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- Neonatal Oncology
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Welcome note president:

Dear Friends and Colleagues

Following the success of Iranian Pediatric Hematology Oncology Society (IPHOS) in all fields in Iran from many years ago to now, it is our great pleasure to invite you to attend the 10th annual meeting of IPHOS Neonatal Hematology Conference (IPHOS2017), which will take place from the 13th-15th of September 2017 in the capital of Iran, Tehran.

Tehran lies in the north part of the country with many historical and attracting sites, you will find a range of pre- and post- conference activities. This city is backed by the Alborz Mountains and Damavand peak, meaning you can delightfully plain at dawn, with good temperate, and enjoys plenty of effusive Iranian hospitality in-between.

As in previous years, the meeting will cover aspects of neonatal hematology. Abstracts are still a key component of the congress and the program has been planned to allow ample time for oral and poster presentations.

We've packed all three days with rousing keynote address, controversies aspects from hematologist and neonatologist, and a chance to meet clinicians, international and national experts who work hard for better pediatric & neonatal practices.

Please join us and be part of a global gathering focused on improving the health of children and neonates around the world.

We look forward to seeing you in Tehran.

Yours Sincerely,

Hassan Abolghasemi, MD

President of Iranian Pediatric Hematology and Oncology Society



Welcome note of Scientific Secretary

Dear Guests

It is my pleasure to welcome you to the 10th annual Congress of Iranian Pediatric hematology oncology society in collaboration with neonatal society and Iranian pediatric society which will take place in Tehran, Iran, September 13-15, 2017.

Neonatal hematology is a complex and dynamic process in the pediatric population. The care of the newborn unlike other areas of medicine affects the care of a changing, expanding, and fast growing patient population.

This congress will provide a general overview of neonatal hematology and common associated disorders to help the participant prepare for better practice. The topics discuss components of blood cells and their importance in physiologic processes; identify causes of anemia, polycythemia, hemorrhagic disease, DIC, thrombocytopenia, inherited bleeding disorders, immune deficiency, stem cell transplant, transfusion, and jaundice in the newborn; describe common physical and lab findings related to the above disorders; indicate appropriate management strategies for the above disorders.

We invite you to attend this congress, where renowned speakers will fascinate us with the latest discoveries in our field, and ample time will be provided for discussion, interaction and social activities in a friendly and congenial environment.

We look forward to providing you an unforgettable event.

Sincerely,

Mohammad Faranoush, MD



ORAL

Mesenchymal Stem Cell therapy in Neonates

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ARTICLE INFO

Keywords:

Mesenchymal stem cell therapy
Neonates
Bone Marrow
Cord blood
Indications

ABSTRACT

Background: Mesenchymal stem cells (MSCs) represent a potentially revolutionary therapy for a wide variety of pediatric diseases, but the optimal cell-based therapeutics for such diversity have not yet been specified.

Definition : The most widely accepted definition of an MSC by the International Society for Cellular Therapy in 2006 includes three criteria: 1- MSCs must be plastic-adherent when maintained in standard culture conditions; 2- MSCs must express CD105 (endoglin-1), CD73 (ecto-5-prime-nucleotidase), CD90 (thymocyte antigen-1) and lack of expression of CD45 (protein tyrosine phosphatase, receptor type, C), CD34, CD14, or CD11b (integrin- α M), CD79- α or CD19 and human leukocyte antigen-DR (HLA-DR) surface molecules; 3- MSCs must be able to differentiate to osteoblasts, adipocytes, and chondroblasts in vitro.

Some of the sources of MSCs studied in pediatric disease include bone marrow-derived MSCs (BM-MSCs), Wharton's jelly or umbilical cord tissue-derived MSCs (UC-MSCs), umbilical cord blood-derived MSCs (UCB-MSCs), placenta-derived MSCs (P-MSCs), amniotic fluid-derived MSCs (AF-MSCs), and adipose tissue-derived MSCs (ADSCs).

Using of MSC therapy in different disorders such as Cerebral Palsy, Spinal Muscular Atrophy, Graft-Versus-Host Disease (GVHD), Autism-Spectrum Disorders, Cardiac Valvular Disease, Reconstructive Surgery and Diabetes Mellitus is reported, but the significant heterogeneity in therapeutic approaches between studies raise new questions. Recently, various preclinical studies have shown that stem cell therapy significantly attenuates injuries in newborn animal models of Bronchopulmonary Dysplasia (BPD), Hypoxic Ischemic Encephalopathy (HIE), and Intraventricular Hemorrhage (IVH). Phase I clinical trials conducted in neonates with BPD, HIE, or severe IVH have shown stem cell treatments to be safe, feasible, and potentially efficacious. But still there are challenges for clinical translation including; Right patients, allogeneic Versus autologous/syngeneic MSCs, Important donor and recipient factors sources of MSC, Right cells, Good manufacture of practice (GMP), Delivery route, Dose and timing of MSCs and safety of MSC transplantation.

Conclusion: Stem cell therapy for currently intractable and devastating neonatal disorders, such as BPD, HIE, and IVH might be a potential paradigm shift in neonatal medicine and stem cell therapy might represent the next breakthrough in therapy of these currently intractable and devastating neonatal disorders with complex multifactorial etiologies.

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ORAL

Fresh Frozen Plasma

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ARTICLE INFO

Keywords:

Fresh frozen plasma

Indication

Complications

GVHD

ABSTRACT

Fresh Frozen Plasma can be obtained by separating both the whole blood and Apheresis. The preparation method is such that the plasma products are prepared (prepared within 8 hours) and freezed at -18°F . The amount of plasma is between 250 - 300 cc and it can be kept at this temperature for about 1 year. In order to limit the exposure of the recipients to less donors, and since the infant needs only a lower amount of plasma per infusion, it is possible to divide the plasma bag into smaller ones and freeze them individually.

In the case of lack of specific factors such as factor X, XI, protein C, S and antithrombin; where their specific concentrates are not available, FFP can be used, but when there is a specific concentrate, it can be used because it has fewer side effects. FFP should not be used in following cases: 1- To increase the blood volume; 2- Accelerator of wound healing; 3- frist line treatment of congenital factor deficiency when either a virally-inactivated plasma driven factor concentrate or recombinant factor is available. Plasma transfusion should be ABO-compatible with the the neonates RBCs to avoid passive transfer of isohemoglotinins from ABO incompatible plasma which may result in hemolysis. Freezing the plasma causes it to leak out from the leukocyte, so the FFP is not detected for CMV antibodies and Leukoreduction and radiation is not necessary for the prevetion of CMV reactivation and TA-GVHD. The usual dose for FFP is 10 CC/kg. Each cc of FFP is equivalent to 1 cc of the Factor's Activity, and thus the factor value to be replaced can be estimated. Side effects of blood transfusion may also occur with FFP infusion with the following differences: 1- Hyperkalemia does not occur in FFP infusions. 2- TRALI is more common in FFP infusions because more antibodies are transmitted with FFP. 3 - Acute hemolytic reactions are less. 4- hypocalcemia caused by citrate may occur, especially when a large amount of FFP is infused very fast.

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ORAL

Protein C deficiency and Ocular Manifestation in Neonates

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ARTICLE INFO

Keywords:

Protein C deficiency
Purpura fulminans
Ocular and extraocular manifestation
Age of onset

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ABSTRACT

Under normal conditions, activated protein C is a natural anticoagulant that cleaves 2 activated coagulation factors, factor Va and factor VIIIa, thereby inhibiting the conversion of factor X to factor Xa and of prothrombin to thrombin. Additionally, activated protein C enhances tissue-plasminogen activator-mediated fibrinolysis by inhibition of plasminogen activator inhibitor-1. This results in an increase in circulatory plasminogen activator levels. Protein C deficiency, a genetic or acquired thrombophilic abnormality, has been demonstrated to predispose to episodes of lethal thromboembolic events and potentially blindness. Heterozygous-deficient subjects usually remain asymptomatic until adolescence or adulthood. In homozygous patients, protein C activity is usually less than 1% (reference range, 70% -140%) resulting in thromboembolism as early as in the neonatal period. The major clinical symptoms in affected newborn infants have been reported to include: purpura fulminans, vitreous hemorrhage, and central nervous system thrombosis. The age of onset of the first symptoms has ranged from a few hours to 2 weeks after birth, usually after an uncomplicated full-term pregnancy and delivery. In contrast to the genetic type, acquired neonatal protein C deficiency occurs particularly in ill preterm babies. Typical complications of prematurity such as respiratory distress syndrome, necrotizing enterocolitis, and neonatal sepsis may also be present. In the medical literature, there are only a few reports of homozygous protein C deficiency in neonates. We present 3 cases of homozygous protein C deficiency with ocular and extraocular manifestation.



ORAL

Necrotizing Fasciitis as an Early Manifestation of Leukemia in a Neonate

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ARTICLE INFO

Keywords:

Congenital leukemia
Necrotizing fasciitis
Skin involvement
Acute myeloid leukemia

ABSTRACT

Background: Congenital leukemia, although uncommon, is usually diagnosed within the first month of life. It constitutes about 1% of all childhood leukemias. AML is observed more common than ALL in neonates. The clinical presentation of neonatal leukemia can be variable. Patients are likely to present with hyperleukocytosis, hepatosplenomegaly, central nervous system involvement, lymphadenopathy and skin involvement. Although necrotizing fasciitis of external genitalia may complicate the clinical course of hematologic malignancies, but sometimes it may present as the first sign of the disease. This aggressive and life-threatening disease is uncommon in children and very rare in neonates and has a high mortality rate in this age group. Predisposing factors vary with age. Prematurity, diaper rash, trauma, poor hygiene, systemic infections, anorectal diseases, immunocompromised status and hematologic malignancies are some predisposing factors in children. Early diagnosis and prompt appropriate treatment is essential.

We present a case of necrotizing fasciitis in external genital and perineal region of a 4-day old term female as an early manifestation of congenital leukemia. Regarding high blast percentage (52%) in complete blood count, bone marrow aspiration and flow cytometry was performed which revealed AML (M4). *Pseudomonas aeruginosa* was isolated from the blood and wound culture of the patient. She was treated with broad spectrum antibiotics (meropenem and amikacin) and received supportive care. Due to the coagulopathy state and her poor condition, our case was not a surgical candidate for debridement. The parents refused to administer chemotherapy to the child and hence the infant was discharged despite medical advise. The baby expired a few days later due to bleeding. The physicians should keep in mind that although cutaneous involvement is commonly benign and self-limiting in neonates, but they may also herald serious underlying diseases and sometimes may represent the first clinical manifestation of rare neoplasms such as hematologic malignancies in this age group.

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ORAL

Retinoblastoma in Infants Less than 3 Months of Age: Report from Mahak Hospital

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ARTICLE INFO

Keywords:

Retinoblastoma

Chemotherapy

Chemoreduction

Treatment outcome

International retinoblastoma classification

ABSTRACT

Background: Retinoblastoma is the most common primary malignant intraocular tumor in children. Treating children with retinoblastoma in the first 3 months of life continues to hold several challenges despite the many advances in retinoblastoma management. The majority of children (>90%) diagnosed in the first 3 months of life have the genetic form of retinoblastoma, the age at which prescribing systemic chemotherapy is also a difficult task due to daily changes in renal clearance during this period (many chemotherapeutic agents used for retinoblastoma are cleared by the kidneys). As a result dosing of the drugs would be imprecise and side effects might be unpredictable. The purpose of this study was to evaluate the outcome of infants diagnosed with retinoblastoma before 3 months of age.

Methods: This is a retrospective review from May 2007-2017 that includes 52 eyes of 30 infants (8 unilateral, 22 bilateral). Systemic chemoreduction was administered when local modalities failed or were considered inadequate.

Results: Out of 30 infants (43% female) diagnosed before first 3 months of age, the youngest patient was 1- day-old. The eyes were classified according to the International Classification of retinoblastoma (ICRB) as; group A (n = 1), B (n = 10), C (n = 3), D (n = 10), E (n = 16) and indeterminate (n= 12). Twelve eye were enucleated due to tumor progression, in two patients both eyes were enucleated. The most frequent symptoms were leukocoria (76.3%), strabismus (9.5%), proptosis (9.5%) and hyphemia (4.7%). 13.3% of the children died and one patient developed bone marrow metastasis. one patient developed second malignancy (osteosarcoma) by the age of nine. Five-year overall survival rate was higher among patients with localized disease (94.6%).

Conclusion: The most frequent symptoms of retinoblastoma were leukocoria and strabismus. All infants ultimately required chemoreduction for globe salvage. Bilateral disease as well as Group D and E disease in at least one eye at presentation increased the need for chemotherapy.

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ORAL

Management of Transfusion Reactions in Neonatal Period

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ARTICLE INFO

Keywords:

Transfusion reactions
Acute hemolytic reactions
Delayed hemolytic reactions
Allergic transfusion reactions
Allomunization
TRALI

ABSTRACT

Neonatal period is defined as infants up to 28 days after birth. The most common group of neonates who are indicated to receive blood transfusion are LBW or preterm infants who are admitted in NICU. The other indications of blood transfusion in older infants and children are : critical conditions in those who are admitted in ICU, the probability of cardiac surgery, congenital anemia such as thalassaemia major and patients with malignancy who receive chemotherapy or radiotherapy.

Nowadays, modern blood transfusion services are very safe, but still we may encounter some transfusion reactions. The most commonly observed transfusion reactions are immune mediated followed by non immune mediated transfusion reactions. The immune mediated transfusion reactions include: Acute hemolytic transfusion reactions mostly due to ABO incompatibility (Clerical error), Delayed hemolytic transfusion reaction due to alloimmunization against RBC minor antigens, Febrile non-hemolytic transfusion reactions due to leukocyte antigens and allergic reactions due to antibodies in recipient against plasma proteins in donor's blood. Non immune transfusion reactions are as follow: volume overload, bacterial contamination, transfusion-transmitted infections, electrolyte imbalance, hypothermia, iron overload and transfusion-related acute lung injury (TRALI).

Acute hemolytic transfusion reactions including identification errors (patients' blood samples and blood components) by hospital staff are the most common cause of the "wrong blood into patient" events. In such situations, the first step is that the transfusion should be stopped and the patient be assessed clinically and resuscitation should be considered if necessary. The further steps are: To check the details on the patient's ID band, documents and records such as results of the compatibility tests, call for medical assistance and contact the blood bank to recheck the blood unit.

Immune-mediated delayed hemolytic transfusion reactions caused by antibody production against Rh alleles, Kell, Duffy or other non-ABO antibodies typically result in extravascular hemolysis, shortened survival of transfused red cells, and relatively mild clinical reactions; however, this event is uncommon in children. Antigen negative blood unit is the treatment option of this situation. Non-hemolytic febrile transfusion reactions caused by cytokines from leukocytes in transfused blood bag is defined as a temperature elevation of 1° C from the basal temperature. The cause of fever due to other problems such as infections should be excluded. Leukoreduced blood units decreased the chance of this transfusion reaction. Allergic reactions typically present as rash, urticaria and are IgE-mediated and are caused by allogeneic proteins existing in donor's plasma. Washed RBC is used in cases with repeated allergic transfusion reactions.

Among non immunologic transfusion reactions, circulatory overload occurs when the volume of the transfused blood is high which will be decreased by

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use of PRBC or use of diuretics. Bacterial contamination and endotoxemia may result from inadequate sterile preparation of the phlebotomy site or opening the blood container in a nonsterile environment or possibility of entry of bacteria into the donor's blood bag. Transfusion-transmitted infection is now a rare event but is not zero yet. Electrolyte imbalance and hypothermia is an inevitable event, but can be decreased by using appropriate components. Iron overload is another complication of blood transfusion in multiply transfused patients. Transfusion-related acute lung injury (TRALI) caused by antibody against HLA of neutrophil antigens in the transfused blood bag which reacts with neutrophil antigens of recipient lead to pulmonary edema in the absence of circulatory overload.

Finally, it is Important to be aware that inappropriate transfusions impose patients to unnecessary risks and reactions. As a result, we should use right product for right patient in right time to decrease the incidence of transfusion reactions.



ORAL

Indications of Neonatal Platelet Transfusion

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ARTICLE INFO

Keywords:

Platelet transfusion
Indications
Rh sensitization
Platelet antigens

ABSTRACT

There are many concerns about the normal or abnormal platelet counts in neonates and specially in preterm neonates. Absolute criteria for platelet transfusion (PTXs) are not still evidence-based and are based almost entirely on "level 4 of evidence" (i.e., expert opinion and reasoning). The policies for PTXs differ in different countries. The bleeding tendency in infants are not only related to platelet counts, but also to their underlying disease; for example in IUGR infants with thrombocytopenia risk of bleeding is low, whereas the incidence of intracranial hemorrhage in neonatal alloimmune thrombocytopenia (NAIT) is considered to be 10-20%.

Many clinicians adopt a fairly aggressive PTXs threshold for the fear of IVH; however, a threshold of 30,000/ μ l was considered safe for the majority of neonates without any previous risk factor such as IVH. It is widely agreed that the platelet count should not fall below 50,000/ μ l in preterm neonates who exhibit active bleeding or are at great risk of bleeding (e.g., when a surgical or invasive procedure such as a lumbar puncture is to be performed). The recommended platelet transfusion levels are seen in table 1.

Table 1: Recommended platelet transfusion levels for neonates

Platelet count($\times 10^3/\mu$ l)	Guidelines
<30	Transfuse all
30–49	Transfuse if: Birth weight <1500 g and ≤ 7 days old Clinically unstable Concurrent coagulopathy Previous significant hemorrhage (i.e., grade 3 or 4 IVH) Prior to surgical procedure Postoperative period (72 h)
50–100	Transfuse if: Active bleeding NAITP with intracranial bleeding Before or after neurosurgical procedures

Platelets are the blood product most prone to bacterial contamination since they are not refrigerated. Platelet bags have a limited shelf life of 5 days. For the same reason, once a unit of platelet is accessed, it must be transfused within 4 hours. They also need to be gently agitated during storage to prevent aggregation.

ABO compatibility for platelet concentrate is not necessary, but ABO compatible platelet provides higher platelet increments. Small amounts of RBCs (0.2-0.3 mL) are present in whole blood derived (WBD) platelets and can cause Rh sensitization in a Rh negative recipient. Administration of Rh immune globulin (RhIg intramuscular dose: 120 IU/mL RBC) should be strongly considered for Rh negative neonates, especially females, within 72 hours of exposure to Rh-positive RBCs through platelet transfusion. When apheresis platelets are used, immunoprophylaxis for Rh sensitization should be discouraged because they contain much less RBC volume than the minimum volume required to cause Rh alloimmunization.

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ORAL

Neonatal Immune Thrombocytopenia

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ARTICLE INFO

ABSTRACT

Immune thrombocytopenia occurs due to the passive transfer of antibodies from the maternal to the fetal circulation. There are two distinct types of immune-mediated thrombocytopenia: neonatal alloimmune thrombocytopenia (NAIT) and neonatal autoimmune thrombocytopenia (NATP)

Neonatal Alloimmune Thrombocytopenia: NAIT is the most common cause of severe thrombocytopenia in the newborn. NAIT typically resolves in 2-4 weeks. 25-50% of the affected infants are first-born infants and subsequent affected pregnancies have increasingly severe presentation and require antenatal treatment. NAIT can be thought of as a platelet analog of Rh incompatibility. In NAIT, the antibody is produced in the mother against a specific human platelet antigen (HPA) present in the fetus but absent in the mother. The antigen is inherited from the father of the fetus. The most common antigen involved is HPA-1a, and then HPA-5b. Mothers who possess the HLA-DR type DRB30101 represent more than 90% of cases of sensitization to HPA-1a. In addition, the combination of severe neonatal thrombocytopenia with a parenchymal (rather than intraventricular) intracranial hemorrhage (ICH) is highly suggestive of NAIT. The treatment options includes: Intravenous immunoglobulin (IVIG), methylprednisolone and platelet transfusion.

Neonatal Autoimmune Thrombocytopenia: The diagnosis of neonatal autoimmune thrombocytopenia should be considered in any neonate who has early-onset thrombocytopenia and a maternal history of either ITP or another autoimmune disease such as SLE and lymphoproliferative disorders. Neonatal thrombocytopenia in NATP is usually less severe than that seen in NAIT and there is a lower risk of ICH. Treatment is required when the infant's platelet count falls below 30,000/mm³ or if significant bleeding is present. The regimen is similar to that of NAIT, utilizing IVIG and methylprednisolone.

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ORAL

Anemia of Prematurity

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ARTICLE INFO

Keywords:

Anemia
Prematurity
Erythropoietin
Blood sampling

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ABSTRACT

Immediately after the birth, oxygen saturation increases which leads to decreased erythropoietin synthesis. In addition, rapid growth of preterm infants elicits a phenomenon called intravascular bleeding. Repeated blood sampling during the first few days of life aggravates the process of anemia in neonates admitted in the hospital. The clinical presentation of anemia of prematurity varies in a broad spectrum from totally asymptomatic to apnea, poor weight gain, tachypnea and increase need to oxygen. In Paraclinic, the peripheral blood smear shows normocytic normochromic red blood cells, decreased reticulocyte count and decreased serum erythropoietin level to less than 10 mU/ml. Even though the erythropoietin administration during the first week of life (early erythropoietin) in extremely low birth weight preterm infants decreased the number of blood transfusions, but in multicenter studies no significant change was seen in the rate of sepsis, IVH, BPD, growth and neurodevelopment. Besides the rate of ROP had been increased in some studies. The late recommendation of erythropoietin also didn't show any significant benefit, so routine usage of erythropoietin is not recommended. In summary, optimal nutrition, limited blood sampling and satellite packs of RBC is the treatment of choice in symptomatic patients.



ORAL

Imaging in Neonatal Thrombosis

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ARTICLE INFO

Keywords:

Neonate
Thrombosis
Imaging modality
Venous thrombosis
Arterial thrombosis

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ABSTRACT

Thrombosis is a significant problem affecting both term and preterm infants. A predisposing factors is usually present in neonatal thrombosis such as sepsis or genetic thrombophilia. There are two types of arterial and venous thrombosis in neonates. Arterial thrombosis includes ischemic perinatal stroke and iatrogenic or spontaneous thrombosis in aorta, iliac and femoral arteries. Venous thrombosis includes catheter related thrombosis, Right atrial and SVC thrombosis, renal vein thrombosis and cerebral sinovenous thrombosis(CSVT). A variety of imaging modalities exist for diagnosis of thrombosis. Diffusion weighted MRI/MRA is used in ischemic perinatal stroke; while Diffusion weighted MRI/MRV is used in cerebral sinovenous thrombosis. Doppler sonography is performed in diagnosis of iatrogenic or spontaneous thrombosis in aorta and extremities' arteries, IVC, abdominal, extremities, renal and portal vein. Echocardiography is the imaging modality of choice which is used in thrombosis of IVC and right atrium.



ORAL

Hematopoietic Stem Cell Transplantation in Primary Immunodeficiency

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ARTICLE INFO

Keywords:

Primary immunodeficiency
Hematopoietic stem cell transplantation
T cell depletion
Gene therapy

ABSTRACT

Hematopoietic stem cell transplantation (HSCT) has been the standard of treatment for primary immunodeficiency disorders (PIDs) in the pediatric population for decades. The first successful pediatric bone marrow transplantation was performed in 1968 on a child with severe combined immunodeficiency (SCID) using a histocompatible sibling donor. SCID, WAS, Phagocytic Cell disorders (Schwachman's syndrome, Granule deficiency, LAD, Chronic granulomatous disease (X-linked/AR), Kostmann's syndrome and Familial Hemophagocytic Lymphohistiocytosis (FHL) are the most common types of PID that can be treated with HSCT. The spectrum of the presentation of these diseases varies from very mild symptoms to serious and potentially lethal illnesses. Children with PID should be diagnosed before they get sick and encounter serious infections which might cause morbidity and mortality. HSCT is an effective treatment for patients with various types of immunodeficiency. As transplant techniques improve, the risk/benefit ratio will continue to progress, warranting application to other diseases with less risk of adverse effects. Improvements in conditioning regimens to reduce toxicity and graft manipulations such as CD3 TCR alpha/beta depletion of haploidentical grafts will improve outcomes and increase donor availability for more patients. Small numbers though continue to make definitive statements difficult about the best candidates and the type of transplant to use. Finally, gene therapy is becoming a viable alternative treatment for some conditions and will have to be considered in decision making for these patients. Because of transplant-related morbidity mortality, the therapy is being offered only to the patients with the highest risk of the disease. The questions such as: who to transplant, when to transplant, how to transplant, from whom to transplant are still not answered clearly. Therefore, looking at every single patient transplanted in detail is critical to understand the disease, its course, the best ways to treat the disease and improve the outcome of the procedure and quality of life for these patients.

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ORAL

Diamond-Blackfan Anemia Complicated by PRES Syndrome

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ARTICLE INFO

Keywords:

Diamond-blackfan anemia
Corticosteroids
PRES syndrome
Intracranial pressure

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ABSTRACT

Diamond-Blackfan anemia (DBA) is a rare disease among inherited bone marrow failure syndromes that is characterized by anemia in early infancy, associated congenital anomalies and cancer predisposition. Management of infants with DBA is focused on definitive diagnosis, corticosteroids, blood transfusions and hematopoietic stem cell transplantation in case of having an HLA-matched sibling donor. Herein, we report a 5-month-old girl who presented with severe macrocytic anemia since 4 months of age. Physical examination was remarkable for wide anterior fontanelle, failure to thrive and cleft palate. Bone marrow aspiration showed scarcity of erythroid series while other cells displayed normal number and maturation. According to physical findings and laboratory findings, DBA was considered for the patient. The patient responded to prednisone; however, she developed signs of increased intracranial pressure; bulging anterior fontanelle and protracted vomiting along with hypertension. MRI demonstrated abnormal T2 signal in both thalami, posterior occipital and parietal white matter which the diagnosis of posterior reversible encephalopathy syndrome (PRES) was made for the patient. As her pressure normalized with medication, her symptoms resolved and the MRI changes improved. Repeated lumbar punctures was performed for the patient which resulted in improvement in occurrence of vomiting and irritability. Her hemoglobin levels remained satisfactory despite tapering the dose of prednisone (Hb was > 10 gr/dL while prednisone was tapered off). To the best of our knowledge, this is the first case of PRES syndrome developed in an infant with DBA.



ORAL

Outcome of Unrelated Umbilical Cord Blood Transplantation for Children with Malignant Infantile Osteopetrosis: An Eurocord and Inborn Errors Working Party (IEWP)-EBMT Study

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ARTICLE INFO

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Cord blood

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GVHD

ABSTRACT

Background: Malignant Infantile Osteopetrosis (MIOP) is a genetic disease characterized by increased bone density due to osteoclast dysfunction, leading to life-threatening multi-systemic complications in early childhood. Haematopoietic stem cell transplantation (HSCT) is the only curative approach for most children with osteopetrosis and can effectively prevent serious complications such as blindness, bone fractures, hydrocephalus and cranial nerve compression. Since timing of transplant is critical in MIOP, umbilical cord blood is an attractive stem cell source due to its prompt availability.

Methods: We analysed the outcomes of unrelated umbilical cord blood transplantation (UCBT) in 41 children with MIOP transplanted in EUROCORD registry area between 1992 and 2007, using data reported to Eurocord.

Results: Median age at UCBT was 7.83 months (0.80-90). Female to male ratio was 2/3. Median interval between diagnosis and transplant was 4.2 months (1.2-56.1). Donor-recipient pairs were matched at HLA-A and -B (antigen level) and DRB1 (allelic level) in 14 or HLA mismatched at 1 (n= 23) or 2 (n= 10) loci. Information on conditioning regimen was available for 35 patients; it was myeloablative (mostly busulfan-based) in 29 children and reduced intensity in 6 patients. GVHD prophylaxis consisted mainly of cyclosporine combined with either prednisolone (n= 20), methotrexate (n=6), or mycophenolate mofetil (n=3). Anti thymocyte globulin (ATG) or alemtuzumab was given to 37/40 patients. Median number of infused total nucleated cell (TNC) and CD34+ was 10.5x10⁷/kg and 3.35x10⁵/kg, respectively. Median follow-up for survivors was 44 months (range 4-144). Neutrophil recovery with donor chimerism was documented in 25/41 patients; 19/25 evaluable patients presented full donor engraftment, while 6 children presented mixed donor chimerism. Median time to neutrophil recovery was 20 (range 10-60) days. Eighteen patients experienced graft failure and 3/18 are alive at last follow up. Information on treatment post-graft failure was available 7/18 children: 6 patients underwent a second HSCT and 3 of them survived. Stem cell dose was associated with a trend for a better probability of donor engraftment: the cumulative incidence of donor engraftment was 46% in patients who received a CD34+ cell dose <2 x 10⁵/kg, versus 71% in children receiving a CD34+ cell dose ≥2x10⁵/kg (p = 0.09). Eleven patients developed grade II-IV acute GVHD (6 grade II, 4 grade III, 1 grade IV) and 5 patients chronic GVHD (3 limited, 2 extensive). Overall survival (OS) at 3 years was 45±8 %. 22 patients died after UCBT due to: infections (n=8), acute respiratory distress syndrome (n=2), veno-occlusive disease (VOD), (n=2) hemorrhage (n=2), GVHD (n=2) or other causes (n=6). VOD was observed in 7/26 evaluable patients. Stem cell dose and HLA disparity

were the only predictors of superior outcome in univariate analysis. The 3-year probability of OS was 50% in patients who received grafts with a CD34+ cell dose $>2 \times 10^5/\text{kg}$ versus 0% in children receiving grafts with a CD34+ cell dose $< 2 \times 10^5/\text{kg}$ ($p=0.001$). According to HLA disparities, 3-year probability OS was 54% versus 58% versus 0% in patients receiving a 6/6, 5/6 and 4/6 HLA-mismatched graft, respectively ($p=0.01$). Interestingly, 4/4 children receiving a treosulfan-based myeloablative regimen achieved donor engraftment and 3 children are alive at last follow up.

Conclusion: These data suggest that transplantation of unrelated UCB is a valid alternative for children with osteopetrosis without a matched sibling or a suitable matched unrelated adult donor. Use of cord blood units mismatched at more than one HLA locus should be avoided due to inferior survival. The incidence of primary graft failure was high and therefore the optimization of the conditioning regimen and/or the use of cord blood units containing a high TNC and CD34+ cell dose must be considered in this setting. The use of treosulfan-based conditioning regimens is worth further investigation, as well as the use of defibrotide prophylaxis to reduce the risk of VOD in this population of high-risk patients.

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ORAL

Challenges in Treatment of Neonatal Thrombosis

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ARTICLE INFO

Keywords:

Neonatal thrombosis
Blood coagulation
Blood flow
Anticoagulation
Fibrinolytic agents

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ABSTRACT

Thromboembolism (TE) is uncommon in the neonatal period, but can cause significant morbidity and mortality. The incidence of symptomatic TE in newborns is approximately 1 case per 400 admissions to NICU or 1 case per 20000 live birth. Three major factors contribute to the formation of thrombi: 1- Abnormalities of the vessel wall (intravascular catheters have become the single most important risk factor for neonatal thrombotic disorders) 2- Disturbances of blood flow. 3- Changes in blood coagulation. The management of neonatal thrombosis is extrapolated largely from data in adults. For asymptomatic thrombosis, we suggest supportive care and close monitoring of the size of the thrombus. For symptomatic thromboses, treatment with anticoagulation and or fibrinolytic agents is recommended.



ORAL

Fetal Transfusion and Neonatal Exchange Transfusion – Trends, Indications and Methods

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ARTICLE INFO

Keywords:

Fetal transfusion
Neonatal exchange transfusion
Rh hemolytic disease of Newborn

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ABSTRACT

Intrauterine transfusion remains a lifesaving procedure for fetuses with severe anaemia. It can prevent fetal death, prolong pregnancy (with benefits including reduced neonatal mortality and morbidity), and reduce the need for invasive procedures such as neonatal exchange transfusion. Mater Mothers' Hospital is a large (>10,000 births per year) maternity hospital that is a referral centre for maternal-fetal and neonatal care. A survey of Mater Blood Bank records for the years 2003-2016 identified 162 intrauterine transfusions administered to 80 fetuses of 72 mothers. Of the transfusions, three quarters were for haemolytic disease of the fetus and newborn (HDFN), mostly for RhD or other Rh antibodies. Fetal anaemia due to Parvovirus infection was the indication for most other fetal transfusions. Exchange transfusions were performed 48 times between 2003-2016, in 42 cases for HDFN (41 Rh or Kell, 1 ABO), with no baby receiving more than one exchange transfusion. The incidence of exchange transfusion has declined, with no exchange transfusion performed since 2013. The incidence of severe haemolytic disease requiring neonatal treatment with exchange transfusion has declined markedly over recent years in Australia. I will discuss the likely causes for this decline, including effective RhD immunoprophylaxis, trends to smaller family size, effective intrauterine treatment, improved screening and early use of intensive phototherapy for severe neonatal jaundice. The newly developed "Australian National Blood Authority Patient Blood Management Guidelines-Module 6; Neonatal and Paediatric" contains guidance about fetal transfusion.



ORAL

Approach to Infantile Hemangiomas

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ARTICLE INFO

Keywords:

Infantile hemangioma
Choice of treatment
Corticosteroids
Propranolol

ABSTRACT

Infantile hemangioma (IH), the most common soft-tissue tumor in children with occurrence rate of 8.7 to 12.7%, presents in up to 60% of cases on the head and neck region. Lesions occur more frequently in premature infants, females, multiple births, with advanced maternal age, and in Caucasians. Classification of hemangiomas is based on the layer of skin they affect: superficial or capillary type, deep or cavernous type, and mixed type. Unfortunately, subsets of IHs rapidly develop to complications, resulting in pain, functional impairment or permanent disfigurement. As a result, the primary clinician has the task of determining which lesions require early consultation with a specialist. "Wait and see" is mainly indicated in involuting hemangiomas or small, stable hemangiomas in non-vital sites, without significant impacts on appearance and function. The growth of the lesions should be observed, recorded and photographed in the follow-up period. Treatment should immediately be taken when the following occurs: (1) fast growth of hemangiomas; (2) hemorrhage, infection or ulceration complicated with huge hemangiomas; (3) functional problems, such as dysfunction of feeding, breathing, swallowing, hearing, vision, excretion or sports etc.; (4) association with Kasabach-Merritt syndrome; (5) its concurrence with high output congestive heart failure; (6) involvement of facial vital structures, e.g. eyelids, nose, lips, auricle etc. Various methods for treating infant hemangioma have been documented including wait and see policy, laser therapy, drug therapy, sclerotherapy, radiotherapy, surgery and so on, but none of these therapies can be used for all hemangiomas. To obtain the best treatment outcome, the treatment protocol should be individualized and comprehensive as well as sequential. Propranolol, although the mechanisms unknown, has become the mainstay treatment for IHs over corticosteroids and other pharmacologic therapies.

Corticosteroids are an alternative therapy if propranolol cannot be used or is not effective. Several months of corticosteroid therapy are often needed, and treatment is usually more successful when initiated during the proliferative phase. The medical and self-esteem needs of the child and the family must be considered in planning treatment.

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ORAL

Indication of Blood Transfusion in Newborns

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ARTICLE INFO

Keywords:

Neonatal blood transfusion
Indications
Prematurity
Low birth weight neonates

ABSTRACT

Blood transfusion is the mainstay of treatment in pediatric and neonatal medicine. Transfusion is performed to improve the anemia and oxygen carrying capacity. Blood transfusion is not a simple procedure like water and electrolyte infusion, but it is kind of temporary tissue transplantation and the reaction such as graft versus host disease and host versus graft and the other reaction phenomena can be appeared. Blood transfusion introduces a multitude of alloantigens and living cells into the recipient's body. This procedure may be repeated in premature and low birth weight newborns, boosting more reaction phenomena. Each component in the blood is able to produce antibodies. Blood antigens such as human leukocyte antigens; class I and II, granulocyte-specific antigens, platelet-specific antigens and RBC-specific antigens can stimulate the immune system and produce alloantibodies. Differences between blood donor and recipient, RBC antigen potency and the recipient's immune status contribute to the development of reaction phenomena. Therefore, there is some regularity in blood transfusion especially in newborn period. Transfusion should not be started based on hemoglobin level only. In addition, the other conditions of the patients such as clinical underlying disorders, gestational age, newborn age and weight of the neonate should also be considered. The benefit of blood transfusion such as rising the Hb, improving oxygen carrying capacity and cardiac output and development of neurocognitive system should be balanced against its side effects.

There are two policies in blood transfusion in newborn period, restrictive and liberal practical policies. The low Hb threshold is considered in restrictive policy and in the liberal approach the selected Hb is considered higher. The management of anemia of premature and LBW neonate is the restricted approach; while for term neonates, the liberal approach is more practical. The type of blood unit that is prepared for newborns is also important. Mother blood characteristics should be tested via blood group, natural and atypical antibody screening test versus newborn blood group.

The selected donors' blood units should be compatible, leukodepleted, irradiated, virus negative and fresh (less than 5-7 days). Such characteristics are more indicated in premature, low birth weight newborns. Donors' blood units should be tested for all kinds of registered viruses especially CMV. Blood donors should be tested for sickle cell trait in high prevalence regions like Khuzestan province.

Satellite and paedipack units are suggested for minimum volume transfusion about 15-20 cc/kg. This approach can avoid multi-donor exposure and save the donor blood volumes.

Blood transfusion reaction in newborns is similar to adults including infectious and non-infectious reactions. Non-infectious reactions consist of allergic and non-allergic ones. Neonatal transfusion reactions are more important in low birth weight and premature newborns.

There is not a definite guideline for newborn blood transfusions.

Each Neonatologist and Hematologist is the final person who decides on blood products transfusion according to the patients' clinical context, gestational age and newborn weight and age.

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ORAL

Infantile Malignancies Incidence and Survival Under 6 Months

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ARTICLE INFO

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Infantile malignancy
Mahak pediatric cancer center
Incidence
Environmental factors

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ABSTRACT

Background: The types of infant malignancies are different from those that develop in other ages. Lifestyle or environmental risk factors do not play an effective role in pathogenesis of infantile malignancies. Instead, it's usually the result of DNA changes or gene mutations in cells that take place very early in their life. The most common malignancies in this period of life include: Acute Lymphoblastic Leukemia (ALL), Acute Myelogenous Leukemia (AML), brain tumor, Neuroblastoma, Retinoblastoma, Wilms tumor, Hepatoblastoma and etc.

Methods: The aim of this study was to classify and evaluate malignancies in infants less than 6 months at MAHAK Hospital and compare with world reports. In addition to causative factors such as low birth weight, persistent fever, diarrhea and chronic underlying diseases, the development of malignancy in infants is commonly linked between diagnosis and treatment protocols.

Results: The records of patients such as genetic, clinical and diagnostic results in infants who had received treatment at our center from April 2007 to July 2017 were retrospectively reviewed. A total of 86 patients were included. The percentage of Infants with malignancies included; Retinoblastoma 65.1 %, Leukemia 8.14%, Neuroblastoma 8.14%, Brain Tumor 5.81%, Sarcoma 2.32%, Wilms tumor 2.32% and others (8.14%).

Conclusion: This evaluation should be considered when finalizing further treatment decisions, especially for infants with genetically background.



ORAL

Disseminated Intravascular Coagulation in Neonatal Period

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ARTICLE INFO

Keywords:

Disseminated intravascular coagulation
Hemorrhagic symptoms
Thrombotic events
Anti coagulation therapy

ABSTRACT

Disseminated intravascular coagulation in the neonatal period is a secondary process triggered by a primary disease state. It is a disruption in the homeostatic balance of the coagulation and fibrinolytic systems. This results in a contradictory state of hypercoagulability with systemic micro thrombi simultaneously occurring with systemic hemorrhage.

The platelet function is diminished in neonatal period, but this is compensated by increased activity of von Willebrand factor. Coagulation factors V, VIII, XIII and fibrinogen in newborns have similar levels compared to those of adults. Nevertheless, vitamin K dependent factors such as II, VII, IX and X and contact factors XI and XII have half of the levels seen in adults. This difference is even greater in premature neonates. The concentration of anticoagulant factors, such as anti-thrombin, protein C and S are low at birth. Most clotting factors attain the normal level by six month of life with exception of protein C level, which remains low until later in childhood. Actually low levels of most coagulation factors and high frequency of vascular disorders and sepsis during and after birth causes newborn infants vulnerable to DIC.

Common causes of DIC in neonates include: viral and bacterial sepsis, hypoxic ischemic encephalopathy, necrotizing enterocolitis, meconium aspiration syndrome, metabolic disorders (galactosemia, tyrosinemia), vascular anomalies (Kasabach-Merritt syndrome, hematologic disorders (purpura fulminans caused by protein C and S deficiency and erythroblastosis fetalis).

Umbilical cord oozing and bleeding, petechiae, excessive bleeding from peripheral venipuncture/heel stick sites and prolonged bleeding following circumcision may be observed in the course of DIC. Large caput succedaneum and cephal hematoma or subgaleal and intracranial hemorrhage occurs without existence of any significant birth trauma history.

Gastrointestinal bleeding must be differentiated from swallowed maternal blood. Pulmonary hemorrhage is most frequently hemorrhagic pulmonary edema not associated with specific coagulation anomaly.

Clinical suspicion has a key role in the diagnosis of DIC. Initial screening begins with CBC, prothrombin time (PT), partial thromboplastin time (aPTT), INR and plasma fibrinogen level.

Laboratory abnormalities seen in DIC include thrombocytopenia, elevated fibrin degradation products (FDP) or D-dimmers, prolonged PT and aPTT, prolonged thrombin clotting time. A serial low fibrinogen testing may be necessary for the diagnosis and treatment.

Armengou L et al. studied on plasma D-dimmer in sick newborn and concluded that increased plasma d-dimmer concentration is significantly associated with the diagnosis of sepsis. Bentz et al. also showed coagulopathy commonly occurs in critically ill neonates especially those with sepsis and septic shock. The blood smear may contain fragmented, burr- and helmet-shaped red blood cells (schistocytes).

Successful treatment of DIC is largely dependent on diagnosis and treatment of the underlying condition and supporting adequate blood flow and oxygen

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delivery. Blood component transfusions (platelets, fresh frozen plasma and cryoprecipitate) have a critical role in supportive treatment of DIC. Generally anticoagulant administration is not recommended; however, in cases of DIC in which thrombosis predominates, therapeutic anticoagulation with heparin may be considered. The Protein C administration is controversial and may increase the risk of intracranial hemorrhage. Replacement therapy with recombinant factor VIIa is recommended in severe neonatal hemorrhagic disease, but thrombotic complications make its use limited to life-threatening hemorrhagic situations.



ORAL

Vitamin K Deficiency in Neonates

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ARTICLE INFO

Keywords:

Vitamin K deficiency
Hemorrhagic symptoms
Childhood cancer
Hemorrhagic disease of newborn

ABSTRACT

Vitamin K was first discovered in early 1930s by Danish biochemist Henrik Dam who described its anticoagulant effect in chickens. Further studies on different foods led to the discovery of "Koagulation vitamin", vitamin K a lipophilic and hydrophobic new vitamin. Vitamin K is a cofactor for the synthesis of factor II, VII, IX, X, and protein C and protein S by carboxylation of specific glutamate residues. (1,2) Phytonadione, Phytomenadione, or phylloquinone also known as vitamin K₁, is a vitamin found in food a naturally obtained compound of vitamin K. Bacterioids and some other bacterias that colonize the human's gut synthesize vitamin K₂ or menaquinone, considered for about 10% adult requirement of vitamin. We have also three synthetic forms of vitamin K : K₃ (used in pet food industry), K₄ and K₅ (inhibition of fungal growth). A water soluble preparation of vitamin K₃ or menadione is also available for adult use.(3) VITAMIN K DEFICIENCY Vitamin K deficiency bleeding (VKDB) is now the preferred term for hemorrhagic disease of the newborn (HDN). Recommended intake between birth and 6 months is 2 mcg/day. A very small amount of vitamin K is necessary for blood coagulation; the deficiency in human is usually associated with profound inadequate dietary, intestinal disorders (resection, inflammation) or hepatic / renal failure. In neonatal period, especially in exclusively breastfed neonate the deficiency may be endogenous and exogenous: the breast milk contain small amount of vitamin K (1-4 mcg/L).

Vitamin K deficiency bleeding (VKDB) is now the preferred term for hemorrhagic disease of the newborn (HDN). Recommended intake between birth and 6 months is 2 mcg/day. A very small amount of vitamin K is necessary for blood coagulation; the deficiency in human is usually associated with profound inadequate dietary, intestinal disorders (resection, inflammation) or hepatic/renal failure. In neonatal period, especially in exclusively breastfed neonate, the deficiency may be endogenous and exogenous. Breast milk contains small amount of vitamin K (1-4 mcg/L).

According to the age of onset, the clinical signs and symptoms may start within the first 24 hours of life in neonates of mothers taking inhibitors of vitamin K (carbamazepine, phenytoin, barbiturate, isoniazid rifampicin, cephalosporin or warfarin). The clinical presentation is often associated with intracranial or intra-abdominal hemorrhage. In cases of bleeding, since 24 hours to 7 days of age the symptoms are usually due to delayed feeding, the clinical presentation is often mild with gastrointestinal blood loss or blood loss from site of punctures or circumcision. The incidence of clinical VKBD vary from 0.25-1.5% to 0-0.44% in more recent studies. From the second to 12 weeks of life, it is usually associated with non-administration of prophylactic vitamin K, exclusive breastfeeding and is precipitated by fat malabsorption (hepatic or GI diseases). Intracranial hemorrhage occurs in 50% of cases with a mortality rate of 20% and persistent neurological sequels in survivors.

Laboratory tests include prolonged PT and INR and in severe cases PTT may be also prolonged. Levels of vitamin K and PIVKA-II (protein induced in vitamin

k absence) are essentially used to monitor patients with disease predisposition.

American association of Pediatrics recommends a single intramuscular administration of 0.5-1 mg vitamin K1 at birth and supplementation of infant formula. UK department of health recommended single IM or Oral dose of 400 mcg/kg (in newborns <2.5 kg) or 1 mg (in newborns >2.5 kg). Recent studies demonstrate inefficacy of a single oral dose of vitamin K for long term protection, specially in exclusively breastfed infants.

Vitamin K toxicity is rare. Vitamin K3 (menadione) can cause hemolytic anemia, hyperbilirubinemia and kernicterus in infant specially in G6PD deficient neonates. Few cases of anaphylactic shock after intramuscular injection of vitamin K in prophylaxis of hemorrhagic disease of the newborn have been reported.

In 1990, Godenn et al. attempted to show an association between intramuscular administration of vitamin K and an increased incidence of childhood cancer. Using data from the National Registry of Childhood Tumors, they estimated the cumulative incidence of childhood leukemia. "American association of Pediatrics" reviewed all reports and information regarding US experiences in 1993 and concluded that there was no association between intramuscular administration of vitamin K and childhood leukemia or other cancers. Recently, researchers have claimed a weak relationship between vitamin K consumption and cancer or childhood leukemia.

Slow intravenous perfusion or subcutaneous injection of vitamin K1 in case of lack of venous access is recommended. Fresh frozen plasma is indicated for all infants with bleeding symptoms. The "Prothrombin Complex Concentrate" (PCC) should be considered in severe forms of the disease.

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ORAL

The History of Rhesus Haemolytic Disease of the Newborn (RHDNB)

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ARTICLE INFO

Keywords:

Hemolytic disease of newborn
RH incompatibility
Hyperbilirubinemia
Hyper immunoglobulin

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ABSTRACT

After the discovery of the Rhesus blood groups in 1940, the cause of most cases of RHDNB became clearer. Over subsequent years, major advances in the diagnosis, treatment and prevention have taken place until today, in developed countries, the disease frequency has been greatly reduced. Immunization of women can occur through exposure to Rhesus positive re cells through injection, transfusion or pregnancy. Once the woman develops rhesus antibodies, her babies are vulnerable to RHDNB and special treatment is required to mitigate the severity of the disease. Diagnosis requires accurate blood group and antibody serology, often including DNA technology. Management may include invasive procedures such intrauterine transfusions during pregnancy, plasmapheresis of mothers, and exchange transfusions of the infant. Maternal treatment with steroids is sometimes used and phototherapy along with intra-venous immunoglobulin in the affected baby. Prevention requires the use of Anti-D hyper-immunoglobulin after and/or during pregnancy. This paper will outline my personal involvement with RHDNB since 1963 with some ideas as to the way forward in countries where a percentage of the population is Rhesus (D) negative.



ORAL

Inherited Disorders of Platelet Function

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ARTICLE INFO

Keywords:

Platelet function disorders
Platelet adhesion
Platelet aggregation
Thrombasthenia

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ABSTRACT

Platelets are very important for primary hemostasis. Platelet function disorders cause abnormal bleeding by a variety of congenital and acquired diseases. Congenital platelet dysfunction may be classified as; adhesion; aggregation and platelet pool diseases. Most of the congenital thrombasthenic disorders are transmitted by autosomal recessive route. The congenital defects of platelet function; although uncommon, have provided important insights into platelet physiology and pathophysiology and as a group are less common, better characterized and more readily classified than the acquired defects. The inherited platelet function disorders are less common, and include several numbers of rare diseases. These include the common von Willebrand disease (VWD) and the less common Glanzmann thrombasthenia, giant platelet disorders (eg, Bernard-Soulier disease), Wiskott-Aldrich syndrome, and storage pool disorders. Acquired platelet function diseases are seen commonly in patients used antiplatelet medications, end stage renal diseases, renal failure, during cardiopulmonary bypass, and hepatic failure. If the disease severity is more than the usual classic manifestation of the disease, another coexisting genetic defect could be suggested. The diagnosis of functional platelet disorders requires measurement of platelet function tests, flow-cytometry, and molecular mutation detection. Proper treatment schedule during bleeding events is HLA-matched single platelet concentration infusion, tranexemic acid, and in Glanzmann thrombasthenia infusion of recombinant factor VIIa. Alloimmunization to platelet is very important and cause platelet refractoriness during bleeding episodes and refractory hemorrhagic symptoms.



ORAL

A Longitudinal Study on the Outcome of Hemoglobin Bart's Hydrops Fetalis in Canada; Implications for Perinatal Care and Family Counselling

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ARTICLE INFO

Keywords:

α thalassemia

Hb barts

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ABSTRACT

With advances in fetal medicine and improved access to intrauterine transfusion (IUT), an increasing number of patients with hemoglobin Bart's hydrops fetalis (homozygous α^0 -thalassemia) will survive. While this improved survival heralds a rising disease burden, studies on the predictors of pregnancy outcome and the pattern of long-term complications of survivors are limited. We retrospectively collected data on genotype, IUTs and pregnancy outcome in all cases of homozygous α^0 -thalassemia diagnosed in Ontario, Canada, from 1989-2014. Clinical data (congenital anomalies, growth pattern, endocrinopathies, postnatal transfusion-related complications and neurocognitive profiles) on all long-term survivors from the four comprehensive thalassemia care centers in Ontario were also collected. Outcome data were compared with longitudinal outcome data from 24 patients with transfusion-dependent β -thalassemia (TDT- β).



ORAL

Australian Neonatal and Paediatric Patient Blood Management Guidelines

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ARTICLE INFO

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ABSTRACT

Module 6 Neonatal and Paediatrics (2016) is the most recently completed module of the suite of 6 evidence-based National Blood Authority Patient Blood Management guidelines. They are available at <https://www.blood.gov.au/pbm-module-6>. We developed specific guidelines for these age groups because of the considerable physiological differences between neonates and children at different developmental stages, and between children and adults. Transfusions can be lifesaving and improve health, but can also have adverse consequences. Both benefits and adverse consequences may be life-long.



ORAL

Vasospasms and Thromboembolism in Neonate

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ARTICLE INFO

ABSTRACT

*Cause: usually occur with indwelling arterial or sometime venous catheters.

More commonly umbilical & less common with peripheral line.

Neonates are at a high risk because of their :

A: immature hemostatic system, B: smaller vessel size

Vasospasm commonly occur in arterial catheterization but thromboembolism common with venous catheterization.

*most medications if given too rapidly can cause vasospasms.

*risk factors :

A) Maternal:

1) Autoimmune disorder, 2) PROM, 3) Diabetes, 4) Preeclampsia, 5) Oligohydramnios, 6) Prothrombotic disorder, 7) Chorioamnionitis, 8) familial history of thrombosis, 9) anti-phospholipid or anti-cardiolipin Ab

B) Delivery:

1) Instrumentation, 2) Fetal heart rate abnormality, 3) C/S Emergency, 4) Traumatic delivery

C) Neonate :

1) C.A.C (central arterial catheter) is the most common risk factor, 2) Central venous catheters, 3) Congenital heart disease, 4) Asphyxia, 5) Sepsis, 6) SGA & IUGR, 7) RDS, 8) NEC, 9) Polycythemia, 10) PPHN, 11) Dehydration, 12) Congenital Nephrotic syndrome, 13) DIC, 14) Impaired liver function, 15) low cardiac output & hypotension, 16) Prothrombotic disorder (protein C & S deficiency, factor V leiden mutation, anti-thrombin deficiency, elevation of lipoprotein A level & other things like impaired liver function.)

A) Vasospasm:

Due to muscular contraction it is commonly arterial

1. catheter, 2. injection of medication, 3. sampling

I. Less severe vasospasm:

Involves a small area of one or both legs

(usually some of the toes and parts of the foot or hand)

* in this type : skin has a mottled appearance & pulses are present but diminished.

II. severe vasospasm:

Involves large area of one or both extremity and sometime progresses to buttocks and abdomen.

* in this type: skin maybe completely white

-Perfusion decreased

-Pulses of affected extremity are weak but detectable

B) thromboembolism: arterial, Venous, Thrombus is a blood clot formation

Embolus is a clot that is mobile

*Thromboembolism: Catheter related (Iatrogen), Spontaneous (non-catheter related)

Thromboembolism also can be:

1. acquired : Deficiencies of protein C & S anti thrombin III with sepsis or Ab transfer from placenta like anti phospholipid -lupus anticoagulant and anti-cardiolipin, 2.

inherited:

Deficiencies of protein C & S - anti-thrombin III - factor V leiden - homocystinemia, elevated lipoprotein - dysplasminogenemias

Arterial thrombosis is a medical emergency in which pulse usually are completely absent & persistent bacteremia & thrombocytopenia may be associated with thrombosis

Venous thrombosis :

More common and it's first sign is catheter dysfunction

Extremities are swollen – cyanotic –hyperemic and discolored with distended superficial veins

but renal vein thrombosis is most common type of spontaneous venous thrombosis

Triad:

1. macroscopic hematuria

2. Thrombocytopenia

3. Palpable abdominal (flank) mass.

Other finding: HTN- proteinuria- renal dysfunction -(70% bilateral 65% left) risk factors : asphyxia - dehydration- prematurity- maternal diabetes & others.

Laboratory studies:

Not usually needed for vasospasm but in suspected thromboembolism following studies should be done:

1. Coagulation profile : PT, PTT, TT, Plasma fibrinogen concentration.

2. Hb & HCT

3. Platelet count & function (BT)

4. CMV workup

5. workup for thrombotic disorder

(Protein C & S & anti-thrombin III - factor V leiden & antiphospholipid & cardiolipin Ab

Imaging:

1. Plain radiograph of the abdomen (for catheter placement)

2. ultrasound (Doppler flow) for thrombosis(also evaluate Brain & kidney sonography)

3. Contrast angiography (gold standard) arterial

Venous

4. magnetic resonance (MR)angiograph arterial

Venous

Is done in some centers especially for suspected stroke.

Some general recommendations for Prophylaxy:

1. Small catheters should be used, 2. heparin is used for patency of peripheral and central Arterial catheter 25-200 u/kg/d(0.5unit/ml)concentration, 3. heparin is not used in peripheral venous line, 4. in central venous and PICC sometimes Heparin is recommended, 5. Umbilical line Should be removed as soon as possible ; arterial line should not be in place longer than 5 days and venous line not longer than 14 days. 6. PICC line has lower incidence of thrombosis. 7. Use peripheral line over umbilical line.

Management:

A) Vasospasm:

Guide lines vary extensively

1. If possible remove the catheter, 2. Warming the contra lateral extremity wrapping of unaffected extremity should cause reflex vasodilation of the affected vessels. continue it for 15-30 min. 3. Gentle massage at the Site of occlusion), 4. Topical nitroglycerin therapy (2% ointment) 4 mm/kg every 8 hours for (2-27 day) improvement usually seen within 15-45 min. 5. If it is not possible to remove the catheter (it is the only line) consider papaverin 60 mg/500cc/N/s with 0/1unit/ml heparin continuous for 48 hr if vasospasm persist removed catheter. 7. lidocaine (controversial) 2mg/kg/hr, 8. morphine, 9. surgery (sympathectomy)

B) thromboembolism:

If suspected & there is loss of pulses in the affected extremity it is a medical emergency : management is controversial & most common treatment are observation.

Treatment depends on the extent & severity of the thrombosis.

I) mild or minor thrombosis:

decreased limb perfusion

hypertension and hematuria

1. revmoval of the catheter, 2. Supportive care, 3. close sonographic follow up

* many resolved Spontaneously

II) moderate thrombosis :

All of the above + oliguria and CHF

1. Systemic heparin therapy, 2. management of systemic hypertension & heart failure

III) major thrombosis :

All of above + multi organ failure

1. Systemic heparin therapy, 2. anti thrombolytic therapy, 3. Supportive care

** Supportive care**

1.prompt removal of the catheter, 2.treatment of volume depletion- Electrolyte abnormality – Sepsis – Thrombocytopenia – anemia, 3.Emergency consultant with surgeon & hematologist, 4.Evaluate for IVH, 5.Rule out contraindication of anticoagulant & thrombolytic therapy (surgery & asphyxia in the last 10 days) – severe coagulation deficiency – platelet under 50000 – fibrinogen under 100 mg/dl – INR>2

****Heparin therapy****

load 50-75 u /kg/IV/over 10 min

then 20-28 u/kg/hr maintenance

for 5-14 days - adjust PTT 4 hours after initiation & after each dosing change

target PTT (60-85 sec)

if PTT> 96sec hold heparin 30-60 min

then start with lower infusion rate (protamine)

-warfarin is not recommended in neonate

****Thrombolytic drugs****

with extensive & life threatening thrombosis - (right atrial thrombosis & limb loss or organ damage)

treatment is controversial

*When using thrombolytic therapy maintain plat > 50000

& fibrinogen >100mg/dl

*monitor PT/INR - PTT, fibrinogen every 4 hours

A) recombinant tissue plasminogen activator (tpA)

(Alteplase) Drug of choice 0.1-0.6 mg/kg/hr/for 6 hours

(may need FFP to be used prior)

B) streptokinase :

2000 u/kg/IV over 30-60 min

1000-2000 U/Kg/hr / for 6-12 hours

C) Urokinase :

4400 U/kg/stat bolus over 10 min then

4400 U/kg /hr 6-12 hours

D) newer agent (bivalirudin – argatroban)

These are direct inhibitors of thrombin that may be used

E) Surgery (thrombectomy & microvascular reconstruction)

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POSTER

Neonatal Malignancies-Brief Review

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ARTICLE INFO

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ABSTRACT

Newborn cancer is a rare event. With the exception of the isolated cases, there is little information on the prevalence or types of tumors found in this age group. Although the occurrence of malignant tumor in the newborn is rare, a large percentage of the neonates can be treated successfully and will be cured. Management of these patients poses great demands on both parents and the physicians. Any proposed treatment and its risks should be discussed thoroughly with the parents before it is implemented. Phototherapy may slightly increase the risk of cancer in children, although the absolute increase in risk would be low. This risk should be taken into account when considering phototherapy for the neonates, especially in infants with bilirubin levels below the current treatment Guidelines. The appearance and behavior of the neonatal tumors often differ from those of older children, resulting in differences in diagnosis and management. The etiology of neonatal cancers are not clear, but genetic factors are likely to play an important role. Congenital anomalies are usually associated beside the tumor. Teratoma and neuroblastoma are the most common histological types of neonatal cancers; however, soft tissue sarcoma, leukemia, renal tumors and brain tumors are also among the common types of neonatal cancers. Prenatal screening, usually in routine ultrasound or as part of a known predisposition to the syndrome is to be employed. Treatment options are problematic because of the particular vulnerability of this population. Search strategy and selection criteria references for this Review were identified through searches of PubMed from January 1995 to December 2017. Only papers published in English were reviewed. Recent articles were chosen, when possible, to reflect current knowledge. The final list is illustrative of the authors' main points and is not intended to be exhaustive. The search strategy included the terms "neonatal", "infant", "paediatric" OR "pediatric", "child" OR "children", "fetus" AND "cancer", "tumour" OR "tumor", "neoplasm", "neoplasia", as well as the various sub-types of cancer. Search results were supplemented by searches of the authors' own files.

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POSTER

Severe Refractory Autoimmune Hemolytic Anemia in an Infant Caused by Warm Reactive IgM and IgG Autoantibodies

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ARTICLE INFO

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ABSTRACT

Described here is a case of IgG and IgM warm autoimmune hemolytic anemia (WAIHA). A 10-month-old girl without previous health problem presented with refractory warm AIHA after an episode of respiratory tract infection. Direct agglutination test (DAT) revealed both IgG and IgM warm autoantibodies. There also have been allo antibodies and ABO incompatibility mismatch lasted for 2 months. In three months from the start of the disease, the patient suffered from relapse of WAIHA. After 14 months, the patient had no problem. The present case of refractory WAIHA is a rare one produced by both IgM and IgG class of autoantibodies. An evaluation for the likely infectious causes is absolutely necessary. Long term follow up is deemed mandatory In WAIHA due to the potentially refractory nature of the autoimmune hemolytic anemia.



POSTER

Management of Neonatal Purpura Fulminans: Case Report

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ARTICLE INFO

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Protein C deficiency
Purpura fulminans
Neonate
Thrombotic events
Daily dressing

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ABSTRACT

Neonatal purpura fulminans is a rare thrombotic, life-threatening condition caused by congenital or acquired deficiencies of protein C or S. The condition is often fatal unless there is early recognition of the clinical symptoms, prompt diagnosis and judicious replacement therapy is initiated. Features include tissue necrosis, small vessel thrombolysis and disseminated intravascular coagulation. Gram-negative organisms are the most common causes of the acute infectious episodes which is often associated with multi-organ failure. An idiopathic variety; however, is often confined to the skin. Acute disseminated intravascular coagulation and hemorrhagic skin necrosis are among the skin manifestations of the deficiency in the mentioned factors. The management includes an acute phase of replacement therapy with fresh frozen plasma or protein C concentrate and a maintenance therapy that includes anticoagulation with warfarin or low molecular weight heparin and approach to wound care. When doppler sonography is normal, wound debridement is performed by hydrocolloid gels. The daily dressing is changed and the wound would be clear from the proliferation in order to get free from proliferation and granulation. Remodeling was conducted over 45 days. This review focuses on the management of severe protein C deficiency.



POSTER

Methylene Blue Toxicity and Hemolysis After Esophageal Atresia Repair in Neonatal Period

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Hemolytic anemia
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ABSTRACT

Background: Several therapeutic and diagnostic uses for methylene blue have been reported. The purpose of this report is to aware about the potential hazard of methylene blue toxicity and hemolysis in neonatal period.

Case Presentation: A 36-week, 2.05 kg female infant delivered by uneventful cesarean section with APGAR score of 9/9 from a healthy mother, underwent surgery for repair of common type esophageal atresia with drainage tube placement on second day of life in Mahdie hospital NICU. The blood group of the newborn was A+ and her mother was AB+ with no family history of hematologic disease. On fifth day postoperation, 2 mL of methylene blue solution was fed via oral route for confirmation of the integrity of esophagus after repair. 8 day after methylene blue ingestion, severe anemia and hyperbilirubinemia was presented.

Conclusion: Methylene blue, in our patient, caused hemolytic anemia and hyperbilirubinemia. Some medical centers consider methylene blue instead of barium meal to check on the esophageal repair. Therefore, attention for methylene blue solution preparation is essential. We recommend determination of G6PD status as the most common enzymopathy with the development of methylene blue toxicity.



POSTER

Pyruvate Kinase Deficiency in Iran: Molecular Aspects of Newborns

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ARTICLE INFO

Keywords:

Pyruvate kinase deficiency
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Missense mutations
Frequency

ABSTRACT

Background: Pyruvate kinase (PK) deficiency is caused by defects on PK-LR gene on chromosome 1q21 which results in mutations of R-PK type in erythrocytes and a broad range of molecular heterogeneity as an autosomal recessive manner. The severity is variable and depends on the homozygous or heterozygous inheritance of the mutations. The frequency of PK deficiency is variable in different geographical areas. In this review article, we discussed the newborns molecular aspects of PK deficiency in Iran.

Methods: Relevant English-language literature were searched and retrieved from PubMed search engine (2000–2017). The following keywords were used: “Pyruvate kinase deficiency”, “Iran” and “molecular genetics”.

Results: About 70% of the identified mutations in PK gene are caused by missense alterations. Heterozygote carriers usually have no clinical symptoms with intermediate PK enzyme activity (40% to 60%). The most common missense mutations are the G1168A and G1529A (54%) at exon 11. In addition, the C1456T and G994A alleles at homozygous state are associated with severely reduced PK activities and very severe hemolytic anemia. Other mutations are C1492T, G1291A, C1594T, G787A, and G1010C.

Conclusion: The frequency of PK deficiency in the south of Iran varies from 0.010 to 0.026,5 and homozygote newborns in this region are predicted 3 per 10,000 individual. According to the prevalence of PK mutations in Iran, molecular study of R-PKs mutants can contribute to predict the diagnosis and prognosis of PK-deficient hemolytic anemia and provide useful guides for genetic counseling.

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POSTER

Prevalence of Swirling Complications in Newborns Treated with Hyperbilirubinemia

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ARTICLE INFO

Keywords:

Hyperbilirubinemia
Exchange of blood
Infants

ABSTRACT

Background: Jaundice is one of the most common problems in neonatal period. The most frequent complications of indirect jaundice are bilirubin encephalopathy. Brain stem response tests screen and diagnose the neurological complications of bilirubin (kernicterus). Transfusion symptoms are classified into three categories: Depending on the blood components, the catheter depends on the exchange of blood. Administering intravenous immunoglobulin may reduce the need for blood transfusions. Inflammation-related inflammation may significantly affect bacteremia. The ratio of bilirubin to albumin has been suggested in recent years as a measure of blood transfusion in some sources.

Methods: This article is a review study describing the use of library resources and databases and web sites of PUBMED, SID, CIVILICA, GOOGLE SCOLAR, SCOPUS, during the years 2000 to 2016 and aimed at an overview of what has been done so far.

Results: An important clinical issue in neonatal hyperbilirubinemia is its correlation with craniocetosis. Signs of blood transfusions are significantly more pronounced in preterm infants than in the seminal period. Complications of exchange transfusion include: thrombocytopenia (55.85%), metabolic acidosis (21.7%), hyperglycemia (22.72%), hypoglycemia (6.7%), hyperkalemia (4.27%), hypocalcemia (30.8%), developed hypernatremia (5%), East Qlby_Tnfsy (5%), convulsion (4.2%), mortality (5%) is the most common complication is between thrombocytopenia.

Conclusion: Common complications of blood transfusion include thrombocytopenia, metabolic acidosis, hyperglycemia, and with regard to the complications of blood transfusion, it is necessary to consider correction with timely diagnosis of complications.

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POSTER

Managment of Intrauterine Transfusion in Fetal Anemia

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ARTICLE INFO

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Fetal anemia
Intrauterine blood transfusion
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ABSTRACT

Fetal anemia remains as a serious complication of pregnancy which can lead to Perinatal morbidity and mortality. For this reason, there have been several studies on the importance of providing intrauterine Blood to the fetus. Intrauterine transfusion (IUT) with enhancing arterial oxygen content, increasing cardiac output, and improving oxygen delivery is an effective and non-invasive method for management of fetal anemia. Although red cell alloimmunization is still the main indication for IUT, it has also been reported to be useful in nonimmune etiologies such as human parvovirus B19 infection, fetomaternal hemorrhage, twin-twin transfusion syndrome, placental/fetal tumors and other rare diseases. IUT is considered as a safe method but fetal death, emergency delivery and infections may occur which may affect the outcome; specially when performed early in the second trimester. This review focuses on interuterine transfusion, perinatal outcome improvement and the risk of its complications.



POSTER

Bernard- Soulier Syndrome Presented in Neonatal Period

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ARTICLE INFO

Keywords:

Bernard-Soulier syndrome
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purpura: giant platelets
Mucocutaneous bleeding

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ABSTRACT

Bernard-Soulier syndrome (BSS) is a rare (1: 1,000,000), genetically inherited platelet function disorder with giant platelets, thrombocytopenia and a prolonged bleeding time. These abnormalities are caused by quantitative or qualitative defect of platelet membrane glycoprotein (GP) Ib/IX/V complex, a receptor for von Willebrand factor on the platelet surface. Platelets in these patients are unable to adhere, leading to an increased bleeding tendency. Easy bruising, nosebleeds and mucocutaneous bleeding are common clinical manifestations in children with BSS. Symptoms begin usually in infancy and early childhood but can rarely present in neonatal period or unrecognized until the third or fourth decade of life. This disease has very close similarity with idiopathic thrombocytopenic purpura (ITP) and is frequently misdiagnosed and treated as it. We report a 1- year- old girl with macrothrombocytopenia and diagnosis of ITP who was referred because of scattered and large bruises on the surface of her body. She had history of prolonged bleeding after first vaccination at birth and large bruising on the hand at 3 months of age that spontaneously was improved. Physical examination was unremarkable and her parents were relative, but there was no family history of bleeding. Because of the history of prolonged bleeding after vaccination at birth, the patient was reevaluated and based on platelet function studies and platelet surface GP expression by flow cytometry, Bernard-Soulier syndrome was diagnosed for the child. In conclusion Bernard-Soulier syndrome should be considered in any neonate with bleeding and macrothrombocytopenia before the diagnosis of ITP is confirmed.

**POSTER****Hereditary Pyropoikilocytosis: Case Report from Iran**

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ARTICLE INFO*Keywords:*

Hereditary pyropoikilocytosis
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ABSTRACT

Neonatal jaundice is commonly observed among newborn infants caused by hyperbilirubinemia. In most cases, hyperbilirubinemia results from a physiological increase in the unconjugated bilirubin concentration, combined with immature mechanisms for conjugation and enhanced enterohepatic circulation. In the cases of pathologic unconjugated hyperbilirubinemia, an increased production of bilirubin due to hemolysis is the most likely cause. We present a newborn with severe neonatal hyperbilirubinemia with signs of hemolysis, which proved to be caused by a rare disorder generally classified in the hemolytic group of unconjugated hyperbilirubinemia.



POSTER

A Neonate with Superior Sagittal Sinus Thrombosis and Homozygous MTHFR A1298C Gene Mutation

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Superior Sagittal sinus thrombosis
Hypercoagulable states
Homozygous MTHFR A1298C gene mutation

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ABSTRACT

Background: Superior sagittal sinus thrombosis (SSST) is the most common type of dural venous sinus thrombosis. Risk factors include: Maternal diabetes (GDM) and preeclampsia, prenatal complications (asphyxia), sepsis and meningitis, dehydration, hypercoagulable states (Factor V Leiden, MTHFR gene mutations), and cyanotic heart disease. Diagnosis of SSST presents challenges specially in first months of life due to its various patterns.

Case Presentation: We report a case of a female term newborn who was born with normal vaginal delivery. Immediately after birth due to low Apgar score, she needed resuscitation. The infant was admitted to NICU for respiratory distress, hypotonia and poor general conditions. Mother had a history of twice abortions in previous pregnancies and hypertension and GDM during last weeks of this pregnancy. Patient experienced seizure attacks 12 hrs after birth who was treated with Phenobarbital and Phenytoin. Because of persistent hypotonia and impairment of consciousness, neuroimaging (T1-T2 brain MRI) was performed that demonstrated isodense clot on T2 and hypodense on T1 suggesting superior sagittal sinus thrombosis. Further work up for hypercoagulable states revealed homozygous MTHFR A1298C gene mutation. Patient was treated with LMWH while anti-Xa activity was 0.8 U/mL and discharged in partial remission.

Conclusion: Cerebral imaging and screening for hypercoagulable state should be considered in evaluation of any neonate with indistinct neurologic presentation and high risk situations.



POSTER

Impact of Maternal Iron-Deficiency in 3rd Trimester on Newborn Jaundice

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ARTICLE INFO

Keywords:

Neonatal Jaundice
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ABSTRACT

Background: Iron deficiency anemia among pregnant women is a widespread problem in Iran. Maternal factors could help determine the potential incidence of hyperbilirubinemia. In this study, we aimed to identify the relationship between the jaundice in newborns and maternal iron-deficiency.

Methods: This cross-sectional study was conducted in 2017. Mothers giving birth between May 2016 and May 2017 were selected from medical records (82 cases). The mothers were classified into two groups based on hemoglobin and serum ferritin levels as iron deficient anemic (41) and non-anemic (41) and their newborns also into two group icteric and non-icteric. for data analysis, statistical tests including t-test, Mann-Whitney, analysis of variance, and Pearson's correlation test were performed, using SPSS version 23.

Results: The results showed that newborns of iron deficient anemic mothers had significantly higher mean total bilirubin levels ($15.1 \pm 3 \text{mg/dl}$), compared to the cases born of non-anemic mothers ($13.1 \pm 3 \text{mg/dl}$) ($P=0.013$). A positive association between the mother's hemoglobin and hematocrit during her 3rd trimester and her infant's bilirubin level was found.

Conclusion: Although factors such as preterm babies and breastfeeding could contribute to development of jaundice, Maternal iron-deficiency in 3rd trimester can be one of its reasons that could be improved during prenatal period by health providers.



POSTER

Factor XIII Deficiency in Khash, Iran: A Unique Mutation in Southeast Iran with an Unexpectedly High Prevalence

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ARTICLE INFO

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Factor XIII deficiency
Rare bleeding disorders
Frequency
Morbidity
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ABSTRACT

Background: Factor XIII (FXIII) deficiency is an extremely rare bleeding disorder (RBD) with an estimated incidence of 1 per 2 million and high rate of life-threatening bleeding such as umbilical cord bleeding, intracranial hemorrhage (ICH) and recurrent miscarriages. Although the precise prevalence of this disorder is not clear, the disorder is more frequent in areas with high rate of consanguinity. Previous studies have revealed an unusual high prevalence of FXIII deficiency in Sistan and Baluchestan province of Iran due to a recurrent missense mutation (p.Trp187Arg, c.559T>C) which is considered as a founder effect. In this study, we assessed the prevalence of congenital FXIII deficiency in the population of the Khash city.

Methods: Initially all participants complete a structural questionnaire and then blood specimens were drawn from 3800 individuals referred to the only governmental hospital laboratory for a routine check-up from June 2016 to February 2017. Genotyping for the c.559T>C mutation was performed by polymerase chain reaction amplification of genomic DNA followed by restriction enzyme digestion (PCR-RFLP). Direct sequencing was performed for homozygous and heterozygous individuals in about 10% of all samples.

Results: Out of 3800 individuals, molecular analysis was performed on 3580 cases. We identified 124 (3.5%) and 7 (0.19%) heterozygous and homozygous carriers of the c.559T>C missense mutation, respectively. A considerable number of heterozygous carriers were living (n=39; 31.5%) or were native (n=26; 21%) from the Poshtkuh rural district. Two of homozygotes (67%) were resident of this area. All affected heterozygotes and homozygotes were Baluch. Almost all heterozygotes and homozygotes patients (92.4%) were born from consanguineous marriages. A total of 23 deaths were occurred in homozygotes families. The causes of death were umbilical cord bleeding (47.8%) and central nervous system (CNS) bleeding (34.8%) that in a family with positive family history of FXIII deficiency were highly suggestive of FXIII deficiency.

Conclusion: Our results showed that prevalence of FXIII deficiency is about four thousand times higher in Khash city than in the rest of the world (1 in 500 vs 1 in 2 million). Based on these data, it is possible to estimate that about 5000 carriers and about 300 severe FXIII deficient patients are living in Khash city.

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POSTER

Prenatal Diagnosis in Rare Bleeding Disorders: An Unresolved Issue?

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ABSTRACT

Intracranial hemorrhage (ICH) is the most dreadful complication and the main cause of death among patients with rare bleeding disorders (RBD) and Prenatal diagnosis (PND) is a preventative lifesaving program. A total of 39 PNDs were reported in the literature, most often for congenital factor (F) XIII and FVII deficiencies and rarely in FX, FV deficiencies and afibrinogenemia. The main cause to request a PND is ICH and related morbidity and mortality. Different molecular methods including direct sequencing and linkage analysis as well as polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) for a specific mutation are the most common used methods for PND while factor assay and combination of molecular and factor assay also were used. A total of 7 severely affected fetuses were identified during PND including 3 fetuses with FXIII deficiency, 3 with FVII deficiency and 1 with FX deficiency. Out of these 7 cases; intrauterine ICH was occurred in 1 case with FXIII deficiency, 1 was electively aborted and 1 case with severe FVII deficiency, received intrauterine factor transfusion. Post-delivery ICH was reported for 1 patient with severe FVII deficiency within first month of life. All other pregnancies were uneventful.



POSTER

Hematologic Complication of Exchange Transfusion in Neonates

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ARTICLE INFO

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Hyperbilirubinemia
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Complications
Metabolic alterations

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ABSTRACT

Background: Jaundice is one of the most common problems in neonatal period which is a leading cause of admissions in neonatal departments. There are different modalities for treatment of hyperbilirubinemia such as phototherapy, exchange transfusion and some medications; however, there are complications reported for each treatment. In this study we evaluated complications of exchange transfusion in neonates admitted in our center.

Methods: 120 neonates which exchange transfusion had been done for them were assessed because of severe jaundice. In this research we measured blood level of bilirubin, Na, Ca, blood sugar hemoglobin and platelet level before and after exchange transfusion.

Results: Complications were seen in 20 neonates (17%). Thrombocytopenia was the most common complication (30%). Hypoglycemia (7%) and hypocalcemia (3%) were the other metabolic complications. There was reduction in hemoglobin level but it was not statistical significant.

Conclusion: Exchange transfusion must be performed with fresh blood and appropriate blood volume should be used along with considering calcium injection and maintenance of blood glucose.



POSTER

Risks of Blood Products Transfusion in Pediatric Patients Undergoing Surgery

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ARTICLE INFO

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ABSTRACT

The decision of when to transfuse blood products to patients is complex and is determined by several factors. On the other hand, there is no minimum hemoglobin level that makes a definite indication to transfuse blood products to pediatric patients undergoing surgery. Red blood cell (RBC) transfusions are one of the most overused treatments in modern medicine and cost billions of dollars. The adverse effects of blood products transfusion include: the transmission of infectious diseases and immune and nonimmune-mediated complications. The incidence of noninfectious transfusion reactions is greater than that of infectious complications. Furthermore, the mortality related with noninfectious risks is significantly higher. In fact, noninfectious adverse events account for 87–100% of fatal complications of transfusions. Reduced the risk of transfusion-related infections, the reported incidence of serious hazards of transfusion has increased, particularly in infants. However, a growing number of prospective randomized clinical trials are finding an association between blood products transfusion and an increased risk of morbidity and mortality. There is a relationship between the volume of red blood cells transfused and the occurrence of adverse outcome. The incidence of transfusion and its relation with adverse outcome warrants development of appropriate patient management guidelines. Nonetheless, the benefits of blood products transfusion must be balanced against its risks. This narrative review describes the risks of blood products transfusion and shows how to minimize the need for blood products transfusion.

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POSTER

The Study of Cord Blood Parameters in 700 Cord Blood Units Stored in Iran National Cord Blood Bank

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ARTICLE INFO

Keywords:

Umbilical cord blood (UCB)
Complete blood count (CBC)
White blood cell differential count (WBC DC)
CD 34+ cells

ABSTRACT

Background: In recent years, the use of umbilical cord blood (UCB) as a source of hematopoietic stem cells in the treatment of malignant and non-malignant blood diseases have been increasing. CBC and WBC DC counting of cord blood units are one of the most important pre-freezing factors to maintain umbilical cord blood units. Neonatal CBC is an important criterion in order to assess the clinical situation. and due to the limitations of the neonatal sampling, the CBC of umbilical cord blood can be a suitable alternative choice to compare the baby's peripheral blood and be useful for pediatrician. This study was performed to determine the CBC and differential WBC count of UCB in Iranian ethnic in order to evaluate the normal reference CBC and differential counts of WBC in umbilical cord blood samples stored in the Iranian Blood Transfusion Organization's umbilical cord blood bank.

Methods: From 2012 to 2015, UCB units from healthy Iranian donors in Iran Blood Transfusion Organization were collected. After completion of consent forms by neonatal parents, Clinical history and screening tests were performed. Cell counting, measurement of hematological indices and differential WBC count of all UCB units were performed by sysmex XS-800i cell counter (Sysmex, Tokyo, Japan). To examine the effects of gender and type of delivery route; parameters on the reference values of CBC and WBC differential count, independent t-test was used for all data

Results: In this study 966 UCB units were analyzed, with an average gestational age of 38.7 ± 0.9 . Normal reference values of CBC and differential with blood cells counts were measured for umbilical cord blood units. The male neonates had higher height, weight and percentage of CD34+ cells, but lower WBC count than female neonates ($p < 0.05$). There was no statistically significant difference in other hematologic indices in these two gender. Newborns born through vaginal delivery had higher WBC counts, hematocrit and percentage of CD34+ cells ($p < 0.05$). There was no statistically significant difference in other hematologic indices in terms of route of delivery.

Conclusion: In this study, the normal CBC and WBC differential count reference values of the umbilical cord blood units in Iran was analyzed. Gender and delivery routes were important factors that influenced the cord blood CBC indices and the percentage of CD34+ cells.

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POSTER

Alpha-Thalassemia as a Cause of Neonatal Hemolytic Anemia

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ARTICLE INFO

Keywords:

Alpha-thalassemia
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ABSTRACT

Background: Alpha-thalassemia is due to impaired production of alpha chains from 1,2,3, or all 4 of the alpha globin genes. The degree of impairment is based on which clinical phenotype is present. In contrast to beta thalassemia; alpha-thalassemia represents with some degree of anemia in the neonatal period. Hydrops fetalis will be expected when 4 of the alpha globin genes are deleted. Hemoglobin H disease usually will be happened when 3 of the alpha globin genes are deleted. In alpha-thalassemia with two α PA2 mutation (α α PA2/ α α PA2) usually mild anemia is expected.

Case Presentation: We would like to present an alpha-thalassemia boy with two α PA2 mutation (α α PA2/ α α PA2) who presented with severe anemia with Hb 5 in neonatal period. He received four times blood transfusion until 2 years of age. He was admitted due to URI for several times. He is 6 years old now. He does not require to receive blood transfusion anymore after the age of 2. The spleen is palpable now. He has not thalassemic face. Patient is evaluated for other causes of hemolytic anemia such as G6PD deficiency, pyruvate kinase deficiency, hereditary spherocytosis, autoimmune hemolytic anemia, pure red cell anemia, and infection associated anemia which all of them proved to be normal.

Conclusion: Alpha-thalassemia with two α PA2 mutation (α α PA2/ α α PA2) usually presents with mild anemia. They are not usually transfusion dependent. Viral infections may exacerbated their anemia. One case with severe anemia in a short time should not be a reason for aborting the alpha-thalassemia fetuses with two α PA2 mutation (α α PA2/ α α PA2).



POSTER

Distribution of ABO and Rhesus Blood Group System in Iranian Glucose-6-Phosphate Dehydrogenase Deficient Newborns

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ARTICLE INFO

Keywords:

ABO blood group system
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ABSTRACT

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited disorder which is common in Iran and may cause neonatal jaundice. As combination of G6PD and ABO or Rhesus incompatibility leads to a higher risk of jaundice, we aimed to evaluate the distribution of ABO and Rhesus blood groups in G6PD deficient newborns.

Methods: This cohort study was conducted on 150 icteric newborns who admitted to the NICU of educational hospitals in Azad University in North-East state of Iran, Mashhad. G6PD deficiency was evaluated and case and control groups were considered on 50 icteric newborns with G6PD deficiency and 100 icteric newborns with normal levels of enzyme, respectively. Distribution of ABO and Rhesus blood group was considered in G6PD deficient newborns and compared with newborns with normal levels of the enzyme. The prevalence of hemolysis was compared in two groups as well.

Results: Prevalence of hemolysis was 22% in case group and 19% in controls. There was no significant relationship between G6PD deficiency and hemolysis. There was no significant relationship between distribution of ABO and Rhesus blood groups in G6PD deficient newborns.

Conclusion: There was no significant relationship between G6PD deficiency and hemolysis. There was no significant relationship between Distribution of ABO and Rhesus blood groups in G6PD deficient newborns in Iran unlike other similar studies.



POSTER

Relationship between Blood Transfusion and Necrotizing Enterocolitis (NEC) in Premature Neonates

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ARTICLE INFO

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ABSTRACT

Background: Necrotizing enterocolitis is a severe intestinal disease with a high mortality rate in premature neonates. The relationship between this disease and blood transfusion (Packed Red Blood Cell Transfusion) in premature neonates has been controversial over the past three decades. We aimed to investigate the relationship between blood transfusion and necrotizing enterocolitis in premature neonates.

Methods: This review study was performed by searching articles related to necrotizing enterocolitis and blood transfusion in premature neonates in Pubmed, Embase and CINAHL databases using three keys: blood transfusion, Infant, Newborn and Necrotizing Enterocolitis and their combination from 2005 to 2017.

Results: During our research, 12 case-control studies and 11 cohort studies (retrospective) were retrieved. The results of 9 studies from 11 cohort studies revealed the relationship between blood transfusion and necrotizing enterocolitis in premature neonates. A study reported a non-association relationship between blood transfusion and necrotizing enterocolitis. Another study introduced the severe anemia in premature neonates as an enterocolitis risk factor. In case-control studies, 7 cases of enterocolitis were reported in premature neonates receiving blood transfusion. Two Blood transfusion studies were identified as an independent risk factor for enterocolitis. An anemia study and subsequent blood transfusion in premature neonates have been shown to increase the risk of enterocolitis. Also, two studies reported that there was no relationship between blood transfusion and necrotizing enterocolitis in premature neonates.

Conclusion: Based on our findings, it seems that there is a relationship between blood transfusion and necrotizing enterocolitis in newborns. But confirmation of the causal relationship between them requires the implementation of randomized prospective studies considering the role of the underlying factors such as birth weight, gestational age, hemoglobin levels and nutrition before and during blood transfusion.

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POSTER

The Correlation of Cardiac and Hepatic Hemosiderosis Measured by T2*MRI Technique with Ferritin Levels and Hemochromatosis Gene Mutations in Iranian Beta-Thalassemia Major Patients

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ARTICLE INFO

Keywords:

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ABSTRACT

Background: Organ specific hemosiderosis and iron overload complications are more serious and more frequent in some β -thalassemia major (BTM) patients compared with others. We investigated whether co-inheritance of HFE H63D or C282Y gene mutations in BTM patients could contribute to the phenotypic variation of iron overload complications. Moreover, the correlation of cardiac and hepatic hemosiderosis with plasma ferritin levels was assessed.

Methods: We studied sixty BTM patients with the mean ages of 17.59 ± 9.16 from the northwest of Iran. HFE gene mutations were analyzed by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism method. Cardiac and hepatic hemosiderosis was assessed by T2*MRI technique. Ferritin levels were measured by enzyme immunoassay method. Statistical analysis was done using SPSS16 software.

Results: Genotype and allele distribution of HFE H63D and C282Y mutation did not differ significantly between patients with and without hepatic or cardiac hemosiderosis ($p > 0.05$). However, carriers of HFE 63D allele had significantly higher ferritin levels compared with non-carriers (1903 ± 993 vs. 992 ± 683 , $p < 0.05$).

Conclusion: HFE H63D is a significant determinant factor for elevated ferritin levels in BTM patients. Cardiac T2*MRI values showed a poor correlation with hepatic T2*MRI values and ferritin levels. So, accurate assessment of cardiac iron overload in BTM patients can be done only by using T2*MRI technique.



POSTER

Congenital Methemoglobinemia in a Neonate with Severe Cyanosis Immediately After Birth: A Case Report

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ABSTRACT

Background: Cyanosis is a physical finding of multiple causes that may be observed since birth. As a result, rapid diagnosis and correct management is very important. Congenital cardiac disease, abnormal lung function, metabolic disease, infections and abnormal hemoglobin can be differential causes of cyanosis. Abnormal molecules of hemoglobin such as methemoglobin can also cause significant cyanosis. methemoglobinemia is an uncommon clinical problem in the newborn infant and usually is caused by environmental toxicity due to strong oxidizing agents. Methemoglobinemia is very rarely an inherited defect of hemoglobin metabolism that includes NADH-cytochrome B5 reductase deficiency and Hb M disease.

Case Presentation: A full-term newborn boy was born in first gravid. The newborn was cyanosed in air room, he had mild respiratory distress and showed oxygen saturation of 67%. After hyperoxymia and hyperventilation test, CPAP and even mechanical ventilation, O₂ saturation was not improved. Arterial blood gas analysis revealed PaO₂: 225 mmHg and coincident oxygen saturation of 67%. Chest-X-Ray and echocardiography was normal. CBC was normal, but appearance of the blood was dark chocolate colored. The level of serum methemoglobin was 3.74gr/dl (equivalent 20%-30%) and Hb electrophoresis of both parents and newborn were normal with no Hb M disease. Glucose-6-phosphate dehydrogenase screening was normal. Therefore, diagnosis of methemoglobinemia was confirmed. Blood oxygen pressure (SpO₂) in right hand of father was 55%. In follow-up, about 17 persons of the family were diagnosed with methemoglobinemia. The neonate discharged with good condition but spo₂ was 75%. In follow-up, the neonate has good developmental growth.

Conclusion: Congenital methemoglobinemia is a rare cause of cyanosis in neonates. The diagnosis should be considered when cyanosis is not responsive to oxygen after exclusion of congenital cardiac disease and when pao₂ is high but spo₂ in pulseoximetry is low.



POSTER

Pathogenesis, Diagnosis, and Management of Sick Cell Anemia in Infancy

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ARTICLE INFO

Keywords:

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ABSTRACT

Sickle cell disease (SCD) refers to the broad group of disorders that feature erythrocyte sickling under physiologic conditions. SCD is an autosomal recessive disorder caused by a number of different genotypes. Sickle cell disease results from the inheritance of two mutated beta globin chains which produce abnormal proteins. The instability of the Hb S polymer leads to oxidative damage (O₂-) of the red cell membrane. The damage to the red cell is initially reversible if the cell is reoxygenated. However, if this happens repeatedly, the red cell becomes irreversibly damaged and adopts the permanently abnormal, sickle shape which is characteristic of the condition. Hemolytic anemia and clinical sign and symptoms of SCA are rare before 2 months of age and develop variably thereafter. At the time of infancy, there is a high risk of life-threatening complication such as splenic sequestration and sepsis and for this reason, designing a timely diagnosis and interventional strategy is very important. In this review after brief discussion about pathophysiology of sickle cell anemia, we discuss about the diagnosis and treatment and prevention of complications in the infancy.



POSTER

Diagnostic Approach to G6PD Deficiency in Neonates (A Review of Articles)

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ARTICLE INFO

Keywords:

G6PD deficiency
Neonatal jaundice
Quantitative measurement

ABSTRACT

Background: G6PD deficiency is a common enzyme deficiency. One of the most common pathologic causes of unconjugated hyperbilirubinemia in the newborn include G6PD deficiency. However, G6PD deficiency may be associated with severe hemolytic episodes with resultant jaundice and anemia after ingestion or contact with the fava bean (favism) and medications or some chemical substances. Therefore, early diagnosis of G6PD deficiency is important. In neonatal period, G6PD deficiency presents with two clinical pictures: A moderate form of jaundice and an extreme hemolytic jaundice. In infants known to be G6PD deficient, prevention of severe hyperbilirubinemia by administration of a single intramuscular dose of tin-mesoporphyrin, an inhibitor of heme oxygenase has been advocated.

Case Presentation: Herein, we report two cases with different presentations. One of them was a male neonate admitted with severe icter and hyperbilirubinemia. He was exchanged in third day of life. The neonate was male with a blood group and Rh compatible with his mother. The first blood tests before exchange did not disclose G6PD deficiency. We requested for quantitative G6PD test, the enzyme level of activity was 16% which was compatible with moderate G6PD deficiency. The second case was a neonate who was admitted in our hospital with recurrent icterus. On third day of admission, G6PD deficiency was detected, while on first and second day it was reported to be normal.

Conclusion: G6PD deficiency has presentations in neonates which are different from other ages. In prolonged severe hyperbilirubinemia, we must perform quantitative G6PD test to rule out G6PD deficiency. Semiquantitative screening test for G6PD deficiency detects severe deficiency but may miss a substantial

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POSTER

Patient Blood Management in Pediatric Transfusion Medicine

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ARTICLE INFO

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Patient blood management
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Blood ordering
Blood transfusion

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ABSTRACT

Background: Allogeneic blood transfusion is one of the most commonly used therapies in hospitalized patients. Despite of the benefits of blood transfusion lifesaving, it has many complications. Limiting blood utilization is called Patient blood management (PBM). Therefore, this treatment should be taken when the benefits outweigh its harm. Patient blood management briefly means that it restricts clinical use of allogeneic blood products with the aim of improving the clinical outcome. Since the normal range of children's hematological tests is less than that of adults, blood administration and its products in this group of patients will be much more limited than that of adults. On the other hand, Children are less than adults likely to have heart and respiratory disorders requiring blood transfusions therapy.

Methods: In this paper we gather latest articles that indexed by pubmed, medline, web of science in 2010-2017 years. Inclusion criteria was investigation of Patient blood management in pediatric transfusion medicine. Among the PBM policies that can be used in children, as follows: acute normovolaemic haemodilution (ANH), reducing Phlebotomy, using tourniquet and oxygen carriers and applying appropriate surgical techniques with minimal bleeding, also, establishment of Guideline maximal surgical blood ordering in Children's hospitals.

Conclusion: The amount of blood ordering should be based on the administration threshold for hemoglobin and platelets, depending on the patient's clinical condition. By adopting strategies for Patient blood management in health centers, provide patient health, in addition, it is economically feasible and reduces the cost of the hospital.



POSTER

The Effect of Iron toxicity on Induction of PARP1 Expression in K562 Cell Line

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ARTICLE INFO

Keywords:

ROS

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Iron overload

Thalassemia

ABSTRACT

Background: Iron overload in vital organs increase the risk of many diseases. Thalassemia is one of the most prevalent monogenic disorder in Middle East and particularly Iran that is related to dysfunctional synthesis of globin chains. Thalassemia patients mainly suffer anemia during lifespan, and many complications in these patients are as a result of blood transfusion to compensate it. Iron overload is a common issue in many transfusion dependent thalassemia (TDT) and non-transfusion dependent thalassemia (NTDT). Iron indices show an accumulation of Iron in the body, therefore, iron toxicity is a major fact among these patients. It has been reported that reactive oxygen species (ROS) increase in erythroid precursors due to α -globin accumulation and Iron toxicity. According to other studies, ROS could cause DNA damage and increase expression of PARP1 gene. PARP1 enzyme has vital role in single-stranded DNA (ssDNA) breaks repair. In current study, we find out that Iron toxicity cause increase expression of PARP1. **Methods:** K-562 cell lines were gifted by Stem Cell Technology Research Center (Tehran, Iran). K562 Cells are cultured in RPMI 1640 Medium supplemented with 10% FBS. These cell were treated by different dose of Iron citrate 0, 30, 50 and 100 ($\mu\text{g/ml}$) according to level of Iron overload in major thalassemia. Then cells were incubated in 37.0 C with 5% CO₂ for 48 hours. Then, RNA was extracted and cDNA was synthesized. Real-time PCR was performed using SYBR Green for assessing expression level of PARP1 in treated groups compared to control. The relative expression of mRNA was calculated using the $2^{-(\Delta\Delta\text{Ct})}$ method, and normalized to the expression of GAPDH.

Results: Our results demonstrated that PARP1 expression was increased after treatment with defined dose of Iron citrate. The expression level of PARP1 shown 4.2, 6.3 and 13.3 folds change on selected iron citrate dose in treated cells, respectively.

Conclusion: We find out that accumulation of iron could directly or indirectly increase level of ROS and subsequently increase expression of PARP1 in TF1 cell line. It is a hope that inhibition of PARP1 could improve the condition of major thalassemia patients.

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POSTER

Psychosocial Risks and Posttraumatic Stress Symptoms among Iranian Parents of Children During Cancer Treatment

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ARTICLE INFO

Keywords:

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Parents
Childhood cancer

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ABSTRACT

Background: Support of parents of children with cancer requires health care personnel to be knowledgeable about the relationship between psycho-social risks and post traumatic stress symptoms. This study thus was conducted to fulfill this aim in South-East of Iran.

Methods: Using the Psychosocial Assessment Tool- Revised (PAT-R) and the Impact of Event Scale- Revised (IES-R) for parents of children with cancer, 200 parents of these children in two hospitals supervised by Kerman University of Medical Sciences was assessed. The PAT-R contains subscales such as family problems (consist of 20 questions; Item Response Anchors are 2= no, 2= Yes), parent stress reactions (consist of 3 questions; 2=Not at All, 2= Sometimes, 0= Often, 3= Very Much), family beliefs (consist of 22 questions; 2=Not at all, 2= true Just a little bit true, 0= Pretty much true, 3= Very true), child Problems (consist of 21 questions; 2=Never a Concern Sometimes, 2=a Concern Currently, 0= Receiving Help) and sibling Problems (consist of 21 questions; Item Response Anchors are 2= no, 2= Yes) and, the Impact of Event Scale- Revised (IES-R) is a 22-item questionnaire that assesses psychological symptoms that occurred within the past week associated with a specific traumatic event. A Kolmogorov-Smirnov test indicated that the data were sampled from a population with normal distribution. So, independent t test was used to examine the correlation between PAT-R, IES-R scores.

Conclusion: There were association between posttraumatic stress symptoms and psychosocial risks. More study is needed to elucidate the Iranian parents' experience of having children with cancer.



POSTER

Diagnosis and Management of Neonatal Thrombosis

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ARTICLE INFO

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Neonatal thrombosis
Anticoagulation therapy
Central venous line
Thrombophilia

ABSTRACT

Thrombotic events in the neonatal period are serious clinical condition. The haemostatic system in neonates is a balanced physiological system. Among children, neonates have the highest incidence of thrombosis due to risk factors such as catheter instrumentation, an evolving coagulation system and congenital heart disease. In neonates and infants, numerous clinical and environmental conditions lead to elevated thrombin generation and subsequent thrombus formation thromboplastin time and a partial thromboplastin time. The diagnostic procedures are more difficult to perform in neonates than in adult patients. The most common sources of thrombus formation in neonates are the renal veins, venacaval occlusion, cerebral venous thrombosis, and perinatal thromboembolic stroke.

Diagnostic imaging methods: In general, the diagnostic procedures are more difficult to perform in neonates than in adult patients because of frequent clinical instability and the lack of comparable data concerning ultrasonographic scans. Duplex sonography, venography, computed tomography and MRI can be used to diagnose venous thrombosis. venography is mandatory to confirm thrombosis in the upper venous system. MRA and MRV and angiography are recommended to confirm the diagnosis of thromboembolic ischaemic stroke. **Prothrombotic conditions:** Numerous conditions such as periparturient asphyxia, fetal diabetes, neonatal infections, dehydration, the use of central lines, trauma or surgery, malignant diseases, renal diseases or autoimmune diseases result in elevated thrombin generation with subsequent thrombus formation in neonates and infants. Inhereditary disorder that consist of thrombosis compose of protein C and S deficiency and mutation protein G20210 and protein V leiden.

Treatment For asymptomatic thrombosis is recommended. Supportive care and close monitoring of the thrombus is also suggested. This avoids development of bleeding complications that may be associated with anticoagulant or fibrinolytic therapy. If the thrombus is associated with a central venous line or umbilical venous catheter, the catheter should be removed. If the thrombus extends, is suggest treatment. For symptomatic thrombosis, treatment with anticoagulation and/or fibrinolytic agents. But neonate with acute purpura fulminans due to homozygous protein C deficiency or protein S deficiency should receive fresh frozen plasma or, if available, protein C concentrate. Anticoagulants used in neonates and infants are standard heparin, low-molecular weight heparin and thrombolytic agents.

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POSTER

The Role of MicroRNA in Neonatal Platelet Disorders

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ARTICLE INFO

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Neonatal megakaryocytes
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MicroRNA (miRNA)

ABSTRACT

Background: Neonates could be affected by megakaryocytic disorders. Statistics indicate 20–35% of all neonates admitted to neonatal intensive care units (NICU) develop thrombocytopenia. Acute megakaryoblastic leukemia (AMKL) comprises 4–15% of newly diagnosed pediatric acute myeloid leukemia patients. Hemorrhage and thrombosis produce significant morbidity and mortality in the newborn period. Approximately one percent of all admissions have significant hemorrhagic complications; also, approximately 40 percent of deaths have associated hemorrhage or thromboses described at autopsy. It was shown that Although megakaryocytopoiesis follows the same steps in neonates and adults, there are substantial developmental differences between them. Specifically, Neonatal MK progenitors are hyperproliferative and generate more MKs per colony but are smaller and less polyploid compared to adult progenitors that generate less platelets per MK. It has been hypothesized that developmental differences between neonatal and adult MKs contribute to the vulnerability of neonates to develop severe thrombocytopenia. Based on findings MiRNAs have importance regulatory role in the self-renewal of megakaryocyte-erythroid progenitors and in platelet generation. MicroRNAs (MiRNAs) provide a posttranscriptional regulatory layer that can silence specific target genes through direct mRNA degradation, translational repression, or both. MiRNAs are involved in several cellular processes; like cell cycle, apoptosis, drug resistance and differentiation, and control the differentiation and function of various cellular systems. There is a strong connection between epigenome and miRNome, and any dysregulation of this complex system can result in various physiological and pathological conditions. The goal is to identify and Introduce the most important MiRNAs in regulating megakaryopoiesis and platelet disorders.

Methods: We reviewed previous studies pertaining for the period of 1990 to 2017, using advanced search based on MESH with the terms, megakaryocytic neoplasms, platelet disorders and MicroRNA.

Results: 64 studies were identified. The present review provides information on 36 miRNA genes shown to be epigenetically regulated in association with megakaryocytic disorders and neoplasms. The review revealed MiR-125b, MiR-9, MIR 99a, and mir155 are the most frequently reported epigenetically dysregulated miRNAs.

Conclusion: There is a need to further study molecular mechanisms of platelet disorders to better understand the crosstalk between microRNA, epigenetics and gene expression and to develop new therapeutic options.

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POSTER

Improved Activity of New Anticancer Agent, Ginsenoside Rh2, on ALL Cancerous Cells by Functionalized Lysine- and Arginine -Treated Graphene

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ABSTRACT

Ginsenoside Rh2 (Rh2) is a promising and strong anticancer agent with broad activity against different cancer cell lines. However, there are two fundamental problems for its application as an effective anticancer agent: fast plasma elimination and enzymatic digestion in the digestive system. To solve above-mentioned problems, Rh2-treated graphene oxide (GO-Rh2), lysine-treated highly porous graphene (Gr-Lys), arginine-treated Gr (Gr-Arg), Rh2-treated Gr-Lys (Gr-Lys-Rh2) and Rh2-treated Gr-Arg (Gr-Arg-Rh2) were synthesized. 3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium Bromide (MTT) assay was used for evaluation of cytotoxicity of samples on ALL and human mesenchymal stem cells (MSCs) cell lines. The hemolysis activity of Rh2-based carbon nanostructures was performed by spectrophotometric assay. Further, the effect on blood coagulation system was evaluated by measurements of prothrombin time (PT) and Partial Thromboplastin Time (PTT). Interestingly, GO-Arg, GO-Lys, GO-Arg-Rh2, and GO-Lys-Rh2 were more active against cancer cell lines in comparison with their cytotoxic activity against normal cell lines (MSCs) with IC₅₀ values higher than 100 µg/ml. Also, GO-Arg-Rh2 has the highest anticancer activity. Results also showed that aggregation and change of RBCs morphology were occurred in the presence of GO, GO-Rh2, Gr-Arg, Gr-Lys, Gr-Arg-Rh2, and Gr-Lys-Rh2. Note that all the samples had effect on blood coagulation system, especially on PTT. After functionalization of nanostructures with Rh2, their toxicity reduced significantly. All nanostructures act as antitumor drug so that binding of drugs to a nanostructures is irresolvable and the whole structure enter to the cell as an effective drug. So, modification with basic aminoacids may be a promising strategy to enhance the therapeutic index for anti-cancer agents such as Rh2 because of reduction of side effects on normal cells, enhancement of their anticancer activity as well as increase of their stability.

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POSTER

Severe Neonatal Hyperbilirubinemia Related to Hemolytic Anemia and Blood Exchange Transfusion

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ARTICLE INFO

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ABSTRACT

Background: Neonatal jaundice is a common condition that could potentially lead to severe neurotoxicity (kernicterus) and is a frequent indication for blood exchange transfusion. The aim of this study was to determine the correlation between the causes of neonatal jaundice and need of blood exchange transfusion.

Methods: 100 neonates treated by blood exchange transfusion in NICU of Amirkola Children Hospital (Babol-Iran). Indications for blood exchange transfusion were serum bilirubin level of more than 20 mg/dl in high risk term neonates and more than 25 mg/dl in no risk neonates. For low birthweight (LBW) infants, a SBR mg/dl less than 1% of body weight in gram was an indication for blood exchange transfusion. Data were analyzed by the X² and Z statistic test.

Results: The need for BET in male sex was 12% higher than females. 41.25% were due to ABO incompatibility, 23.75% due to G6PD deficiency, 13.75% idiopathic, 12.5% due to prematurity, 5% Rh incompatibility, 2.5% sepsis and 1.25% polycythemia. ABO incompatibility and G6PD deficiency were the most common causes (P=0.001). Need for blood exchange transfusion in LBW infants were higher than term neonates (P=0.001).

Conclusion: According to the high incidence of ABO incompatibility and G6PD deficiency in this region, for prevention of severe neonatal hyperbilirubinemia we suggest to do the umbilical cord G6PD screening and blood group typing in neonates who have a mother with O blood group.



POSTER

Transient Myeloproliferative Disorder in a Preterm Newborn Without Down Syndrome: A Case Report

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ARTICLE INFO

Keywords:

Transient myeloproliferative disorder
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ABSTRACT

Transient myeloproliferative disorder (TMD) is commonly seen in Down Syndrome (DS) infants. We report a male newborn infant with 31 weeks of gestation and birth weight of 1060 grams without Down Syndrome who presented neonatal transient leukemia and achieved spontaneous remission. In case of TMD chemotherapy is not advised, as it is not useful due to transient nature of disorder and its potentially more toxicity in newborn infants. Nevertheless, the risk of developing later leukemia seems high, and close follow up is recommended.



POSTER

Risk of Neonatal Hemolysis and Death Because of Severe Alloimmunization in Multi Transfuse Mothers

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ABSTRACT

Background: Thalassemia is most hereditary anemia in our country with chronic blood transfusion. Nowadays with improvements in quality of treatment, we have adult thalassemic patients who are in child bearing age and want to be married and have baby. On the other hand, alloimmunization is one of the major side effects of regular blood transfusion in thalassemic patients. These alloantibodies against the minor blood groups some times can significantly complicate transfusion therapy. If these alloantibodies are produced in female patients, they can complicate the pregnancy and delivery. We introduce a 26-year-old female with Thalassemia intermedia who was on hydroxyurea since age of 5. She got married at 22 years of age. One year later, she stopped taking hydroxyurea with plan for pregnancy. With discontinuation of HU, her Hb level dropped to less than 8gr/dl. She had few episodes of transfusion with low Hb levels. she got pregnant. During pregnancy, the Hb of the patient significantly dropped. Antibody screening test was positive for anti-E, anti-JK, anti S and auto-antibody. She was on low dose of oral prednisone and was receiving transfusion every 14 days with complete matched blood provided by IBTO, but She had low fetal growth. Her gynecologist decided to terminate the pregnancy because of intrauterine growth retardation, so cesarean section was performed at gestational age of 32 weeks. She delivered a live infant girl weighing 1800 g. The Preterm baby admitted to NICU due to his low birth weight. The baby was relatively well and they wanted to discharged the baby after 15 days, but because of mild anemia they decided to Transfuse him. Unfortunately, the baby died due to severe hemolysis.



POSTER

Neonatal Thrombosis: Incidence and Risk Factors in a Tertiary Care Hospital in Iran

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ARTICLE INFO

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ABSTRACT

Background: Neonatal thrombosis is one of the most important challenges in Neonatal Intensive Care Unit (NICU) patients which can lead to an asymptomatic condition, limb loss or even death. This study was performed to determine the incidence and risk factors of neonatal thrombosis in a tertiary care hospital in Tehran, capital of Iran.

Methods: In this historical cohort, all neonates admitted to Ali-Asghar children's hospital, Tehran, since Sep 2014 till Mar 2015 were enrolled. With using a check list, data of the neonates were collected from their files. If thrombosis happened and was proved with doppler ultrasound, the data about the type and place of the thrombosis, occurrence of complications, recurrence of thrombosis and the swelling of the extremity distal to the thrombosis area were collected. The significant level was considered less than 0.05. Software of SPSS version 16 was used for data analysis.

Result: The neonatal thrombosis incidence was 2.87% (14 cases out of 489). The mean age of cases at thrombosis onset was 31 days (Standard Deviation (SD) 22 days). The mean birth weight and gestational age in cases were 1890 gram (SD: 968 gram) and 33 weeks (SD: 4.3 weeks), respectively. Most of the cases (13, 92.9%) had venous thrombosis and one case (7.1%) had arterial thrombosis. Femoral vein thrombosis following catheter insertion has occurred in 9 cases (64.2%) of thrombosis. All the cases have involved with at least a critical illness and had positive history of receiving at least one blood product. In multivariate analysis with multiple regression, a statistical significant relation between thrombosis and neonatal age at admission, using of central vein catheter, history of exchange transfusion, and exclusive breast feeding was found that means higher age at admission, using of a central vein catheter or positive history of exchange transfusion; the using the latter had a protective effect.

Conclusion: Most of our findings were in agreement with the results of other studies. Some interesting results included the significant relation between thrombosis and neonatal age at admission, history of exchange transfusion or exclusive breast feeding, none of them mention about in other articles. It seems that approval of these relations needs conducting more extensive and prospective studies in neonates admitted in NICUs.

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POSTER

Neonatal Screening for Anemia

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ARTICLE INFO

Keywords:

Neonatal anemia
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ABSTRACT

Background: The high incidence of α thalassemia, Sickle cell anemia and spherocytosis are major reasons that newborn screening should be routine in order to decrease morbidity especially in the southern provinces of Iran. The object of this study was neonatal screening for anemia in healthy, full-term Iranian newborns.

Methods: One thousand neonates were screened over a nearly three-year period for detection of the cause of anemia. All neonates were Iranian and lived in Fars Province, southern Iran, and were healthy and full term. This study was conducted in two Hospitals affiliated to Shiraz University of Medical Sciences, Shiraz, Iran. The screening was performed on cord blood samples collected on EDTA and the method was approved by the Ethical Committee. After sample collection, complete blood cell count, osmotic fragility test and hemoglobin electrophoresis were done for each sample.

Results: Total prevalence of anemia in this neonatal screening program was 12.2 %; the most prevalent one was α thalassemia (6.4 %), followed by hereditary spherocytosis (4.8 %) and sickle cell anemia (1.2 %). The total analysis for detection of alpha thalassemia suggested that screening methods by mean corpuscular volume (MCV) ≤ 94 fl, mean corpuscular hemoglobin (MCH) ≤ 27 , and hemoglobin level ≤ 16 g/dl plus MCHC > 35 , were the appropriate cut-off points for our population.

Conclusion: Our study suggests new cut-off points for the MCHC (35 as a screening index for hereditary spherocytosis. This cutoff points are very cost effective for early detection of α thalassemia; because of clearance of the Hb Barts after third week of the birth and misdiagnosis as iron deficiency.



POSTER

Correlation between Hematocrit and Neonatal Thrombosis, A Systematic Review

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ARTICLE INFO

Keywords:

Neonatal thrombosis
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ABSTRACT

Background: High level of hematocrit (HCT) is a prominent feature in neonatal period. On the other hand, the natural history of Polycythemia Vera (PV) is complicated by thromboembolic events; patients with myeloproliferative disorders suffer from both arterial and venous thrombosis, which accounts for 40% of the mortality associated with these disorders. A growing number of recent studies have observed an association between elevated hematocrit levels and thrombosis. However, the mechanism behind this pathway yet has not been fully understood. **Methods:** A systematic review on the correlation between hematocrit and risk of thrombosis in the English language literature which has been published in the recent 20 years were surveyed.

Results: Eleven papers had inclusion criteria. A recent in vivo study induced an elevation of hematocrit levels in otherwise healthy mice. Compared with control mice, mice with elevated hematocrit had a shorter time to artery occlusion (13.2 vs 5.3 minutes, $P < 0.05$).



POSTER

Neonatal Screening Program for G6PD Deficiency in Fars Province, Iran

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ARTICLE INFO

Keywords:

G6PD deficiency
Neonatal screening
Screening program
Blood transfusion

ABSTRACT

Background: According to Hospital documents since 20 years ago; G6PD deficiency hemolysis consisted more than 20% of admissions in Pediatric Emergency Room (PER) and Pediatric Wards in the spring. Also significant mortalities related to the severe anemia had been recorded annually.

Methods: When national neonatal screening was suggested by Ministry of Health, in our Province a committee was established for organizing and conducting this program. This committee decided on screening for G6PD deficiency. Filter paper method was suggested. Radio and Television programs were prepared and handouts were distributed for teaching of parents whose neonates were diagnosed as G6PD deficient. A proposal of research was submitted and approved. Number of Hospital admissions and blood transfusions and mortalities in the five years before the screening program was extracted retrospectively, and same information was recorded prospectively in the five years after the program.

Results: Data of the five years before program showed that in the spring from 600 admissions in the PER, 250 admissions (24%) and from 1000 admissions in the Pediatric Wards, 150 admissions (15%) were due to G6PD deficiency hemolysis. Blood transfusion was needed in 10% of the patients who were admitted in the PER, but it was recorded in the 60% of the patients who were admitted in the Wards. Male to female ratio was 2:1. Three mortalities were recorded annually. But three years after screening program, rate of admission in the PER gradually decreased to 100 and Pediatric Ward admissions decreased to 50; suggesting that more severe hemolysis occurs less frequently. Surprisingly male to female ratio became about 1:1; and need to transfusion decreased to 10% both in the wards and PER. Lyon hypothesis for random inactivation of X chromosome may be the cause of lesser sensitivity of paper method for screening, suggesting that girls should have quantitative method testing of G6PD Enzyme assay before starting Fava bean feeding.

Conclusion: Neonatal screening program is effective in decreasing mortality, morbidity and packed cell transfusion rate.

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POSTER

Hemolysis in Iranian Glucose-6-Phosphate Dehydrogenase Deficient Newborns

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ARTICLE INFO

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Hemolysis
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ABSTRACT

Background: Glucose-6- phosphate dehydrogenase (G6PD) deficiency is an inherited disorder which is common in Iran and may cause neonatal jaundice. As combination of G6PD and ABO or Rhesus incompatibility leads to higher risk of jaundice, we aimed to evaluate the distribution of ABO and Rhesus blood groups in G6PD deficient newborns.

Methods: This cohort study was conducted on 150 icteric newborns who were admitted to the NICU of educational hospitals in Azad University in North-East state of Iran, Mashhad. G6PD deficiency was evaluated and case and control groups were considered of 50 icteric newborns with G6PD deficiency and 100 icteric newborns with normal levels of enzyme respectively. Distribution of ABO and Rhesus blood group was considered in G6PD deficient newborns and compared with newborns with normal levels of the enzyme. The prevalence of hemolysis was compared in two groups as well.

Results: Prevalence of hemolysis was 22% in case group and 19% in controls. There was no significant relationship between G6PD deficiency and hemolysis. There was no significant relationship between Distribution of ABO and Rhesus blood groups in G6PD deficient newborns.

Conclusion: There was no significant relationship between G6PD deficiency and hemolysis. There was no significant relationship between

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POSTER

Hemophagocytic Lymphohistiocytosis in a Neonate: Case Report

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of pathologic immune activation, occurring as either a familial disorder or a sporadic condition, in association with a variety of triggers. This article will introduce a neonate with HLH in Iran. We report a case of HLH presenting with respiratory distress and fever, hepatosplenomegaly, jaundice and pancytopenia on the second day of life. Typical clinical and laboratory findings were detected in the neonate. HLH was diagnosed according to HLH-2004 guidelines. In spite of initiating the treatment, the disease did not cure. Post-mortem, extensive hemophagocytosis was found in multiple organs. No specific genetic defect was identified. Since HLH is a potentially lethal childhood illness, early diagnosis of this disorder and immediate starting the therapy is indicated.



POSTER

Successful Treatment a Neonate with Transient Leukemia: A Case Report

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ARTICLE INFO

ABSTRACT

Increased WBC count with circulating blasts often accompanied by anemia and thrombocytopenia may be seen in 5% of newborns with DS.^{1,2} The blast cells almost invariably have cell surface antigens characteristic of megakaryoblasts.² The percentage of blasts is often higher in blood than in BM, and a BM aspiration is of limited additional diagnostic value.^{1,2,3} The condition is referred to as transient abnormal myelopoiesis (TAM), or transient myeloproliferative disorder.^{1,3,4,5} The presentation is indistinguishable from leukemia and some have therefore favored the name transient leukemia.^{1,3} Infants with TAM are often asymptomatic presenting with elevated WBC count and hepatomegaly.^{1,3,4}

Life-threatening complications, mainly progressive hepatic dysfunction, may occur in 10% to 20% of patients with TAM, but spontaneous remission appears in the majority within 1 to 3 months.^{1,2,3} Generally no chemotherapy is indicated in TAM; however in those with progressive hepatic or pulmonary problems, WBC count above $100 \times 10^9/L$, or bleeding diatheses a short course of low-dose cytarabine (e.g., 1.5 mg/kg/day for 4 to 7 days) may be very effective and improves survival.¹ ML develops 1 to 3 years later in about 25% of the children who have recovered from TAM.^{1,2,3,4,5} We report an infant with severe respiratory distress and leukocytosis and blast in PBS.

Case Report: A 3 days old neonate with down syndrome admitted to NICU because of poor feeding and lethargy. he was a term neonate born by cesarin section. On examination, the baby was lethargic and suffered from severe respiratory distress. he had dismorphic feature of down syndrome and he was icteric but he was not pallor. he was severly tachypenic and respiratory insficiency so intubation was done. The baby was evaluated for sepsis. And his Hb was 21g/dl, WBC :56500/ μL and platelet count : 96000 / μL . Abdominal examination was revealed hepatomegaly. Others were normal. PBS showed several atypical blast with cytoplasmic projection (blebbing) suggestive to AML (M7). Bone marrow aspiration was not done. Because of respiratory insufficiency chemotherapy with low dose Ara-C (1.5mg/kg for 5 days) began and after 5 days the patient extubated and discharged with normal CBC and good condition. He has normal CBC after 1 year follow up and is wellbaby now.

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POSTER

Pyruvate Kinase deficiency and its gene mutations in newborns with jaundice in East Azerbaijan province, Iran

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ABSTRACT

Background: Jaundice is a common finding in newborns and deficiency of pyruvate kinase (PK); an enzyme in “Embden Meyerhof pathway” of glycolysis in erythrocytes can be one of the main etiologic factors in development of jaundice. PK deficiency could be one of the etiologies of “hereditary non-spherocytic hemolytic anemia”. In this study, the prevalence of PK deficiency is determined in newborns with jaundice in East Azerbaijan province for the first time.

Methods: In this study on 1750 newborns of whom 200 affected with non-conjugated hyperbilirubinemia were assessed for activity of pyruvate kinase. Routine laboratory tests were extracted from hospital records. PK activity was determined by Coupled Enzyme Assay by using the ELISA technique. Common PK-LR gene mutations were studied by PCR-RFLP method.

Results: Pyruvate kinase normal range was determined in 30 umbilical cord blood samples, and it was from 3.52-8.45 miliunit/ml. In 32 out of 200 newborns (16%), there was more than 60% decrease in PK activity. 16 out of 32 patients with PK deficiency were heterozygous for G1529A PK-LR gene mutation, while the G1168A mutation was not detected.

Conclusion: This study showed a relatively high prevalence of PK deficiency in newborns with jaundice in East Azerbaijan province. So, the PK deficiency should be considered in differential diagnosis of neonatal jaundice. Further molecular studies are recommended in this population to find more common mutations for this candidate gene.



POSTER

Transient Myeloproliferative Disorder in a Preterm Newborn Without Down Syndrome: A Case Report

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ARTICLE INFO

Keywords:

Transient myeloproliferative disorder
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Non down syndrome

ABSTRACT

Background: Transient myeloproliferative disorder (TMD) is commonly seen in infants with Down Syndrome (DS). We report a 31-week male newborn infant with birth weight of 1060 grams without Down Syndrome who presented with neonatal transient leukemia and achieved spontaneous remission. In case of TMD, chemotherapy is not advised, as it is not useful due to transient nature of the disorder and its potentially more toxicity in newborn infants. Nevertheless, the risk of developing later leukemia seems high and close follow up is recommended. Transient myeloproliferative disorder (TMD), also referred to as transient leukemia (TL), is a unique disorder characterized by the presence of blasts of megakaryocytic lineage, commonly seen in Down Syndrome (DS) infants. It is estimated to occur in 4% to 10% of newborns with DS, and is due to a mutation in the GATA-1 gene on the X-chromosome that results in the lack of full-length GATA-1 protein required for normal differentiation of megakaryocytes. About 20% of newborns with TMD have severe disease, and 10% expire in infancy. Some of the patients are asymptomatic (10% - 31%), and 48% have a mild symptomatic course, experiencing a gradual decrease in number of blasts, and achieve spontaneous remission within the first three months of life. However, the risk of developing non-transient acute megakaryoblastic leukemia (AMKL), few months or years later is estimated to be 25-30%.

Case Report: A male newborn infant delivered at 31 weeks of gestation by cesarian section due to fetal distress in a 31-year-old mother with preeclampsia. He was the second child of non-consanguineous healthy parents of Persian origin. The patient was intrauterine growth restricted (IUGR) with birth weight of 1060 grams (under 5 percentile) and was admitted to NICU for respiratory distress syndrome. His respiratory symptoms recovered by the third day of life with surfactant replacement therapy and nasal CPAP. Physical examination was unremarkable and no sign of Down Syndrome was seen in this newborn.

Blood count performed on day 1 showed hyperleukocytosis (44,400 white blood cells/ μ l with 55% lymphocytes, 35% PMN, 7% monocytes, 3% eosinophils), with normal platelets and hemoglobin. Complete blood count performed on the third day of life revealed higher degree of leukocytosis (68,300 white blood cells/ μ l), thrombocytopenia (84,000/ μ l), and anemia (hematocrit of 34%). Blood smear at the same time showed no blast. At this time, physical examination did not show any hemorrhagic signs or hepatosplenomegaly.

Supportive measures, antibiotics, and total parenteral nutrition continued. Complete blood count on the 10th day showed normal leukocytes (7,900 white blood cells/ μ l), but anemia and thrombocytopenia was aggravated. Blood culture which was negative at the first day of life, became positive with candida at 15th day, as a result amphotricin was started for the patient. CRP was elevated to 48 μ g/ml. cerebrospinal fluid and urine analysis and cultures were negative. Cultures of eye discharge and skin pustules recovered E. Coli sensitive to meropenem

and colistin; appropriate antibiotics cleared skin lesions. Patient and his mother were immunologically assessed for HIV which were negative. Anemia and thrombocytopenia needed to be treated with multiple transfusions of irradiated packed red blood cells and platelets. IVIG and erythropoietin were also prescribed for the newborn.

On 50th day of life, leukocytosis recurred again, and blast cells were seen in peripheral blood smear. Bone marrow aspiration showed diluted bone marrow, severe hypoplasia in erythroid lineage, and 28% premature white blood cells. A preleukemia state was diagnosed. But, as the patient was toxic and ill, chemotherapy was not initiated and supportive care continued. Three weeks later peripheral blood smear, bone marrow aspiration, and flowcytometry all were within normal limits and the patient was discharged from the hospital when he was 80 days old, with normal physical examination, 1630 grams body weight, and normal complete blood count (WBC=10,050/ μ l; Hb=9 g/dl; plt=172,000/ μ l).

Subsequent follow up performed at the age of 5 months was normal; however, follow up needs to be continued.

Conclusion: Attention should be paid to the rare transient myeloproliferative disorder, even in preterm infants without Down Syndrome. All newborns described in the literature achieved spontaneous remission. Chemotherapy is not advised, as it is not useful due to transient nature of the disorder and its potentially more toxicity in newborn infants. Nevertheless, the risk of developing later leukemia seems high and close follow up is recommended.

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LECTURES

The Relationship Between Maternal Anemia During Pregnancy with Preterm Birth: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Iron deficiency anemia is the most common cause of anemia during pregnancy. Other causes of anemia include parasitic diseases, micronutrient deficiencies, and genetic hemoglobinopathies. Maternal anemia during pregnancy is the most important public health problem. Since, the relationship between maternal anemia by the months of pregnancy and premature birth has been reported differently in various studies; thus, this study aims to determine the relationship between maternal anemia during pregnancy and premature birth. **Methods:** The current study has been conducted based on PRISMA guideline. That systematic review and meta-analysis study was performed from 1999 to 2015. Articles extracted using related keywords such as maternal, anemia, premature birth, pregnancy in databases, including: Cochrane, Medline, Medlib, Web of Science, Pubmed, Scopus, Springer, Science Direct, Embase, Google scholar, Sid, Irandoc, Iranmedex and Magiran. Relative risk and its confidence interval were extracted from each of the studies. The random effects model was used to combine study results and heterogeneity among the studies measured using I² index. Data analysis was conducted using STATA Ver11.1 and $P < 0.05$ was considered significant.

Results: Seventeen studies with sample sizes of 770555 were entered into the meta-analysis. Maternal anemia in the first trimester increases the risk of premature birth (relative risk, 1.31 [95% CI: 1.15 to 1.51]). But, this relationship was not significant in the second (relative risk, 1.32 [95% CI: 0.44 to 3.25]) and third trimester (relative risk, 1.56 [95% CI: 0.82 to 2.87]).

Conclusion: Maternal anemia during pregnancy can be considered as a risk factor for premature birth.



LECTURES

A Report of Rare Case with D- Phenotype

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ARTICLE INFO

Keywords:

Rh phenotyping

RBC

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D- phenotype

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ABSTRACT

Background: Rh-deleted RBCs are presented by a lack of expression of Rh CE antigens and an over-expression of the D antigen. The frequency of the -D- phenotype (Rh:17 phenotype) is very rare, with only few unrelated and consanguineous families documented worldwide.

Case Presentation: A 28-year-old woman from Shiraz was being evaluated after delivery for the need of blood transfusion in her baby. The baby was a girl who needed to be transfused due to Hb 6 g/dl. The first pregnancy was aborted at 2 months of gestational age. The second pregnancy had no problem and the result is a healthy 7- year-old girl. The patient's serum sample was agglutinated in an antibody screening test with all screening panel cells. In Antibody Screening test, Anti Rh-17 was positive. The patient's blood group was A +, agglutinated strongly with anti D. In Rh phenotyping, it was found that only antigen D existed on the patient's RBC surface, and no C, c, E and e antigens were expressed. Anti-Rh-17 positive was detected by the D-phenotype. After performing Antibody screening, it was found that the sister of the patient also had the same blood group.

Conclusion: An appropriate assessment of the interval between sensitization and pregnancy and also antibody titer, IgG subclass determination, and fetal doppler ultrasonography findings, might help to avoid some of the invasive interventions and prevent the second immune responses, resulting in prolongation of the pregnancy.



LECTURES

The Relationship Between the Epidemiology of Infants and Children Acute Lymphoblastic Leukemia (ALL) with Gender in Iran: A Meta-Analysis Study

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ARTICLE INFO

Keywords:

Acute lymphoblastic leukemia (ALL)

Epidemiology

Gender

Iran

Infants and children

Sex predilection

ABSTRACT

Background: Cancer is the third leading cause of the death after cardiovascular diseases and accidents in Iran. In infancy and childhood, the incidence of cancer is rare and it accounts for less than 1% of all cancers. Yet, it is one of the main causes of mortality and as one of the most important health problems in the community. The most common type of cancer in infants and children is Acute Lymphoblastic Leukemia (ALL). The epidemiological study of these age groups is an important step towards prevention in delays in diagnosis and treatment and subsequently reduction the social, psychological and physical problems associated with cancers of this age group. Therefore, we decided to study the epidemiology of ALL among infants and children with gender in Iran, through a meta-analysis of these studies.

Methods: The present study is a meta-analysis review of the relationship between ALL and gender in children in Iran by searching for the keywords 'Cancer', 'Children', 'Sex' and 'Epidemiology' in the SID, Magiran, Iran Doc, MEDLIB, Google Scholar, PubMed and ISI. Seven papers that were conducted in Iran during 1992 to 2016 were extracted and the results of the studies were combined using a randomized meta-analysis model. Data analysis was performed using CMA software (version 2.2.064). In heterogeneity test, p value less than 0.000 was considered significant.

Results: In the seven articles studied, which one of them was a meta-analysis of the relationship between ALL and gender, The meta-analysis showed that there was a meaningful relationship between the incidence of infants and Childhood ALL and gender in Iran. The incidence of ALL was more in boys.

Conclusion: The results of this study indicated that in terms of statistical and epidemiological data of infants' and Children's ALL in Iran, boys are more likely to develop ALL than girls. Therefore, it is recommended that in the case of screening for infants' and Children's ALL, attention should be paid to boys, and also suggested that further studies on the relationship of the etiology of ALL with male gender in order to reduce and prevent i

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LECTURES

Discrepancies between Forward and Reverse Grouping in Neonates Blood Grouping

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ARTICLE INFO

Keywords:

Neonate blood grouping
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ABSTRACT

Up to 90% of infants with a birthweight <1000 g receiving at least one red blood cell (RBC) transfusion during their stay in the neonatal nursery. ABO remains the most important blood group system in transfusion and transplantation medicine. The proper and accurate typing of ABO blood group of donors and recipients is important for compatible transfusion of RBCs. Having immature immune system, Infants do not produce antibodies until 3-6 months of age. Therefore verifying the accuracy of cell type blood grouping through the back type method is not accessible for this population. Checking the neonate's blood group by its parents could be beneficial. However there are many discrepancies between cell type and/or back type of parents that makes it complicated. In emergency need for blood transfusion, this problem is more obscure and the neonate life depends on the proper decision of laboratory specialists and physicians. Having background on the field of common discrepancies and their troubleshooting could be very advantageous for solving this puzzle. Proper and prompt decision is a critical step on the way of saving neonates with these discrepancies in immediate blood products necessities. In this article we discuss the most common discrepancies that complicates the neonates blood grouping and also explain how they can be solved.



POSTER

The Relationship Between Maternal Anemia During Pregnancy with Preterm Birth: a Systematic Review and Meta-Analysis

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ARTICLE INFO

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Anemia
Maternal
Pregnancy
Premature birth

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ABSTRACT

Background: Iron deficiency anemia is the most common cause of anemia during pregnancy. Other causes of anemia include parasitic diseases, micronutrient deficiencies, and genetic hemoglobinopathies. Maternal anemia during pregnancy is the most important public health problem. Since, the relationship between maternal anemia by the months of pregnancy and premature birth has been reported differently in various studies; thus, this study aims to determine the relationship between maternal anemia during pregnancy and premature birth. **Methods:** The current study has been conducted based on PRISMA guideline. That systematic review and meta-analysis study was performed from 1999 to 2015. Articles extracted using related keywords such as maternal, anemia, premature birth, pregnancy in databases, including: Cochrane, Medline, Medlib, Web of Science, Pubmed, Scopus, Springer, Science Direct, Embase, Google scholar, Sid, Irandoc, Iranmedex and Magiran. Relative risk and its confidence interval were extracted from each of the studies. The random effects model was used to combine study results and heterogeneity among the studies measured using I² index. Data analysis was conducted using STATA Ver11.1 and $P < 0.05$ was considered significant.

Results: Seventeen studies with sample sizes of 770555 were entered into the meta-analysis. Maternal anemia in the first trimester increases the risk of premature birth (relative risk, 1.31 [95% CI: 1.15 to 1.51]). But, this relationship was not significant in the second (relative risk, 1.32 [95% CI: 0.44 to 3.25]) and third trimester (relative risk, 1.56 [95% CI: 0.82 to 2.87]).

Conclusion: Maternal anemia during pregnancy can be considered as a risk factor for premature birth.



POSTER

Evaluation of the Cytotoxic Effects of the Melatonin Treated RAW 264.7 on the Erythroleukemia Cell Line K562

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ARTICLE INFO

Keywords:

Childhood leukemia
K562
Melatonin
MTT assays

ABSTRACT

Background: Macrophages comprise the most abundant population of immune cells in the tumor microenvironment that undergo differentiation into functional phenotypes depending on the local tissue environment. Melatonin modulates a wide range of physiological functions with pleiotropic effects on the immune cells like macrophages. However, there is no information about the role of melatonin on the shaping of macrophages in the tumor environment. The purpose of the present study is evaluation of the effects of RAW 264.7 macrophages treated with melatonin on the growth rate of erythroleukemia cell line K562.

Methods: RAW264.7 cells were cultured in the 24-well plates at a density of 6×10^4 cells per well. After culture for 24 h, the cells were treated for 24 h with melatonin at concentrations 0, 50, 75, 100, 150, 200 $\mu\text{mol/L}$. After removal of supernatant, macrophages and K562 were co-cultured in 1:10 ratio. K562 vitality was then determined by MTT assay. Briefly, MTT was added to cultures at a final concentration of 5 mg/mL and the samples were incubated for 4 h at 37°C. After gentle removal of the media, 150 μL DMSO was added to each well to dissolve the formazan product. The absorbance was then measured on a micro-plate reader at a wavelength of 492 nm.

Results: The vitality of K562 cells co-cultured with melatonin treated macrophages was increased at concentrations of 50 and 75 $\mu\text{mol/L}$. Nevertheless, at higher concentrations of melatonin, this process was reversed so that at the highest concentration, there was no significant difference between cytotoxic effects of untreated macrophages and melatonin treated macrophages (200 $\mu\text{mol/L}$) on the proliferation of K562 cells.

Conclusion: These results indicated that treatment of macrophage with melatonin, especially at lower doses (50 and 75 $\mu\text{mol/L}$) could remarkably influence the K562 proliferation.

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POSTER

Hemolytic Disease of Fetus and Newborn (HDFN) and Maternal Antibody Screening

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ARTICLE INFO

Keywords:

HDFN

Maternal antibody screening

Anti- D antibody

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ABSTRACT

Background: Hemolytic disease of fetus and newborn (HDFN) is a highly dangerous condition that is caused by maternal alloantibodies resulted from maternal immune system sensitized by fetal RBC's antigens. These alloantibodies can be formed against Ag-D or other blood group system antigens that cause hemolysis of fetal and newborn's RBCs whether in first or subsequent pregnancies. In severe conditions of HDFN intrauterine transfusion is required. By maternal antibody screening in the first-trimester we can detect the occurrence of the HDFN.

Methods: This review is extracted from surveying in the field of HDFN.

Results: Based on a population-based study in Netherland, positive antibody screening in the first-trimester occurs in about one percent of pregnancies that almost one third of that is related to the alloantibodies other than anti-D that of which around two third has the risk of HDFN occurrence.

Conclusion: Antibody screening in the first-trimester of pregnancy can result in appropriate on time treatment of HDFN caused by alloantibodies like anti-D or others such as anti-K or anti-c, and even rare anti-Jra antibodies.



POSTER

Prevalence of Positive Coombs Test in Icteric Neonates

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ARTICLE INFO

Keywords:

Coombs test
Neonatal Icter
Hemolysis

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ABSTRACT

Background: hyperbilirubinemia and jaundice, including common diseases in newborns. In this context, understanding the factors that cause or aggravate jaundice is of particular importance. One of those entered in the immunological cause hemolysis, which can be positive Coombs test. The test to detect antibodies partially sitting on red blood cells and sensitize them is used. Coombs test to determine the results of diagnostic tests, especially important in the reduction of neonatal jaundice. In this study, the incidence of positive Coombs test conducted in icteric neonates.

Methods: This study was a cross-sectional study on 100 icteric neonates admitted to hospital because of hemolysis Fatemeh and Khatam was conducted in shahrood in 2016. Sample collection method was available. Jaundice was defined based on clinical observation. In infants, to determine the Rh and ABO blood group, blood samples were also examined. Hemoglobin, CBC, maternal and neonatal indirect Coombs test, G6PD, total bilirubin were also explored. The baby's gender, gestational age, birth weight, Apgar score, mode of delivery, birth trauma, pottory hematoma, skin ecchymosis, require resuscitation and infant feeding methods were investigated.

Results: In this study, the incidence of positive Coombs test in icteric neonates admitted due to hemolysis was zero percent. 72 percent of babies had icterus, hemolysis was confirmed by the reticulocyte counts.

Conclusion: Based on the results obtained in this study, coombs test in any icteric neonate admitted for hemolysis would not be positive.



POSTER

The Role of Clinical Hematology Laboratory in Prevention and Diagnosis of Neonatal Anemia

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ARTICLE INFO

Keywords:

Hematology laboratory
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Diagnosis

ABSTRACT

Anemia is a common health problem in neonates and its evaluation is one of the most common problems seen in clinical practice. Based on the symptoms observed in the baby, various diagnoses, from natural neonatal anemia, to the critical pathological cases are suggested. The clinical hematology laboratory plays an important role in identifying, categorizing and determining the causes of the hereditary and acquired neonatal anemia, its treatment and even preventing the occurrence of anemia. Generally, anemia occurs in newborns for three reasons: 1) hemolysis due to blood transfusion incompatibilities (especially ABO and less Rh), deficiency of specific enzymes such as glucose 6-phosphate dehydrogenase (G6PD), pyruvate kinase (PK), as well as infections of infants before birth with toxoplasmosis, rubella, cytomegalovirus, and inherited diseases such as hemoglobinopathies and membrane defects such as spherocytosis. The major role of the hematological laboratory activity is in this section. 2) Hemorrhage that occurs in various clinical contexts and causes anaemia during pregnancy and postpartum which leads to serious consequences for both mother and child. 3) Bone marrow failure, which rarely occurs in the fetus and causes inadequate red blood cell production and anemia. Examples of these diseases are rare genetic disorders, such as Fanconi anemia and Diamond-Blackfan anemia. Some infectious like syphilis and HIV can also lead to this type of anemia by bone marrow suppression. Treatment of the underlying condition depends on whether the blood loss is acute or chronic, the degree of anemia and hypovolemia. A constellation of signs and symptoms with assistance of accurate laboratory clues may lead in arriving at the correct diagnosis. In this systematic review, we summarize recent findings about neonatal anemia and explore new strategies for detecting and preventing anemia in infants, with a focus on laboratory hematology activities.

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POSTER

A Review of Complications of Bone Marrow Transplantation in the Treatment of Wiskott-Aldrich Syndrome

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ARTICLE INFO

Keywords:

Wiskott-Aldrich syndrome
Primary immunodeficiency
Bone marrow transplantation

ABSTRACT

Background: Wiskott-Aldrich syndrome (WAS) is an X-linked recessive combined immunodeficiency characterized by thrombocytopenia with small platelets, eczematoid dermatitis, and recurrent infections caused by immunodeficiency, and an increased incidence of autoimmunity and malignancies. One of the treatments for this disease is bone marrow transplantation (BMT). According to the studies, this treatment method will be associated with complications for the patient that has varied over the years. This study tries to review the studies in this area to report on the side effects of BMT and efficacy of this therapeutic approach in WAS over the years.

Methods: This article is a review of studies on BMT complications in the treatment of WAS from 2002 to 2017 on information databases such as SID, WILEY, CIVILICA, SCIENCE DIRECT, GOOGLE SCHOLAR, PUBMED. Words that were searched included: Wiskott-Aldrich syndrome, immunodeficiency, bone marrow transplantation. Finally, 8 articles were investigated in this period and in direct relation with this subject.

Results: In two studies, WAS who underwent BMT expired. The reason for this was the progressive multifocal leukoencephalopathy which affects the neuronal membrane of the CJ virus, which afflicts the nervous system and ultimately weakens breathing and death. Autoimmune diseases such as thyroiditis, liver toxicity, proteinuria, and hematuria can be mentioned as other complications. One of the most common complications after transplantation was reported to be GVHD for which prophylaxis consisted of cyclosporine, methotrexate and prednisolone.

Conclusion: It has been shown that autoimmune complications and infections develop after BMT in the course of WAS. It has been found that the survival rate after transplant has evolved over the years. So, treatment will be more successful with accurate knowledge of possible complications after bone marrow transplantation and follow up of clinical studies.

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POSTER

Association of Weight Reduction and Neonatal Icter

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ARTICLE INFO

Keywords:

Neonatal jaundice
Icter
Weight loss

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ABSTRACT

Background: Neonatal icter is an important common problem in newborns and determination of contributing factors would decrease the burden of disease. This study was performed to determine the association of weight reduction and neonatal icter.

Methods: In this observational descriptive-analytical cross-sectional study, 245 consecutive neonates admitted to a training hospital in Tehran, Iran in 2016 were selected. The association of weight reduction higher than ten percent in first birth week and the neonatal icter was assessed.

Results: 46 neonates (18.8%) had icter. 30 neonates (12.2%) had weight reduction more than 10%. 11 neonates (36.7%) among those who had weight loss more than 10 percent and 35 neonates (16.3%) among those who had weight loss less than 10 percent had icter that showed significant difference ($P=0.007$).

Conclusion: According to the obtained results and comparison with other studies, it may be concluded that icter and weight reduction are interrelated and so the neonates with weight loss more than ten percent should be evaluated for icter.



POSTER

Anti-Leukemic Effect of Emend on Hematologic Malignant Cell Lines

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ARTICLE INFO

Keywords:

Apoptotic cell death
Emend
Cell survival
Hematologic malignancies
Neurokinin-1 receptor signaling pathway

ABSTRACT

Background: Genotypic and phenotypic studies have recently extended the molecular landscape of hematologic malignancies by identifying the variety of molecular and signaling events which are critical for the sustained proliferation of malignant cells. In the panoply of pathways, contribution of the neurokinin-1 receptor (NK1R)/ substance P (SP) network, which originally involves in myriad of processes related to the central and peripheral nervous system, has reported in a wide assortment of adult and pediatric malignancies. Intrigued by the constant activation of this signaling in leukemia, we aimed to investigate the anti-cancer effects of Emend, a competing non-peptide antagonist of the NK1R, in a panel of hematological cell lines consist of multiple myeloma, pre-B acute lymphoblastic leukemia (ALL), and acute promyelocytic leukemia (APL) cells.

Methods: To explore the cytotoxic and anti-proliferative effects of Emend, each cell line was subjected to the increasing concentrations of the NK1R antagonist and subsequent cell viability, growth kinetics, and metabolic activity were investigated using trypan blue and MTT assays. Next, to ascertain whether Emend-induced anti-leukemic activity could be attributed to the induction of apoptosis, annexin-V staining analysis was performed. The genes expression of anti-apoptotic target genes of Bcl-2 family was further examined by real-time PCR.

Results: We found that abrogation of the NK1R exerts a short-term cytotoxic and anti-proliferative effect against hematologic malignant cells both in a dose-dependent and time-dependent manner. However, the IC50 varied among different cell lines. In addition, our results showed that Emend-induced cytotoxic effect is mediated at least partially by the induction of apoptosis as a result of alteration in the gene expression level.

Conclusion: Overall, due to the pharmacological safety and potent anti-tumor activities of Emend, our study suggests that this inhibitor seems to be a promising agent for the treatment of hematologic malignancies in the near future.

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POSTER

The NK1R Antagonist, Emend, Demonstrates Anti-Leukemic Activity on Pre-B ALL REH Cells through Induction of Apoptotic Cell Death and G1 Cell Cycle Arrest

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ARTICLE INFO

Keywords:

Emend
NK1R antagonist
Pre-B acute lymphoblastic leukemia
REH
Anti leukemic effects

ABSTRACT

Background: There are lots of well known signaling pathways associated with leukemia. The latest investigations in the field of neuroscience demonstrated that substance P (SP) and its receptor, the neurokinin-1 receptor (NK1R) play fundamental role in both initiation and malignant progression of ALL through bifurcating at many points and regulating a considerable number of downstream targets. In this study, we aimed to examine the restrictive potential of well-known NK1R antagonist, Emend, on REH pre-B-ALL cells.

Methods: To evaluate the cytotoxic and anti-proliferative effect of Emend, REH cells were cultured with Emend at different concentrations and cell proliferative rate and metabolic activity were assessed using trypan blue and MTT assays, respectively. In addition, to evaluate whether cytotoxic effect of NK1R inhibitor is attributed to either cell cycle arrest or induction of apoptosis, drug-treated cells were subjected to flowcytometry analysis. Finally, to gain further insights into the anti-survival effects of Emend, we scrutinized the expression of key genes involved in apoptosis.

Results: We found that Emend not only reduced the survival rate of REH cells in both dose- and time-dependent manner, but also restricted the proliferative capacity of leukemic cells, at least partially, through induction of G1 cell cycle arrest. Moreover, the results obtained from Annexin-V staining and RQ-PCR analysis suggest that up-regulated Bax/Bcl-2 molecular ratio and subsequent induction of apoptotic cell death may contribute to the cytotoxic effect of Emend in this cell line.

Conclusion: Overall, due to the pharmacologic safety of Emend and its potent anti-leukemic effects, our study suggests that this antagonist could be considered as a promising agent for the treatment of acute lymphoblastic leukemia.

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POSTER

Investigating the Relationship Between Breastfeeding with Childhood Leukemia in Sistan and Baluchestan Province

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ARTICLE INFO

Keywords:

Childhood leukemia
Breastfeeding
Sistan and Baluchestan

ABSTRACT

Background: Leukemia is the most common childhood cancer, accounting for about 35.8% of all cancers in this period. The incidence of this cancer in children due to unknown causes is one of the major health problems in developed and developing countries. This study was conducted to determine the factors associated with leukemia in children of Sistan and Baluchestan province.

Methods: This study was performed on 120 children under the age of 18 years old with leukemia referred to Imam Ali hospital in Zahedan during 2011 - 2016 and 240 children hospitalized in other hospitals of the province due to other diseases that were not related to leukemia. Children were matched in group by age and gender. The variables including age, sex, mother's level of education, family income, breastfeeding, breastfeeding at birth and exclusive breastfeeding were examined. To determine the relationship between variables and the risk of leukemia, odds ratio (OR) with 95% confidence intervals through logistic regression was analyzed using SPSS-16 through logistic regression which was analyzed using SPSS-18 software and Chi-square test.

Results: Of 120 children with leukemia, (57.5%) were male and (42.5%) were female. The results of this study showed that breast feeding as a protective factor in children with leukemia was significantly different in case group (94.2%) and control group (97.9%). (OR=0/28, CI=%95 :0/08-0/95). In such a way that odds of morbidity in children were not fed with breastfeeding is 72% higher than that of breastfeeding children. Although the risk of leukemia in infants who were not fed with breastfeeding at birth was higher than infants who were breastfed, they were not statistically significant ($P>0/05$). Exclusive breastfeeding and maternal education were not statistically significant with development of leukemia.

Conclusion: The study found that breastfeeding is one protective factor of morbidity to leukemia and low income family is one of the risk factors for leukemia in children.

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POSTER

Cord Blood Stem Cell Transplantation in the Treatment of Diamond-Blackfan Anemia : A Review

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ARTICLE INFO

Keywords:

Diamond-Blackfan anemia
Cord blood stem cell
Bone marrow transplantation

ABSTRACT

Background: Diamond-Blackfan Anemia (DBA) is a rare congenital anemia which presents in early infancy and is considered as erythroblastopenia of bone marrow. This disease is caused by symptoms like macrocytic anemia (Moderate to severe) and uncommon bone marrow pattern which is erythroid hyperplasia. In these infants, various growth disorders and associated congenital anomalies, especially in head and upper extremities is seen. Treatment of this disease is often by drugs like Steroids. If the patient does not respond to drug therapy, the use of other methods such as Blood transfusion, stem cell transplantation from bone marrow and cord blood stem cell transplantation (CBT) is recommended. Bone marrow transplantation has been successfully employed in the treatment of DBA. However, the procedure causes considerable toxicity including both acute and chronic GVHD.

Methods: This article is a review and descriptive study. This occurs through reviewing the articles published in the database like: pubmed, civilica, irandoc, magiran and sid over the past 15 years By searching words; Diamond-Blackfan anemia, cord blood stem cell. As a result of this search, by examining the disease and the difference between the method of bone marrow transplantation or CBT, we focused our search on CBT.

Results: In the studies reviewed, it is claimed that CBT has a therapeutic effect and recovery in the course of the disease and reduces the risk of acute and chronic GVHD while increasing the risk of infertility in the patient. Also, This method is also used in the treatment of other hematologic diseases, but the patient after the transplantation certainly needed immunization against diseases like Diphtheria, Rubella, BCG and Pertussis. That has been successful and had a positive result. In one of the articles, a case is reported to be complicated by lymphoproliferative disease (LPD) with the origin of the donor. The reason for the malignant growth was Epstein-Barr virus (EBV). Despite the reported complications, using busulfan and cyclophosphamide resulted in successful results.

Conclusion: CBT by drug therapy for DBA reduces the risk of acute and chronic GVHD. Almost no case of GVHD has been reported since CBT; however, this method has its own complications such as infertility and more commonly LPD. while the number of DBA patients treated with CBT is very few to assess the outcome of this method, but the articles claim the probability of a LPD; however, in this method no case of GVHD has been reported compared to the Bone marrow transplantation and this superiority of CBT is related to this method.

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POSTER

Hemolysis in Preterm Infants: A Review Study

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ARTICLE INFO

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Hemolysis
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Hemolytic disorders
Rh incompatibility

ABSTRACT

Background: Hemolysis is contracted into erythrocyte degradation with release of hemoglobin in plasma. If a person does not have an antigen, contact with that antigen causes the immune system to become susceptible and an immune response that can occur in pregnancies where the mother is RH Negative, but the RH positive fetus is responsible for the immune response and fetal death in involved pregnancies. The aim of this study was to investigate hemolysis in primitive neonates and their differences with term neonates.

Methods: This is an overview of studies on hemolysis in infants from 2007 to 2017 in databases such as SCIENCE DIRECT, GOOGLE SCHOLAR, PUBMED. Words that were searched included: Hemolysis, preterm neonates, preterm infants.

Results: Among the articles, the main group of neonatal hemolysis were among those preterm infants who were born to those who had received anti-D treatment recently. Therefore, there is a higher level of IgG anti-D in the blood that causes hemolysis in Rh positive infants. In one of the studies, G6PD deficiency has been shown to cause acute hemolysis in infants.

Discussion: Hemolysis in newborns is often due to congenital conditions including erythrocyte membrane disorders, deficiency of enzymes such as glucose 6-phosphate dehydrogenase, hemoglobin disorders, antibody build-up, drugs and infections. Transmission of Ig G Anti D in a pair of negative RH mother to a Positive RH embryo causes hemolysis of fetal red blood cells and death. The immature age is the protective system of red blood cells against oxidation which can cause hemolytic anemia due to the use of certain drugs or chemicals. According to the studies, hemolysis-induced hepatocellular dysfunction could be followed by peripheral edema, kernicterus, brain disabilities, neuropathy and death.

Conclusion: Given the dangerous side effects of hemolysis, the treatment team advises to consider hemolytic complications in newborns and appropriate interventions should be started quickly.

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POSTER

Umbilical Cord Bleeding - A Presenting Feature for Congenital Afibrinogenemia

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ABSTRACT

Background: Congenital afibrinogenemia is a rare blood disease that occurs due to low levels of fibrinogen.

Case Presentation: A 9-day-old baby, born of consanguineous marriage by cesarean section with birth weight of 2700 grams and gestational age of 39 weeks, was admitted to our hospital with history of bleeding from the umbilical cord of two days' duration. Investigations revealed hemoglobin of 12.1 g/dL, white cell count of 13000/mm³, Platelets of 513000/mm³. Prothrombin time (>120 sec, control 12 sec), Prothrombin time/ INR (>10 sec, control 1 sec), Activated partial thromboplastin time (>180 sec, control 33 sec), thrombin time (>240 sec, control 17 sec) were all abnormally prolonged. Liver and renal function tests were normal. Peripheral blood film did not reveal any evidence of microangiopathy, hemolysis, infection or thrombocytopenia. Factor X level was 73 mg / dL (normal 70-120 mg / dL) and level of factor XIII was abnormal. Absolute fibrinogen level was <10 mg / dL (normal 200-400 mg / dL). The patient was discharged with instructions of avoiding aspirin containing compounds and for the measures to be taken in the future in the event of trauma, injuries or operations. The baby's mother was asked to refer on regular visits for the baby to receive fibrinogen injections on regular intervals.

Conclusion: Afibrinogenemia should be considered as a differential diagnosis in patients with bleeding from any part of the body. In congenital bleeding disorders with bleeding from the umbilicus, afibrinogenemia should be suggested.



POSTER

The Effect of Early Detection of Thalassemia In Childhood on Survival of Patients

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Thalassemia major

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ABSTRACT

Background: Thalassemia is the most common inherited hemoglobinopathy worldwide. Structural defect make RBCs to be rapidly removed in spleen, liver and the bone marrow. Following reduction of lifespan of RBCs, patients need to receive blood transfusion and chelation therapy (DFO injection). Regular blood transfusion causes iron poisoning resulting in cardiac and endocrine complications. It can also affects patient's lifespan. This study aimed to analyze the patients' overall status considering early diagnosis and prevention programs.

Methods: In this descriptive analytical study, we analyzed the most recent medical records of 100 patients referred to the AL Zahra hospital in Isfahan, Iran during year 2016. Demographic and clinical indicators were extracted from the log files and were imported to spss 23 using descriptive statistics method to process the data.

Results: 100 log files were analyzed. Patient age range varied between 5-57 years. The mean age was 26.47 ± 8.3 years. 59% of patients were women and 41% of them were men. 100% of referred patients suffered from thalassemia major. 70% of patients were diagnosed under the age of 1. The rest of the patients were diagnosed sporadically below 8 years of age. 41% of patients were splenectomized.

Conclusion: The age distribution of the thalassemia patients suggested success in preventive strategies and also an increase in patient's life expectancy due to modern treatments. Early diagnosis of thalassemia is a key to health improvement as patients' age in our country has reached over 40 years. Since, most patients are young, they need more blood and chelator to thrive for many years. However, still the most important action to take is to reduce the birth number of patients with Beta thalassemia major.

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POSTER

NOTCH1 Signaling and Related Pathways in Infant T-ALL and Therapeutic Approaches

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T-cell ALL
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ABSTRACT

Background: Infant T-cell acute lymphoblastic leukaemia (T-ALL) is a kind of cancer with increasing T cells in the thymus associated with poor prognosis. Studies have demonstrated that NOTCH1 signaling pathway as a crucial regulator of cell growth could have numerous mutations in T-ALL cells. Aim to: review NOTCH1 and other dependent signaling pathway aberrancies in T-ALL.

Methods: Information have been extracted from NOTCH1 signaling pathways-related reliable articles and deductions were fulfilled.

Results: Notch1 can negatively control PTEN transcription. So, phosphorylation of PTEN (by CK2-mediation) results in PTEN-overexpression in T-ALL cases. Functional PTEN inactivation cooperates to hyperactivation of PI3K/Akt pathway. Gain-of-function mutations in NOTCH1 in T-cell lymphoblastic leukemias (T-ALL) can make it a target for γ -secretase inhibitors.

Conclusion: Although iT-ALL prognosis have been improved due to multiagent therapeutic protocols, chemotherapy resistance indicates very poor survival in patients. Initial activation of AKT lead to resistance to NOTCH1 inhibition. Regardless of PTEN, hyperactivation of AKT can be resulted from a variety of molecules such as PI3K, AKT, MYC, IL7R and IGF1R. AKT inhibitors could be considered a promising therapeutic procedure for T-cell ALL in addition to current protocols. furthermore, PI3K and/or CK2 inhibition promotes death in T-ALL cells not normal T cell precursors. However, the therapeutic beneficial of combined PI3K/AKT and NOTCH1 antagonists in human cancer have been shown, targeting these mechanisms simultaneously can open new avenues for neonatal T-ALL treatment.



POSTER

Maternal Anemia After Delivery: Prevalence and Risk Factors

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ARTICLE INFO

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Postpartum
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Blood loss
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ABSTRACT

The purpose of this study was to assess the prevalence of postpartum anemia and determine the clinical risk factors for this condition to provide a viable alternative to postpartum hemoglobin measurement. In total, 415 patients, who underwent postpartum hemoglobin measurement were included and risk factors for Hb level <10 g/dl were determined. We found that 29% of the mothers were anemic, and birth canal lacerations, caesarean delivery, and episiotomy were identified as the main risk factors for this condition. When we examined the performance of each risk factor alone in the prediction of postpartum anemia, none of them achieved a sensitivity of 30%. Selective screening of women who had any of these five risk factors resulted in 23% of cases remaining unidentified. Despite the high incidence and disease burden of this condition, management of puerperal anemia is not standardized and this condition is not easy to predict. Universal screening should be considered in high-prevalence settings. World Health Organization (WHO) describes the postnatal period as the most critical and yet most neglected phase in the lives of mothers and infants. It is a common knowledge that a woman's adjustment to life with her new infant is very difficult. This period, known as the puerperium, often involves poor sleep quality, pain and fatigue, if not other major complications. In this context, we must face the challenge of increasing breastfeeding rates, which is why health care providers should be aware of the medical and psychological needs of the new mother. This work reports that postpartum anemia, a potentially preventable or treatable condition that can make it more difficult to resume everyday activities, is highly prevalent. It remains to be seen whether ensuring the appropriate diagnosis and treatment of anemia after delivery will result in improvements in the physical and psychological well-being of obstetric patients.

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POSTER

Toxoplasmosis of Central Nervous System in Relapsed Hodgkin's Lymphoma: A Case Report

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ABSTRACT

Patients with immunosuppression have an increased incidence of toxoplasmosis characterized by involvement of the central nervous system. Only a few cases of toxoplasmosis associated with immunosuppressive agents have been reported. Such cases have been reported in immunosuppressed patients outside the Iran, but a search of the literature has not revealed any previous reports from Iran. We describe a 17-year-old male, a known case of Hodgkin's lymphoma with the diagnosis of central nervous system (CNS) toxoplasmosis. As a conclusion, CNS toxoplasmosis should be considered in the differential diagnosis of immunosuppressed patients who present with neurological manifestations.



POSTER

Osteoporosis in Severe Congenital Neutropenia: Sequel of Long-Term Treatment with G-CSF

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ARTICLE INFO

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ABSTRACT

Background: Severe congenital neutropenia (SCN) or Kostmann syndrome is a hematologic disorder characterized by maturational arrest of myelopoiesis at the level of promyelocyte or myelocyte. This arrest results in severe neutropenia leading to absolute neutrophil counts below $0.5 \times 10^9/L$ associated with recurrent bacterial infections and risk of leukemic transformation from early infancy. Patients with SCN require lifelong recombinant human granulocyte colony-stimulating factor (G-CSF) therapy. This study was aimed to ascertain the long-term outcomes of G-CSF therapy in patients with SCN.

Methods: This study was a review conducted on Pubmed, Scopus, Web of Science and Google Scholar databases using keywords: neutropenia, severe congenital neutropenia, G-CSF and osteoporosis in english articles from 2000 to 2017. A total of 16 papers were reviewed.

Results: G-CSF has substantially improved the life expectancy for patients with severe congenital neutropenia. The use of G-CSF has extended the life expectancy for these patients from 2-3 years to adulthood. Osteoporosis within the context of SCN and G-CSF treatment was first described by Zeidler at 1993, who reported radiologic signs of osteoporosis in 38% of patients. The mechanism of bone loss in SCN is unclear. SCN is characterized by enhanced production of phagocytic mononuclear cells with increased numbers of circulating macrophages and osteoclasts that are the principal bone resorbing cells. In addition, under the influence of G-CSF, neutrophils produce cytokines, including IL-1 which strongly stimulates osteoclast-mediated bone resorption. Many other factors could contribute to the process, including reduction in exercise, malnutrition, chronic illness with repeated episodes of infection and the effects of steroid therapy. These patients are also at increased risk of MDS and/or AML, but again it is not clear if this is due to G-CSF or the underlying disease.

Conclusion: We conclude that G-CSF speeds the recovery of the ANC and given the morbidity and mortality associated with this syndrome, is highly recommended. Severe osteoporosis and also increased risk of MDS or AML, reported in this population may be related to the disease process itself or be a therapeutic side effect due to long term use of G-CSF. Thus close follow-up of this condition is essential.

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