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Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

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Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Thalassemic patients have ineffective erythropoiesis and accelerated red blood cell turnover owing to the short life span of red blood cell, which results in increased body demand of nutrients to maintain normal erythropoiesis.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- There are controversial issues in terms of folic acid supplementation for patients with thalassemia in protocols because it is supposed that regular blood transfusions prevent bone marrow hyperfunctioning.

- β-thalassemia major patients with undertransfused condition may need more folic acid as they continue to have ineffective erythropoiesis.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Patients with thalassemia who are on low transfusion regimens have increased consumption and may develop a relative folate deficiency.
- Supplements (1 mg/day) may be given if this occurs.

- Patients on high transfusion regimens rarely develop this condition, and usually have no need for Supplements.

- TIF, 2ND Revised edition, 2008:152

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Patients on high transfusion regimes rarely develop folate deficiency, in contrast to those on low transfusion regimens.
- In view of the fact that many patients with thalassaemia major are transfused at low haemoglobin levels (and their folate status is unknown, as well as possible benefits from folic acid supplementation in reducing risks of thrombosis related to homocystein levels and atherosclerosis (Qin 2012), the possibility of providing folic acid supplements at up to 1mg/day to all patients may be considered.

- TIF, 3RD edition, 2014, 228-229

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

Effect of folic acid supplementation on the progression of carotid intima-media thickness: A meta-analysis of randomized controlled trials

X. Qin et al. / Atherosclerosis 222 (2012) 307–313

We conducted a meta-analysis to assess whether folic acid supplementation reduces the progression of atherosclerosis as measured by carotid intima-media thickness(CIMT).

Our findings indicate that folic acid supplementation is effective in reducing the progression of CIMT, particularly in subjects with CKD or high CVD risk and among trials with higher baseline CIMT levels or a larger homocysteine reduction.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

Folates are compounds consisting of a pteroyl group conjugated with one or more glutamic acid units.

Folic acid, or pteroylglutamic acid, is an oxidized folate consisting of pteroic acid conjugated with a single glutamate residue.

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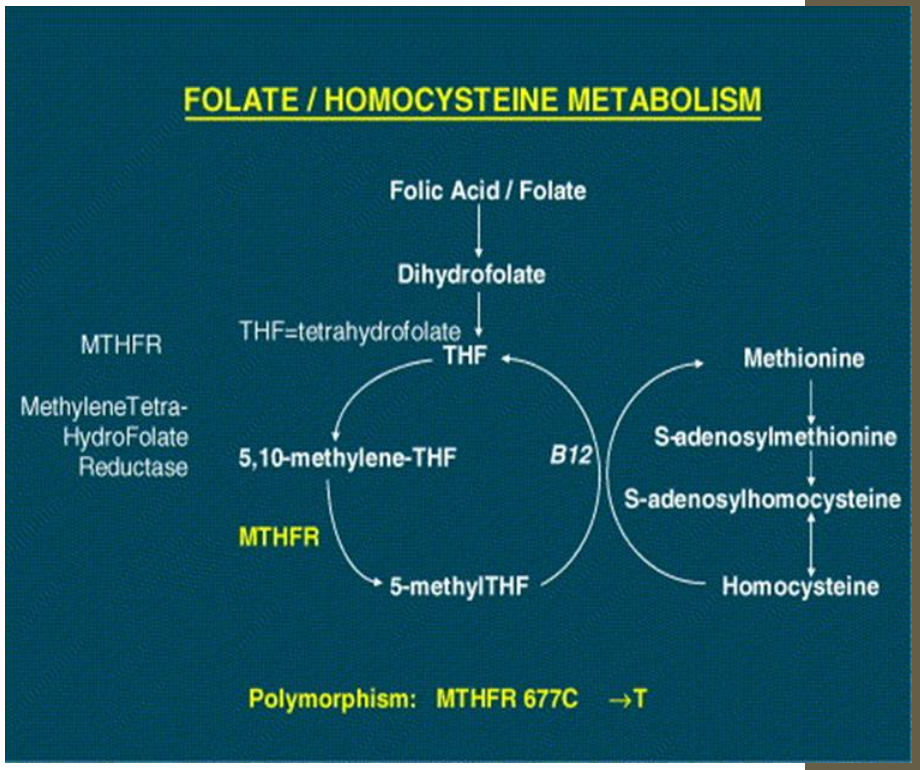
Biologically active folates are derived from folic acid by reduction of its pterin ring to form dihydrofolate (DHF) and tetrahydrofolate (THF).

Intracellular folates exist primarily as one-carbon group substituted tetrahydrofolate polyglutamates.



Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

Hyperhomocysteinemia is a well-defined factor for artherosclerosis.

Many observational studies showed an association between elevated tHcy and cardiovascular disease

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Patienta and Methods

This study was a before-after controlled clinical trial conducted in 17th Shahrivar Hospital, Rasht, North of Iran,during May to October, 2016

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Study Population

The patients enrolled in this study had thalassemia major on regular blood transfusion and were older than 2 years of age.

They had at least a 6-month history of folic acid supplement consumption before enrolment in the study(1 mg/daily).

We also excluded pregnant patients or lactation patients

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- Sample Size
- We used the following formula for sampling and calculated 40 patients for enrollment:
- α = 0.05
- Power = 0.95
- P1 = 0.20
- P2 = 0.05
- z for 95 % confidenc interval
- z1- α/2=1.96
- n¼

$$n = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 (P_1(1-P_1) + P_2(1-P_2))}{(P_1 - P_2)^2}.$$

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Measurement

Before patients stopped their consumption of folic acid, 10 mL of fasting blood sample was obtained from each of them.

CBC, serum folic acid, and serum Hcy were measured.

Folic acid and Hcy measurement were performed using the chemiluminescence method

We asked patients to stop the folic acid consumption for 1 month and then, we again repeated the tests for patients

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TABLE 1. Baseline Characteristics of Beta Thalassemia Major Patients

Variables		Minimum	Maximum
Age ($M \pm SD$) (y)	21.39 ± 11.17	3	40
BMI ($M \pm SD$) (kg/m^2)	21.38 ± 3.32	10.94	29.3
Duration of transfusion ($M \pm SD$) (y)	18.30 ± 7.63	3	38
Duration of folic acid consumption ($M \pm SD$) (y)	11.82 ± 6.64	2	30

BMI indicates body mass index; *M*, mean.

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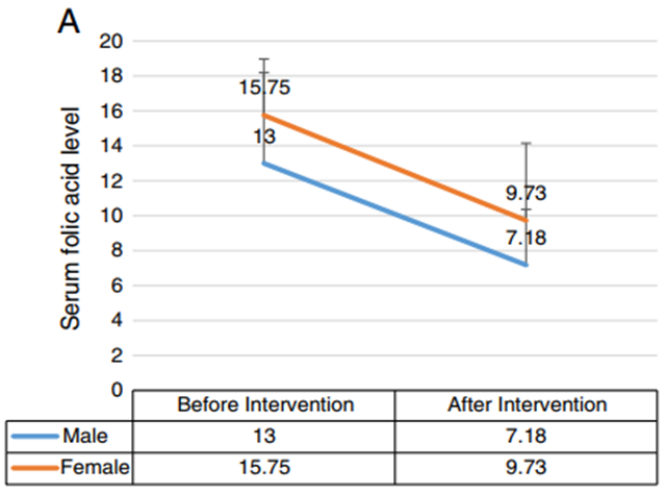

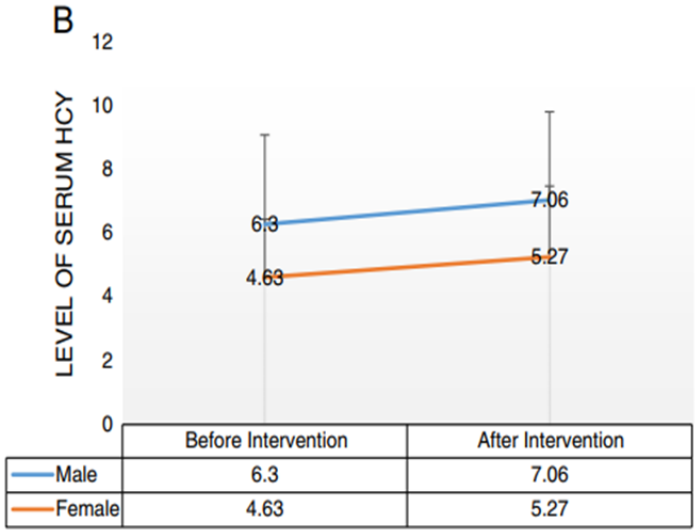

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TABLE 2. Changes in Serum Folic Acid and Homocysteine Before and After the Intervention in Beta Thalassemia Major Patients

Variables	Time	Mean	SD	*t*	*P*
Serum Hcy	Before	5.24	2.35	2.79	0.008
	After	5.93	2.56	—	—
Serum folic acid	Before	14.74	4.2	10.58	0.0001
	After	8.8	4.16	—	—

Hcy indicates homocysteine.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Results showed a statistically significant difference between the level of serum folic acid before and after intervention and showed the need for folic acid supplementation in their treatment regimen.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- The effect of folic acid supplementation in beta-thalassemia major: A randomized placebo-controled clinical trial
- Mehrnoush Kosaryan , Archives of Iranian Medicine, 2006:

- They found that folic acid deficiency was present in 29 – 68% of subjects

- They recommend prophylactic and routine folic acid supplementation for all patients with β-thalassemia major and intermedia.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Behavior of blood folate in children with thalassemia major under transfusion therapy and in thalassemia trait
- Castagna PC et al, Acta Vitaminologica et Enzymologica, 01 Jan 1984

- The folic acid plasma level in 12 out of 13 children with thalassemia major was lower than 3 ng/ml.
- Therefore the necessity of folic acid treatment in thalassemic children with a low blood transfusional has been recommended.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Serum Folate Levels in Major Beta Thalassemia Patients
- Bibi Shahin Shamsian et al,Iran J Pediatr; Vol 18 (Suppl 1), Dec 2008

- They conducted a cross sectional study performed on 100 β major
- thalassemia patients receiving regular blood transfusion.
- Serum folate level is determined with Electrochemiluminescence method. Normal serum folate level was 3-17.5 ng/ml.
- Serum folate level was in the range of 1-19 ng/ml and median of 9 (± 4.9) ng/ml.
- Serum folate was less than 3 ng/ml in 3% of evaluated patients.

- It seems that if major β thalassemia patients receive regular blood transfusion, their serum folate level would be in normal range and supplementation therapy with folate will not be necessary.

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- Folate deficiency is also linked to the increased incidence of arterial and venous thromboembolic events because of hyperhomocysteinemia, a well-known inducer of hypercoagulability states.

- Hcy is an amino acid that plays an important role in atherosclerosis.
- Increase of this amino acid can lead to injury in endothelium, platelet activation, low density lipoprotein cholesterol oxidation, increase in von Willebrand factor, and smooth muscle proliferation

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- In this study, there was a significant difference before and after the intervention in the Hcy level and it increased from 5.24 ± 2.35 to 5.93 ± 2.56.
- The results also showed that the decrease in serum folic acid in women was higher than that in men.
- In addition, there was a significant difference in the Hcy level after the intervention in women, but not in men.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- We found that, in all age groups, there was a significant decrease in the serum folic acid level.
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- However, Hcy was increased significantly in patients older than 20 years of age before and after the intervention.

Assessment of serum folic acid and homocysteine in thalassemia major patients before and after folic acid cessation

- Patients on high transfusion regimens, which suppress endogenous erythropoiesis in thalassaemia major, rarely develop folate deficiency, in contrast to those on low transfusion regimens.

- In view of the fact that many patients with thalassaemia major are transfused at low haemoglobin levels as well as possible benefits from folic acid supplementation in reducing risks of thrombosis related to homocysteine levels and atherosclerosis (Baghersalimi et al., 2018; Qin et al., 2012), the possibility of providing folic acid supplements at 1-5 mg/day especially to patients on low transfusions, should be
- considered.
- This is especially so since we now have an ageing thalassaemia
- population more prone to thrombotic complications and atherosclerosis (Farmakis et al., 2020).

- TIF, 4RD edition, 2021, 233


photo : Mohammad Ranjbar