

Effects on Hematopoiesis in Children Suffering from Iron Deficiency Anemia with Vitamin A Supplementation

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ABSTRACT

Objective: To study the effect of the supplementation of vitamin A along with standard dose of iron on hematopoiesis in children with documented iron deficiency anemia.

Design: A hospital based prospective study.

Place and Duration: Carried out for 6 months on children with documented iron deficiency anemia in OPD and indoor patients of the department of paediatric medicine, Medical College Kolkata.

Methods: Thirty children (1-12 years age) presenting with iron deficiency anemia (hemoglobin less than 10g/dl, mean corpuscular volume (MCV) < 75fl, and serum iron < 55 mcg/dl) were studied in two groups of 15 each. Group I was supplemented with iron (ferrous sulphate 3 mg/kg/d) while group II in addition to iron was also supplemented with vitamin A (5000 IU/d). Collected data were expressed as mean +/- SE. Comparison of variables was done by using student t test or chi square test as applicable. $p < 0.0001$ was taken as statistically significant.

Results: Hemoglobin concentration was found significantly

increased after 4 weeks of iron supplementation. Rise in hemoglobin was comparatively more in-group II, as compared to group I, after 4 and 8 weeks.

Conclusions: The result of this study suggests that supplementation of vitamin A improves hematopoiesis.

Key Words: Vitamin A, Hematopoiesis, Anemia.

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Article History:

Received: 26-08-2016, Revised: 17-09-2016, Accepted: 23-09-2016

Access this article online

Website: www.ijmrp.com	Quick Response code 
DOI: 10.21276/ijmrp.2016.2.5.030	

INTRODUCTION

Vitamin A deficiency predominantly produces ocular manifestations, which include metaplasia, Bitot's spots, conjunctival and corneal xerosis, and keratomalacia. Extra ocular manifestations include follicular hyperkeratosis, anorexia and growth retardation (Marcus and Coulston, 1996).¹ Ghatpande et al (2002)² reported that Vitamin A is an important cofactor for normal hematopoiesis though its precise role is difficult to define. Jang et al (2000)³ suggested that iron deficiency inhibits mobilization of Vitamin A stores and may decrease its absorption. Role of VitA in iron deficiency was studied in rats⁴ and role of vitamin A deficiency as a contributing factor to anaemia has also been examined in human.⁵ In a study by Gamble MV et al.⁶ among preschool children in the Republic of the Marshall Islands, it was shown that both iron and vitamin A deficiencies were independent risk factors for anemia, but inflammation was not a significant risk factor for anemia among these preschool children. Hashizum et al.⁷ in his study also concluded that anemia among school-aged children in rural Kazakhstan appears to be related to iron indices and vitamin A status. None of the above studies had demonstrated the effect of vitamin A therapy on iron deficiency

status in children, so it was planned to study the effect of the supplementation of vitamin A along with standard dose of iron on hematopoiesis in children with documented iron deficiency anemia. The study was approved by the ethical committee of medical college and hospital.

MATERIAL AND METHODS

This prospective study was done for one year on the children in the age group 1-12 year who had attended the outpatient department of Medical College and Hospital, Kolkata due to any reasons. All children with clinically suspected anemia were advised to do a complete hemogram before prescribing any forms of therapy. Iron deficiency anemia is evidenced by hemoglobin less than 10g/dl, mean corpuscular volume (MCV) < 75fl, red cell distribution width (RDW) < 10gm/dl, and serum iron < 55 mcg/dl. Thirty children with documented iron deficiency anemia were studied in two groups of 15 each.

The study protocol was approved by our institutional review board and informed written consent was taken from parents of each patient involved. Children having congestive heart failure,

symptoms and signs of vitamin A deficiency, children already on iron therapy in any form, unwilling patients or parents were not included. Group I (the control group) was supplemented with iron as ferrous sulphate, at a dose of 3mg/kg/d, as a single dose for four weeks. Group II (the study group), in addition to iron (as in group I) was also supplemented with vitamin A (5000 IU/d) for four weeks.

Hemoglobin levels were assayed by Cyanmethemoglobin method

before the start and after four weeks of therapy and also after eight weeks. Besides hemoglobin, red cells count, reticulocytes counts, mean corpuscular volume (MCV), serum iron (Higgen, 1981)⁸ were also determined. Collected data were analyzed using statistical package for social sciences (SPSS 11.5) program and expressed as mean +/- SE. Comparison of variables was done by using student t test or chi square test as applicable. $p < 0.0001$ was taken as statistically significant.

Table 1: Hemoglobin percentage

Hemoglobin %	Baseline	End of 4 th wk	End of 8 th wk	P value
Control Group (Iron Only)	9.1	9.73	10.56	0.0001
Study Group (Iron + Vit. A)	8.46	10.09	12.37	<0.0001
P Value	0.0056	0.1594	<0.0001	

Table 2: Total RBC count

RBC count	Baseline	End of 4 th wk	End of 8 th wk	P value
Control group (iron only)	4.07	4.48	4.87	0.0006
Study group (iron + vit. A)	4.08	4.77	5.46	<0.0001
P value	0.97	0.117	0.0004	

Table 3: Serum Iron

Serum Iron	Baseline	End of 4 th wk	End of 8 th wk	P value
Control Group (Iron Only)	52.01	54.42	56.99	<0.0001
Study Group (Iron + Vit. A)	51.08	58.40	63	<0.0001
P Value	0.7186	0.0007	<0.0004	

RESULTS

We included 30 children divided into two groups in our study. The baseline parameters to document iron deficiency anemia were same in both groups and as follows,

Hemoglobin less than 10g/dl, mean corpuscular volume (MCV) < 75fl, and serum iron < 55 mcg/dl.

Group I (the control group) was supplemented with iron as ferrous sulphate, at a dose of 3mg/kg/d, as a single dose for four weeks. Group II (the study group), in addition to iron (as in group I) was also supplemented with vitamin A (5000 IU/d). After 4th and 8th week the same baseline parameters are repeated. (Table 1, Table 2 and Table 3)

Results of the present study demonstrate that hemoglobin concentration is significantly increased after 4 weeks of supplementation of iron in children. Mean hemoglobin concentrations after 4 and 8 weeks were significantly higher ($p < 0.001$) in-group II that was supplemented with iron and vitamin A, (10.09 and 12.37 g/dl, respectively) as compared to group I that was supplemented with iron alone (9.73 and 10.56 g/dl respectively).

DISCUSSION

Numerous studies using humans have supported the notion that vitamin A has an impact on iron status and, in turn, iron-deficiency anemia, both in human⁹ and in animal like rats.¹⁰ Early research suggested that people deficient in vitamin A were prone to anemia that was reversed when sufficient doses of vitamin A were taken. A study by Mohanram M et al showed that apart from deficiency of iron, vitamin A deficiency may also have a contributory role in the development of anemia in children.¹¹

Another study by Wieringa FT et al. showed that due to redistribution of retinol after iron supplementation, which might

induce vitamin A deficiency, iron supplementation in infants should be accompanied by measures to improve vitamin A status.¹²

Many studies in humans have been performed in countries where nutritional anemia and vitamin A deficiency are major public health problems.¹³ One study focused on pregnant women in Indonesia who were anemic due to nutritional status, which the authors reported to affect 50-70% of all pregnant women in that country.¹⁴ In another study the relationships between biochemical indicators of vitamin A and iron status and the intestinal helminthes *Ascaris lumbricoides* and hookworm in primary school children in Bangladesh was explored.¹⁵

Another study of this type focused on children in Guatemala, with four groups of children receiving either vitamin A or iron or vitamin A and iron or placebo for two months. Various hematological measures were taken, and the results supported an effect of vitamin A on iron status. The major finding in this study was that vitamin A raised the level of serum iron in anemic children, which, according to the authors, could lead to greater hematopoiesis and thus recovery from anemia. Also, the increase in serum iron is maximal when both vitamin A and iron are administered, with either alone resulting in an increase of lesser magnitude.¹⁶

In a comparable cross-sectional study with children in north-east Thailand, serum retinol was positively associated with haematocrit and serum iron. An association was found between serum retinol and serum transferrin or serum ferritin, but none between serum retinol and haemoglobin.¹⁷ In a study in Ethiopian children, however, a significant correlation was found between serum retinol levels and haemoglobin.¹⁸

While these authors imply that nutritional-deficiency anemia might be best treated using both vitamin A and iron, their conclusions are not drawn directly from the hemoglobin data, since there was no significant difference between the iron group and the vitamin A

and iron group in many studies. Perhaps the observed changes in hemoglobin concentration represent physiological maximums, and the iron available for hematopoiesis, as indicated by serum iron, is greatest when both vitamin A and iron are supplemented in one's diet, even though it may not be used immediately for hematopoiesis.

Suharno et al (1993) demonstrated that there exists a correlation between vitamin A status and hemoglobin level.¹⁴ In a study by Zimmerman et al, it was concluded that in children deficient in vitamin A and iron, vitamin A supplementation mobilizes iron from existing store to support increased erythropoiesis, an effect likely mediated by increase in circulating erythropoietin.¹⁹ Furthermore, addition of retinyl palmitate to iron fortified maize-bread has been reported to enhance the absorption of iron (Davidson et al, 2003).²⁰ Comparatively more rise in hemoglobin with the supplementation of iron along with vitamin A also supports the interaction between iron and vitamin A metabolism even in the present study.

CONCLUSION

Results of our study showed that supplementation of vitamin A along with standard iron therapy are beneficial in terms of long term outcome in children with documented iron deficiency anemia. Since iron and vitamin A deficiencies are common nutritional problems in this part of the world, it is suggested that both the nutrients should be given simultaneously to overcome the problem of microcytic hypochromic anemia, even if the symptoms and signs of vitamin A deficiency are not apparent.

ACKNOWLEDGEMENTS

We would like to thank Dr. Eshita Bhowmik and Dr. Sunil Kr Hembram of the Department of Pediatric Medicine, Medical College & Hospital, Kolkata, 88, college street, kolkata-700041, India.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

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Cite this article as: Arnab Biswas, Isita Tripathy, Kaberi Basu. Effects on Hematopoiesis in Children Suffering from Iron Deficiency Anemia with Vitamin A Supplementation. *Int J Med Res Prof*. 2016; 2(5):149-51.