#### In the name of the only pain healer

ركم Procedural pain management in pediatric cancer patients
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# Approaches to Procedural Comfort management

- Developing an individualized plan for procedural comfort can enhance both psychosocial (e.g., coping, increased understanding of hospital procedures) and physical (e.g., walking, returning to regular diet, decreased opioid requirement) patient outcomes.
- Nonpharmacologic and/or pharmacologic interventions based on the patient's unique characteristics, care setting, procedure being performed, and skill of the HCP performing the procedure.
- Individuals prescribing and administering pharmacologic agents must be knowledgeable about the onset, duration, and mechanism of action for these agents and be skilled in managing adverse effects and complications should they occur.

# Cancer treatments - There are a variety of treatments for cancer and some of them are less than pleasant. Some examples of treatment-related pain include:

i) Chemotherapy produces numerous side effects that cause pain like mucositis, peripheral neuropathy, constipation, diarrhea, nausea, vomiting and abdominal cramps. ii)

Radiotherapy also similarly produces pain due to mucositis, peripheral neuropathy, burning sensations etc. iii)

Surgical treatments apart from producing acute post-operative pain, it can also produce long term post amputation phantom limb pain, stump pain, post-mastectomy pain etc.

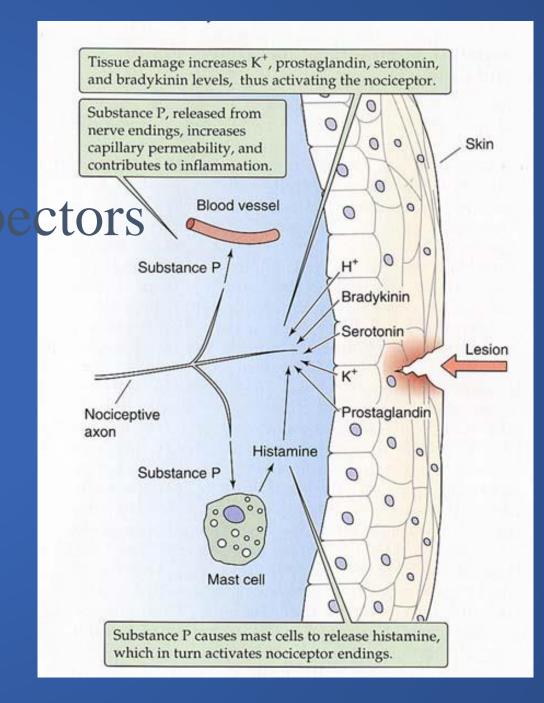
#### Adequate Stimulation

- -Temperature
- -Mechanical damage
- -Chemicals (released from damaged tissue)

Bradykinin, serotonin, histamine, K<sup>+</sup>, acids, acetylcholine, and proteolytic enzymes can excite the chemical type of pain.

Prostaglandins and substance P enhance the sensitivity of pain endings but do not directly excite them.

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# Non-pharmacologic intervention

- relaxation techniques, meditation, imagery, massage, thermal measures, positioning, play activities, and music
- Additional interventions specifically for neonates include administration of oral sucrose, nonnutritive sucking, swaddling, facilitated tucking, skin-to-skin contact, breastfeeding, and reduction of external stimuli

# Pharmacologic Interventions

- The cornerstone of procedural pain and comfort management.
- Local anesthetics, nonsteroidal antiinlammatory drugs (NSAIDs), acetaminophen, opioids, anxiolytics, and sedatives.
- Some particularly invasive and painful procedures may benefit from the use of regional (e.g., peripheral nerve block) or general anesthesia.
- Several factors should be considered when selecting appropriate pharmacologic agents for patients undergoing procedures, including the type and length of the procedure, how much pain is associated with the procedure, the setting in which the procedure will be performed, age of the patient, accessibility to pharmacologic agents and techniques, and availability of skilled personnel to administer and monitor the effects of the selected pharmacologic interventions)

### Local anesthetics

- are the most commonly used agents for dermal procedure pain management.
- They are injected S.C or I.D or Topically(Spray, Cream, Patch).
- Regional anesthetic techniques for more invasive painful procedures.
- Topical anesthetics: for needle stick procedures (particularly in infants and children.
- A drawback of topical preparations is that they all have an extended application time because they must transverse the skin barrier to reach the site of action.
- Application time varies from 30 to 120 minutes depending on the fformulation and depth of anesthesia desired.
- Injectable bacteriostatic saline or lidocaine using a small-gauge needle (e.g., \$27) has been shown to be particularly effective for intravenous catheter insertion, suturing, biopsies, and other needlestick procedures.

### Local Anesthetics

- Needleless of 1% buffered lidocaine using the J-Tip (National Medical Products, Irvine, CA) to provide greater anesthesia than a 30-minutes application of topical lidocaine, based on the self-report of children aged 8-15 years undergoing peripheral intravenous catheter insertion.
- Such findings, if able to be generalized, offer an advantage to other options by eliminating the 30-minute wait time required for topical administration and the subcutaneous needle stick required for injectable anesthetics.
- Regardless of the local anesthetic formulation or technique of administration, care should be taken to allow the anesthetic to take effect before beginning the procedure.

# Non-opioid Analgesics

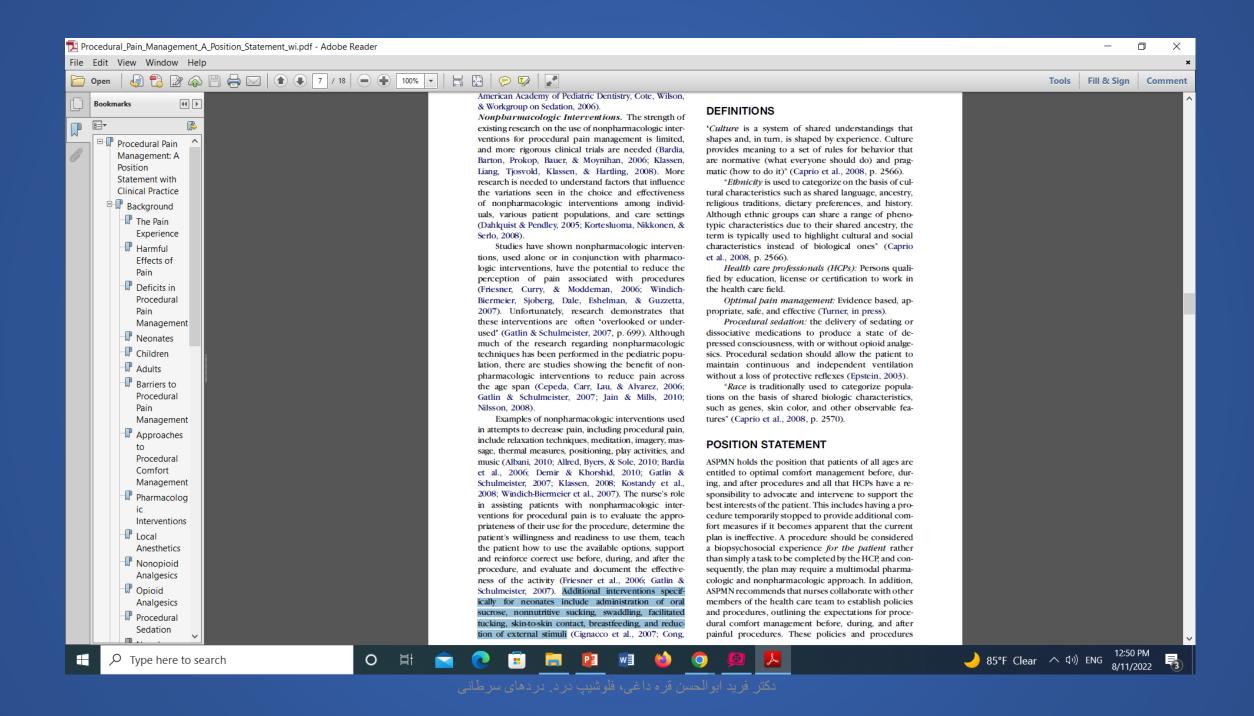
- Acetaminophen, and NSAIDs, can be very beneficial when given in preparation for a procedure or for postprocedural pain.
- Acetaminophen alone may be effective for mild pain, and some NSAIDs (e.g., ketorolac or ibuprofen)alone may be effective alone for moderate pain.
- Both acetaminophen and an NSAID may be given together with other pharmacologic agents such as opioids, anxiolytics, and sedatives.

# Opioid Analgesics.

- Indicated when procedural pain is expected to be of a moderate to severe intensity.
- Opioids are available in a variety of fast-acting formulations, which can be used for short, painful procedures.
- The most commonly used are fentanyl, hydromorphone, and morphine, administered in titrated doses usually by the intravenous route for rapid analgesia.
- You have to differentiate: between Procedural Sedation and Analgesia. .

### Procedural Sedation

- Is used most often when procedures are expected to cause moderate to severe pain or to require extended periods of immobilization or the patient expresses great concern or distress at the thought of being awake during the procedure.
- Procedural sedation provides two benefits, sedation and amnesia; it does not provide analgesia.
- For some procedures, a mild anxiolytic before a procedure may induce amnesia and increase cooperativeness and willingness to undergo a similar procedure in the future, but an anxiolytic alone provides no reduction in pain.
- · Likewise, sedatives do not relieve pain and should only be used in
- conjunction with an analgesic when pain is expected to be moderate to severe.
- Procedural sedation must be performed only by HCPs experienced and knowledgeable with this technique and airway management



• Potentially painful procedures can range from "simple" procedures, such as venipunctures or dressing changes, to more invasive procedures, such as lumbar punctures, fracture reductions, or biopsies, and can occur in a variety of settings, urethral catheterization, drainage tube ,....

### POSITION STATEMENT

- Goal: Optimal comfort management before, during, and after procedures
- procedure should be considered a biopsychosocial, pathophysioanatomical, cultural, spiritual,... experience for the patient and her/him relatives, rather than simply a task to be completed by the HCP, and consequently, the plan may require a multimodal pharmacologic and nonpharmacologic approach.
- This position statement refers to "comfort management" as incorporating the management of pain, anxiety, and any other discomforts that may occur with procedures.

### **Ethical Consideration**

- Pain relief has been declared a basic human right by the World Health Organization (Green et al., 2006)
- And "the unreasonable failure to treat pain is viewed as an unethical breach of human rights" (Brennen et al., 2007, p. 217).
- Several ethical principles apply to procedural pain management, including beneficence, nonmaleficence, justice, autonomy, fidelity, dignity, and veracity (Brown & Bennett, 2010).

### Before the Procedure

- Establish a plan for managing patient comfort if the procedure is likely to produce pain or anxiety.
- Select appropriate pharmacologic and nonpharmacologic interventions.
- Establish a mutually agreed upon comfort goal with the patient and family if indicated (e.g., young children, cognitively impaired).
- Develop a plan to help the patient cope during the procedure (e.g., distraction, breathing, relaxation)

# Consider procedural sedation if:

- i. The procedure is believed to be significantly painful.
- ii. Immobility of the patient is required for a longer period of time.
- iii. The patient expresses great concern or distress at the thought of being awake during the procedure.
- e. If procedural sedation is in the best interest of the patient but cannot be administered in the current setting, consider transfer to an alternate location where the administration procedural sedation is possible.

### Prepare:

- Patient and family: i. Provide education tailored to meet the patient and family needs (e.g., discussion, written materials, videos, etc.).
- ii. Acknowledge patient's fears/concerns and modify the comfort management plan accordingly.
- iii. A family member should be allowed to remain with the patient during procedures (if possible)
- when the patient believes this would be helpful (American Association of Critical Care Nurses, 2004).
- (1) Provide coaching to family members regarding their role.
- (2) If a family member is to be present, their role is to support the patient, not participate in or interfere with the procedure.
- (3) The family member should be allowed to step away if needed.

# Timing and location of procedure:

- i. Negotiate the time and location of the procedure with patient/family.
- ii. Consider the following in choosing the location:
- (1) Adequate space.
- (2) Maximum privacy.
- (3) Adjustable lighting.
- (4) Minimal noise and interruptions.
- (5) Accessibility to pharmacologic agents.
- (6) Availability of supplies for nonpharmacologic techniques.
- (7) Selection of music for relaxation if appropriate.

### Agree upon optimal patient position.

- c. Prepare relaxation, distraction, and coping techniques based on patient preference, capabilities, and experience.
- d. Decide how the patient will communicate unrelieved pain or anxiety to the nurse during the procedure

# Discuss the need for any premedication with the health care team:

- Analgesic if pain is anticipated.
- ii. Topical anesthetics if indicated.
- iii. Anxiolytic if anxiety is present/anticipated.
- iv. Sedation if patient is required to be immobilized for long periods of time or if significant pain is expected.
- v. Appropriate monitoring devices as needed.
- Provide maximum safe treatment for pain and anxiety during the first procedure to minimize the development of anticipatory anxiety before subsequent procedures.
- Ensure that medications are ordered, available, and administered to allow sufficient time for effectiveness before the procedure.

# During the Procedure

Use agreed-upon distraction/coping techniques.

- 2. Assess pain and anxiety (if patient is awake).
- 3. If pain and/or anxiety are not well controlled during the procedure, ask the HCP performing the procedure to stop so that further evaluation can be conducted and the need for additional support (pharmacologic and/ or nonpharmacologic) determined.
- a. Be ready to use all pharmacologic and/ or nonpharmacologic intervention.

# During the Procedure

- Multiple people trying to lead, confusion.
- iv. Patient who is moaning, crying, or striking out.
- v. An upset family member.
- vi. A feeling the need to "get it over with" instead of calmly performing the procedure.
- 4. Remember to remain calm and confident, do not rush. Respectfully remind others to do the same as needed.
- 5. Provide verbal coaching in a calm reassuring manner.
- a. Evaluate if other interventions (pharmacologic or nonpharmacologic) are required before continuing.
- 6. Monitor family member and staff behavior and provide feedback to ensure that the environment remains safe and relaxed for the patient.
- 7. Use supplies known to minimize tissue trauma as appropriate

### After the Procedure

Discuss/evaluate the procedure with patient and family if applicable.

- 2. Document the procedure, including an evaluation of the patient's experience, from the patient, family, and HCP perspectives including recommendations for future procedures in the medical record.
- 3. Develop and implement a comfort management plan for after the procedure, because the pain resulting from the procedure itself may not subside when the procedure is completed and must be treated appropriately.
- a. Multimodal (pharmacologic including opioids and adjuvants, and non pharmacologic) treatment may be indicated.
- b. The comfort plan should include care in the event the patient is no longer in the health care setting (i.e., home) after the procedure.

#### APPENDIX C: PROCEDURAL PAIN MANAGEMENT CHECKLIST

#### Before the Procedure Establish a plan for managing patient comfort if the procedure is likely to produce pain and/or anxiety: ——1. Select appropriate pharmacologic and nonpharmacologic interventions. ----2. Establish a mutually agreed-on comfort goal with the patient, and family if indicated (e.g., young children, cognitively impaired). ----3. Develop a plan to help the patient cope during the procedure (e.g., distraction, breathing, relaxation). 4. Consider procedural sedation if: ----a. The procedure is believed to be significantly painful. ——b. Immobility of the patient is required for a longer period of time. ----c. The patient expresses great concern or distress at the thought of being awake during the procedure. If procedural sedation is in the best interest of the patient but cannot be administered in the current setting, consider transfer to an alternate location. Prepare patient and family: ----1. Provide education tailored to meet the patient and family needs (e.g., discussion, written materials, videos, etc.). ———2. Acknowledge patient's fears/concerns and modify the comfort management plan accordingly. ----3. Provide coaching to family member(s) regarding their role if they stay with the patient. If a family member is to be present, their role is to support the patient, not to participate in or interfere with the procedure, and they should be allowed to step away if needed. ——4. Negotiate the time and location of the procedure with patient/family and HCPs. ——5. Agree-on optimal patient position. ——6. Prepare relaxation, distraction, and coping techniques based on patient preference, capabilities, and experience. ----7. Decide how the patient will communicate unrelieved pain or anxiety to the HCP during the procedure. ——8. Discuss the need for any premedication with the health care team. ----9. Ensure that medications are ordered, available, and administered to allow sufficient time for medication to be effective before the procedure. Prepare the health care team: ——1. Know the procedure specifics. ——2. Gather appropriate supplies and equipment. ——3. Know if additional support staff are needed and their role. ----4. Identify someone who will lead the distraction and coping techniques so the patient is not confused or overstimulated (if multiple staff present). During the procedure: ——1. Use agreed-on distraction/coping techniques. ——2. Assess pain and anxiety (if patient is awake). ---3. If pain and/or anxiety are not well controlled during the procedure, ask the HCP performing the procedure to stop so that further evaluation can be conducted and the need for additional support (pharmacologic and/or nonpharmacologic) determined. 4. Provide verbal coaching in a calm reassuring manner. ----5. Monitor family member and staff behavior, and provide feedback to ensure the environment remains safe and relaxed for the patient. After the procedure: ——1. Discuss/evaluate the procedure with patient and family if applicable. ----2. Document the procedure, including an evaluation of the patient's experience, from the patient, family, and HCP perspectives including recommendations for future procedures in the medical record. ---3. Develop and implement a comfort management plan for after the procedure as the pain resulting from the procedure itself may not subside when the procedure is completed and must be treated appropriately.

Chemotherapeutic agent	toxicity	Impact on pain
Vinca alkaloids (vincristin, vinblastin)	neurologic	Peripheral neuropathy ( glove and stocking distribution), autonomic neuropathy (abdominal pain, constipation, paralytic ileus, urinary retention, and arthostatic hypotention)
Paclitaxel / Docetaxel	Bone marrow depression, neurologic	Neutropenia, mucositis ( painful mouth ulcerations), peripheral neuropathy

Platinum complexes ( cisplatin, carboplatin)	Renal, Bone marrow depression, neurologic	Decrease creatinine clearance, peripheral neuropathy (cisplatine)
Etoposide	Bone marrow depression	Leukopenia , thrombocytopenia , mucositis ( high dose )
Nitrogen mustards Mechlorethamine,chlora mbucil,cyclophosphami de,ifosphamide)	Bone marrow depression	Leukopenia , thrombocytopenia , hemorrhagic cysitis(cyclophosphamid e )

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Nitrogen mustards Mechlorethamine,chlora mbucil,cyclophosphami de,ifosphamide)	Bone marrow depression	Leukopenia , thrombocytopenia , hemorrhagic cysitis(cyclophosphamid e )

Methotrexate	Bone marrow supression, neurologic marrow supperssion, renal	Pancytopenia, Mucositis (early indicator of toxicity),chronic renal failure
bleomycin	Pulmonary	Mucositis ( dose – related ) , lung fibrosis

#### **Baseline assessment: ANALGESIA MONITORING GUIDLINE**

Obtain RR, HR, BP,O2 saturation, sedation score, and pain score before administering a single or intermittent dose or initiating continuous infusion

Intermittent intravenous administration

RR, HR, BP, and sedation score every 5 min x 4, then every 30 min x 2, and then as per child's condition/ preexisting orders pain score every 20-30 min Continuously monitor O2 saturation only for children whose underlying condition predisposes them to respiratory depression

#### Continuous IV infution / PCA

RR , HR , BP , pain score , and sedation score every 1 h x 4 , then RR and sedation score every 1 h , and then HR , BP , and pain score every 4 h  $\,$ 

Continuously monitor O2 saturation and document reading every 1 h

#### Intermittent epidural administration

 $\rm RR$  ,  $\rm HR$  , and  $\rm BP$  every 5 min for the first 20 min following a bolus dose , and then  $\rm RR$  and sedation score every 1 h

HR, BP, pain score, and motor block score every 4 h

Continuously monitor only for children whose underlying condition predisposes them to respiratory deprssion

#### Continuous epidural infusion<sup>a,b</sup>

RR, HR, BP, sedation score, and pain score

#### TABLE 21-14 Acetaminophen Drug Combinations

Combination acetaminophen	Brand Name	Strength (mg )	Dose by pill PRN (max#/d)	Usual use	comments
+aspirin+caffeine	Excedrin extra-Strength Excedrin migraine	250+250+65	1q12-24hr(2)	Tention headaches, migraine attacks	In Canada, no aspirin OTC
+butalbital+caffeine Above w codeine	Fioricet Fioricet with codeine	325+50+40 325+50+40+30	1q4hrpRN(6) 1-2q4hr(6)	Tention headaches, pain following minor procedures/surgeries	
+caffeine +dihydrocodeine	panlorDC panlorSS	356.4+30+16 712.8+60+32	1-2q4hr(10) 1q4hr(5)	Moderate to moderately severe pain	Good for postoperative and breakthrough pain
+codeine	Tylenol#2 Tylenol#3 Tylenol#4	300+15 300+30 300+60	1-2q4hr(6)	Moderate to moderately severe pain	Good for postoperative and breakthrough pain Available in liquid .2.5mg codeine Per ml
+dichloraphenazone +isometheptene	Midrin	325+100+65	1q 1hr(12)	Migraine attacks	Lost popularity with evolvement of Triptans
+hydrocodone	Lorcet, Lortab  Maxidone Nocro Vicodine Zydone	500+2.5,500+5,500+7.5 500+10,650+7.5,650+10 750+10 325+5,325+7.5 500+5,660+10,750+7.5 400+(5/7.5/10)	1-2q4hr(6)	Moderate to moderately severe pain	Good for postoperative and breakthrough pain Available in liquid.0.5mg hydrocodone per ml Most popular item of diversion in the US
+oxycodone	Endocet Percocet Roxicet Tylox	325+(5/7.5/10),650+10 325+(2.5/5/7.5),650+10 325+5,500+5 500+5	1-2q6hr(8-10)	Moderate to moderately severe pain	Good for postoperative and breakthrough pain Available in liquid.1mg oxycodone per ml.second-most popular item of diversion in the US
+pentazonic	Talacen	650/25	1q4hr(6)	Moderate pain	Good for postoperative and breakthrough pain
+propoxyphen	Wygesic Darvocet	650+65 325+50,325+100,650+100	1q4hr(6)	Mild to moderate pain Mild pain	Good for postoperative and breakthrough pain
+tramadol	Ultracet	<b>325+37.5</b> رشیپ در د. در دهای سرطانی	1-2q4-6hr(8) والحسن قره داغي، فلو	Acute pain دکتر فرید اب	Good for postoperative and breakthrough pain Available in liquid

TABLE 26-3Acquition Costs of Long-Term Opioid Therapy: Comparison of Average Wholesale Prices in the United States

Drug	Dose b	Schedule	AWP per dose (\$us)	AWP per day (\$us)
Mild-to-moderate pain				
Short-acting oral preparations Codeine Dextropropoxyphene Hydrocodone(+paracetamol,acetaminophen) Oxycodone (+acetaminophen)	60 mg	q4h	0.80	4.80
	100 mg	q4h	0.33	1.98
	10 mg	q4h	0.53	3.18
	10 mg	q4h	0.52	3.12
Moderate to severe pain				
Short-acting oral preparations Oxycodone, immediate release Morphine, immediate release Hydromorphone Levorphanol	20 mg	q4h	0.32	1.86
	30 mg	q4h	0.31	1.86
	8 mg	q4h	1.22	7.32
	4 mg	q4h	0.87	3.48
Transmucosal preparation Oral Transmucosal fentanyl cirate	200 μg	q6h	6.95	27.80
	400 μg	q6h	8.93	35.72
	600 μg	q6h	10.91	43.64
	800 μg	q6h	12.90	51.60
	1200 μg	q6h	16.87	67.48
	1600 μg	q6h	20.83	83.32
Long-acting oral preparations Oxycodone, controlled release Morphine, controlled release(MS Contin) Morphine, controlled release (kadian) Methadone	60 mg	q12h	6.60	13.20
	90 mg	q12h	5.58	11.16
	150 mg	q24h	9.63	9.63
	5 mg	q8h	0.09	0.27
Transdermal preparations Transdermal fentanyl	25 μg 50 μg 75 μg 100 μg	q72h q72h q72h q72h q72h	12.33 20.37 32.63 40.65	4.11 6.79 10.88 13.55

AWP, average wholesale price; qxh, every Xhours.a AWP ware averaged for all suppliers using the 2001 edition of RedBook™ for Windows version 4.0(Medical Economic Data,Mntvale,NJ,USA). Costs to patients are variable and approximately 10%-20% above AWPs for outpatients and 50%-200% above AWPs for inpatients.Costs to pharmacies are based on product volume discounts and can be considerable less than AWP. b Doses are not intended to be equianalgesic. c Mean AWP for available products multiplied by the number of doses required in a 24-hr period. From Komick CA.Benefic-risk assessment of transdermal fentanyl for the treatment for cancer pain. Drug Safetly 26:969,2003.

Туре	Description	Risk and Associated Considerations	Infusion Type	Use Duration
Percutaneous catheter	Intrathecal or epidural insertion	Infection, Epidural fibrosis, encapsulation	Bolus	Acute postoperative pain, drug trials, inability to undergo invasive procedures
Tunneled catheter	Intrathecal or epidural	Less infection risk	Bolus or continuous	Anticipated use for weeks to months
Implanted reservoir	Surgical implantation, precutaneus filling. Costly	Less infection or catheter failure risk than percutaneous or tunneled catheters	Bolus or continuous	Anticipated use for months to years
Implanted mechanical delivery system	Surgical implantation, precutaneous access. Patient-activated dose titration	Not FDA approved	Bolus	Anticipated use for months to years
Implanted drug delivery pump	Continuous delivery; periodic pump refills	Dose change requires pump refill with different concentrations	continuous	Anticipated use for months to years
Programmable implanted delivery pump	Allows dose Programming without solution exchange	Most costly	continuous with bolus capability	Anticipated use for months to years

TABLE 38-1 Potentialy Useful Agents in the Management of procedural related visceral Pain

Kappa opiod agonist	Peripheral kappa receptor agonists on visceral afferents reduces substance P and calcitonin gene-related peptide
Mu and delta opioids	Central mu and delta receptors reduces primary nociceptors actually and central hypersensitivity through periaqueductal grey
Nonsteroidal anti-inflammatory drugs	Block spinal cord and peripheral prostaglandin and central hypersensitivity
Ketamine, methadone	Block dorsal horn NMDA receptors
Corticosteroids	Block expression of spinal cord nitric oxide synthase and reduces hypersensitivity
Gabapentin	Reduces central glutamate levels and NMDA binding for hypersensitivity
Alpha-2-adrenoreceptor agonists (clonidine )	Facilitate descending inhibitory tracks through periaqueductal grey
Tricyclic antidepressants	Facilitate descending track inhibitory tracks in periaqueductal grey
Anticholinergics	Reduce colic and reduce intenstinal secretion
Somatostatin	Inhibits vasointestinal peptide and decreases colic and intestinal secretion. Reduces central hypersensitivity.
NMDA,N-methyl-D-aspartate.	

FIGURE 42-2 options for helping children cope with pain and preventing modification of personality structure and behavior.

How to help children better cpe with pain and prevent modification of personality structure and behavior

**Pharmacologic interventions** 

Sedation/analgesia

- 1. Topical (skin, mucossa)
- 2. Inhalational
- 3. intravenous

Nonpharmacologic interventions (not to be used in children less than 3-7 yr, nor in severaly developmentally delayed)

**Cognitive-behavioral therapy** 

- 1. Breathing exercises
- 2. Psychological preparations
- 3. Relaxation
- 4. Distraction(i.e., hypnosis)
- 5 .imagery
- 6. Positive reinforcement

**Both techniques** 

#### Orally Administered NSAIDs

Name of Drug	Pediatric Dose (<60kg)	MaximumDose /kg/Day	adultDose (>60kg)	Maximum Dose / Day
Acetaminophe n	10-15 mg/kg q4-6hrsPO	75mg	500-1000 mg q4-6hrs PO	4000mg
Naproxen	5-10 mg/kg q12hrsPO	20mg	250-375 mg q12hrs PO	1000mg
Iboprofen	5-10 mg/kg q8-12hrsPO	40mg	400-600 mg q6hrs PO	3200mg
Choline magnesium trisalicylate	10-15 mg/kg q8-12hrsPO	Information not available	1000-1500 mg q12hrs PO	3000mg
Ketorolac	0.5 mg/kg q6hrsIV	Give no more than 5 days	15-30 mg q8hrs IV	Give no more than 5 days
NSAIDs, nonsteroidal anti-inflammatory drugs:PO.per os .				

Nonopioid Drugs of Pain Relief in Children

Drug	Dosage	Comments
Acetaminophen	10-15mg/kg PO , every4-6h Dose limit of 65 mg/kg/day or 4 g/day, whichever is less	Lacks gastrointestinal and hematologic side effects;lacks anti- inflammatory effects(may mask infection-associated fever)
Ibuprofen دهای سرطانی	5-10 mg/kgPO,every 6-8 h Dose limit of 40 mg/kg/day;max dose of 2400mg/day دكتر فريد ابوالحسن قره داغي، فلوشيپ درد. در	Anti-inflammatory activity. Use with caution in patients with hepatic or renal impairment, compromised cardiac function or hypertension (may cause fluid retention, edema), history of GL bleeding or ulcers, may inhibit platelet aggregation
Naproxen	10-20mg/kg/dayPO,divided every 12 h Dose limite of 1 g/day	Anti-inflammatory activity. Use with caution and monitor closely in patients with impaired renal function. Avoid in patients with severe renal impairment
Diclofenac	1mg/kg PO, every 8-12h Dose limit of 50 mg/dose	Anti-inflammatory activity. Similar GL renal and hepatic precautions as noted above for ibuprofen and naproxen

Note: increasing the dose of nonopioids beyond the recommended therapeutic level produces a ceiling effect (i.e.,there is no additional analgesia but there are major increases in toxicity and side effects). PO,per os; GL,gastrointestinal. From McGrath PA,BrownSC:Paediatric palliative medicine: pain control. In Doyle D,Hanks GWC,Chemy NI, Calman K(eds): Oxford Textbook of palliative Medicine, 3<sup>rd</sup> ed. Oxford, Oxford University press,2004, p 781, with permission.

#### Thank you so much for your attention