Curr Pediatr Res 2012; 16 (2): 153-155 ISSN 0971-9032
Scientific Publishers of India

Iron stores and menstruation in healthy adolescent girls – pilot study.

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Abstract

Tissue iron stores are commonly assessed by measuring serum ferritin. Adolescent girls are more prone to develop iron deficiency due to menstrual blood loss. Menstruation is an inflammatory process and we hypothesized that serum ferritin levels may be elevated during menstruation as it is an acute phase protein and hence serum ferritin measurement alone may not be truly reflective of iron status in menstruating girls. The present study was conducted to compare Iron stores in healthy adolescent girls who have attained menarche with age matched healthy adolescent girls who have not attained menarche. Consecutive healthy adolescent girls who have attained menarche and with no illness in the preceding one month were enrolled as cases and consecutive healthy age matched adolescent girls who had not attained menarche served as controls. Hemoglobin, serum Iron and Ferritin were measured in both groups and compared. Serum ferritin levels were significantly high in girls who had attained menarche compared to girls who have not attained menarche (37.2 vs. 8.61 p value 0.0373). There was no significant difference in the hemoglobin and serum iron levels between the two groups. Serum ferritin levels are elevated in healthy menstruating adolescent girls and care should be exercised in relying on ferritin alone for determination of iron status in these girls.

Keywords: Adolescent girls, Serum ferritin, Menstruation, Inflammation, Iron status

Accepted March 04 2012

Introduction

Anemia is a highly prevalent disease in developing countries. Anemia is common during adolescence due to demands of increased growth and menstrual blood loss. Studies have shown that iron deficiency exists in both clinical as well as subclinical forms in adolescent girls [1, 2]. In adolescent girls, the onset of menstruation can alter the iron status of an individual not only by creating a demand for more iron due to blood loss but also due to the pro-inflammatory nature of menstrual cycle itself. The fact that menstrual cycle is pro- inflammatory in nature has been supported by literature [3] and markers of inflammation like CRP are found to be elevated during menstruation supporting this hypothesis [4]. Serum ferritin is widely used as a surrogate marker of storage iron. Serum ferritin can be elevated in acute infections or inflammatory states as it is an acute phase reactant like CRP. Some authors have advocated having a higher cut-off level for diagnosing iron deficiency in areas of high infection transmission [5]. In menstruating adolescent girls, serum ferritin levels can be elevated due to acute phase response. In this study we attempt to find out whether serum ferritin levels are elevated in menstruating adolescent girls compared to non menstruating healthy adolescent girls and explore the relationship between iron status and menstruation.

Material and methods

Consecutive healthy post menarchial adolescent girls between 10 and 12 yrs attending the pediatric OPD accompanying a sick child or relative were enrolled in the study as cases and an equal number of pre menarchial healthy adolescent females of same age served as control. An informed consent was taken and the study was approved by the institute ethics committee of our hospital. Children with history of medication use, use of nutrient supplements, history of any acute illness or injury in the preceding 1 month or any chronic ailment were excluded from the study. Eighteen girls were found eligible for the study and they were divided into two groups consisting of nine pre and nine post menarchial girls. Hemoglobin (Hb), serum iron levels and serum ferritin were measured in both groups. Hb was estimated using BC5200 auto analyzer. Serum Iron levels were estimated by Ferrozine

method using Kit available from CREST BIOSYSTEMS, GOA. Serum ferritin levels were measured by electro-chemi-luminescence method using Elecsys ferritin assay (REF 03737551), Roche Diagnostics GmbH. The results were compared in the two groups and results tabulated and analyzed using Graphpad Quickcalcs t test calculator.

Results

A total of 18 girls in the age group of 10-12 years were enrolled for the study out of which 9 girls had attained menarche. The mean Hb, serum ferritin and Iron levels are given in table 1. The mean Hb in the postmenarchial group was 11.67(SD 0.828) gm/dl. The mean serum ferritin and serum iron levels were 37.2 (SD 34.01) ng/ml and 99.98(SD 63.17) ug/dl respectively. The mean Hb of pre menarchial girls was 11.7(SD 0.935) gm/dl. The mean serum ferritin and iron levels were 8.61 (SD 2.31) ng/ml and 68.97 (SD 28.37) ug/dl respectively. The age and Hb in both groups were comparable. The difference in serum ferritin between the two groups were statistically significant [p value 0.0373 (95% CI 2.16 to 55.01]). There were no statistical difference in Hb [p value 0.9479 (95%CI -1.173 to1.107)] and serum iron levels [p value 0.2807 (95%CI -30.798 to 92.820)] between the groups.

***Table 1**. Comparison of mean serum ferritin, serum iron levels and Hb concentration between the two groups.*

Variables	Post menarchial	Premenarchial	P value*
S.ferritin levels (ng/ml)	37.2 (sd 34.01) ng/ml	8.61 (sd 2.31) ng/ml	0.0373 (95% CI 2.16 to 55.01)
s.iron (ug/dl)	99.98 (sd 63.17) ug/dl	68.97 (sd 28.37) ug/dl	0.2807 (95% CI -30.798 to 92.820)
Hb (gm/dl)	11.67 (sd 0.828) gm/dl	11.7 (sd 0.935) gm/dl	0.9479 (95% CI -1.173 to 1.107)

** p value by paired t test (two tailed).*

Discussion

The pathophysiology of menstruation has been a subject of debate for several researchers. Some authors have hypothesized that menstruation occurs due to anoxia and resultant cellular degeneration while others believe that tissue inflammation plays an important part [6]. The features of inflammation seen during menstruation include cellular edema and cellular infiltration. Another finding is that decidual cells seen during menstruation have features similar to granulation tissue fibroblasts seen in inflammation [6]. Several chemokines like Interleukin(IL) 8,Monocyte Chemotactic Protein (MCP) 1, MCP 2 and Eotaxin have been found in endometrium during menstruation [3]. Macrophage activation also plays a role in regeneration of endometrium through several factors like TGF α, FGF, PDGF, VEGF, TGF β and inhibin β [7, 8]. Withdrawal of progesterone during menstruation results in increased matrix metalloprotein production (MMP) and activation and release of tissue inhibitors of MMP (TIMP) which cause matrix degradation and massive tissue destruction [9]. In a study by Blum and co authors, C-reactive protein (CRP), an acute phase protein was found to be highest during menstruation; however independent effects of hormone & menses and ovulation have not been studied [10]. From the above discussion it seems reasonable to view menstruation as a pro-inflammatory state.

Ferritin is an indicator of iron stores and also an acute phase protein. Hence ferritin can be elevated during any infection or inflammation. In third world countries, infection contributes significantly to iron deficiency anemia. In such population the utility of ferritin in diagnosing iron deficiency has been a subject of debate forcing world bodies like World Health Organization (WHO) and Centres for Disease Control (CDC) to encourage further research on influence of acute phase proteins and iron deficiency anemia [11]. Since menstruation itself has been shown to be inflammatory in nature, the same level of precaution should be exercised in defining iron deficiency in menstruating females. Unfortunately studies looking at the influence of menstruation on indicators of iron status in healthy adolescent girls are lacking.

In our study, we find Serum ferritin levels to be significantly high in young healthy adolescent girls who have attained menarche compared to those who have not attained menarche for the same age and health status. The decreased iron stores in non menstruating healthy adolescent are a cause for concern as their iron status will become further compromised by blood loss when they attain menarche.

Conclusion

We emphasize that caution should be exercised in relying on serum ferritin alone for determination of iron status in adolescent girls who have started menstruating. Correlation with other biomarkers of inflammation and or using a higher serum ferritin cut-off to diagnose Iron deficiency may be useful during menstruation. Whether serum ferritin levels and serum iron levels influence the onset of menarche needs to be investigated in a well designed cohort study with adequate sample size. In premenarchial adolescent girls prelatent iron deficiency is common and should be treated with iron supplementation.

The nutritional anemia control program should be strenghthened and expanded to include adolescent girls also in its ambit. Iron fortification of common food substances should be undertaken on an urgent basis as majority of children in India are iron deficient.

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