Single Iron supplementation versus combined Vitamin A and Iron supplementation in treatment of Iron Deficiency Anemia in children less than 5 years visiting tertiary care hospital of Islamabad: A randomized Control Trial

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ABSTRACT

Objective: To compare Vitamin A supplementation along with iron supplementation and iron supplementation alone in treatment of iron deficiency anemia in terms of mean Hb improvement in children less than 5 year.
Study Design: Randomized Controlled Trial
Place and Duration: Department of Pediatrics, Pakistan Institute of Medical Sciences Hospital, Islamabad from 1st July 2016 to 31st December 2016.
Methodology: Total of 80 diagnosed cases of iron deficiency anemia patients were enrolled with 40 in each group. Patients were randomly assigned into group-A (iron and Vitamin A supplementation) and group-B (iron supplementation only) by using simple random sampling. A baseline venous sample of 5ml was taken to obtain patient's Hb, MCV, MCHC, Ferritin and Iron. Follow-up blood samples were obtained of patients in both groups for Hemoglobin level after two months.
Results: Both groups were comparable for age and gender and baseline Hemoglobin levels which were 8.9 ± 0.36 in Group A and 8.8 ±0.38 in Group B (iron supplementation only). There was significant improvement in hemoglobin level in group A compared with group B, mean hemoglobin 11.9 ± 0.99 in Group A and 9.6±1.03 in Group B respectfully, p-value was 0.00.
Conclusion: Addition of Vitamin A along with iron supplementations significantly improve hemoglobin levels in iron deficiency anemia patient in pediatric age group less than 5 years.
Keywords: Children, Hemoglobin, Iron deficiency anemia, Management, Vitamin A, Iron supplementation

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INTRODUCTION

Iron deficiency is important nutritional problem primarily affecting preschool children. WHO estimates prevalence of anemia to be 40-60% in developing countries half of which attributable by iron deficiency.[1] Anemia affects 43% of children under five years globally. In Pakistan reported prevalence of IDA in children under five years is 40-70%[2]. In India prevalence of anemia is nearly 60% in children under five years age[3].

Iron and Vitamin A deficiencies are amongst most prevalent micronutrient deficiencies globally affecting particularly young children[4]. Global prevalence of Vitamin A deficiency is estimated to be 33%. Insufficient dietary intake of Vitamin A and presence of infectious process are predominant causes of vitamin A deficiency. Vitamin A can affect several stages of iron metabolism including erythropoiesis and release of iron from ferritin stores[5].

Iron deficiency anemia is a recognized public health problem that impacts adversely on childhood mortality, morbidity and cognition[2]. It increases the risk of behavioral problems and developmental delays in young children[6]. Several factors account for the high prevalence of IDA in Pakistan including poverty, malnutrition, illiteracy, inadequate and lack of policy and legislation[2]. Iron deficiency anemia is highest in cost of treatment after tuberculosis throughout the world[7,8].

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The rationale of this study is to gather evidence based data in our local population to determine the role of Vitamin A supplementation along with iron supplementation in treatment of iron deficiency anemia so that it will help us in developing our own recommendations compatible with international standards for better management of this health problem. We conducted this study with an objective to compare Vitamin A supplementation along with iron supplementation and iron supplementation alone in treatment of iron deficiency anemia in terms of mean Hb improvement in children less than 5 year.

METHODOLOGY

This Randomized controlled trial was carried out from 1st July 2016 to 31st December 2016 at Pediatric OPD Shaheed Zulfiqar Ali Bhutto University, PIMS Children Hospital, Islamabad. Simple random sampling technique was used[8]. All children of age 1 to 5 years, who were recently diagnosed to have iron deficiency anemia were included in the study. Children who were severely anemic i.e. Hb <7g/dl, already on iron supplements, malnourished, having thalassemia trait, malabsorption syndrome, active infection or have been treated with drugs that interfere with iron absorption were excluded from the study.
Patients were assigned into Group A (iron supplementation and Vitamin A) and Group B (iron supplementation only). Sample size was calculated by using WHO sample size calculator with the assumptions of study power 80%, level of significance 5% population mean= 17.5±1.0 g/dL, Test value of population mean = 22.1±1 g/dL, probable S.D=1[9]. A total of 80 cases were enrolled in the study, 40 in each study group. A venous sample of 5ml was taken to obtain patient's Hb, MCV, MCHC, Ferritin and Iron. All tests were sent to hospital laboratory and verified by pathologist. Vitamin A was given in the form of vitamin A drops with daily dose of 2,666 IU (one drop) for a period of 3 months. Oral iron preparation which contains elemental iron (50mg = 5ml) with dose (5mg/kg/day) was administered for a period of 3 months. Group B received only iron preparation. Contact numbers were taken for follow up and it was done after 2 months. Blood samples were obtained for Hemoglobin. All the data was recorded on Performa attached.

Data Analysis: SPSS version 20 was used to analyze the data. The Mean and S.D was collected for continuous variables like age, Haemoglobin at baseline, 2 months and mean change, MCV, MCHC, Iron and Ferritin. Frequency and percentage was calculated for categorical variables like gender. Student t-test was applied to compare mean Hemoglobin change between two groups P-value less than 0.05 was considered statistically significant.

RESULTS

A Total of 80 diagnosed cases of iron deficiency anemia were enrolled in study 40 in each group. Demographic data like age and gender distribution of the patients involving the two groups showed that there were increased number of children aged 1-3 year in Group-B i.e. 82.5% while 67.5% was found in Group-A & vice versa noted in the age group 4-5 year i.e. 32.5% in Group-A and 17.5% in Group-B, however this distribution did not had an effect on Hb level and mean change in Hb. Group-A included 57.5% male and 42.5% female while Group-B included 55% male and 45% female children. Mean Hb, MCV, MCHC, Iron and Ferritin levels were recorded at baseline as shown in Table-I.

Table-I: Mean Hb at baseline, MCV, MCHC, Iron and ferritin levels (N=80)

At baseline, Hb MCV, MCHC, iron and Ferritin levels	Group A (n=40)		Group B (n=40)		P-value
	Mean	SD	Mean	SD	
Hb (g/dl)	8.9	0.36	8.8	0.38	0.76
MCV (fl)	63.25	1.25	62.9	1.57	0.27
MCHC(pg/l)	18.75	0.98	17.90	1.05	0.00
Iron (µg/dL)	54.70	2.04	56.65	1.25	0.00
Ferritin µg/dL	8.15	1.17	7.97	1.07	0.48

This study showed baseline Haemoglobin levels to be 8.9 ± 0.36 in Group A and 8.8 ± 0.38 in Group B, p value 0.76. Ferritin level was 8.15 ± 1.17 in Group A and 7.97 ± 1.07 in Group B, p-value 0.48. Mean change in Hb levels was recorded after treatment for two months as shown in Table-II. The hemoglobin after two months treatment was 11.9 ± 0.99 in Group A and 9.6 ± 1.03 in Group B, p value was 0.00.

Table-II: Mean Hb and mean change Hb level after 2 months of treatment (N= 80)

Blood parameters	Intervention group N=40	Reference group N=40	Mean difference 95% confidence interval	T test	P-value
Hb	11.925±.997	9.60± 1.032	2.325 1.873-----2.776	10.243 df 78	.000

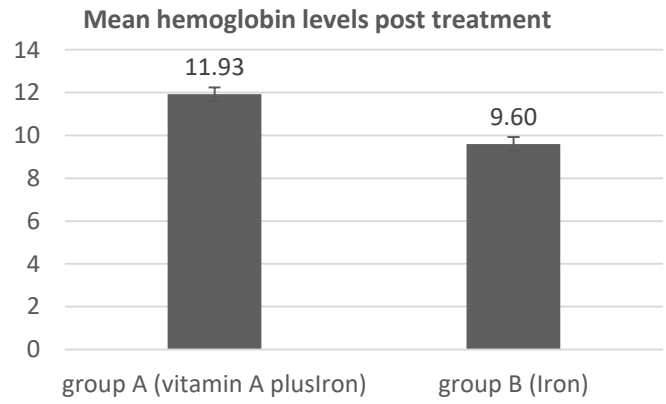

Figure-1: post treatment error bar chart along with 95% confidence interval showing mean difference in blood Hb levels between two study groups (N=60)

DISCUSSION

In summary, our study concluded that Vitamin A supplementation along with iron supplementation is significantly better in treatment of iron deficiency anemia in terms of mean Hemoglobin change when compared to iron alone. Baseline Hemoglobin levels was higher (8.9 ± 0.36 in

intervention group) as compared to control group (8.8 ± 0.38) with p value 0.76. Ferritin level was also found significantly higher (8.15 ± 1.17, p value 0.48) as in interventional group. Mean change in Hb level was recorded after treatment for two months i.e. 11.9 ± 0.99 in interventional group as compared to 9.6 ±1.03 in control group (p value was 0.00).

Literature search shows that a study conducted on anemic school children aged 9 -12 year in Tanzania shows a rise in Hemoglobin levels in 88% of children who supplemented with Vitamin A and iron, were no longer anemic in comparison to only 3% improvement in the placebo group[9]. Patel et al conducted a study on anemic adolescent girls in urban Agra and reported that mean hemoglobin improved from 10.128±0.196 gm/dL to 12.216±0.215 gm/dL among girls receiving vit A supplementation with iron[10]. In another randomized controlled trial by Chen et al from China on pre-school children observed Iron deficiency anemia observed hemoglobin levels are markedly lower in children with iron therapy only as compared with children receiving vit A supplementation (P <0.05)[11]. Our results are comparable to the findings of all above mentioned trials. Different studies from literature by Biswan and colleagues[12], Abizari et al[13] also support our study that vitamin A supplementation improves hematopoiesis.

Regarding addition of supplementation in staple food, the Rahman and colleagues conducted a double-blind cluster (bari) randomized controlled trial on school children of a rural community in Bangladesh to evaluate the impact of consumption of chapatti made of micronutrient-fortified wheat flour with vitamin A on hemoglobin and iron status. They observed that the consumption of fortified chapattis demonstrated a significant improvement in the vitamin A status, but not in iron, hemoglobin or anemia status[14]. Similarly, Chen et al also found out in his study that impact of vitamin A supplementation on iron metabolic homeostasis was mainly on iron storage and there was no direct effect on total body iron content or absorption of iron in intestines[15].

In another randomized, double-blind, controlled study participating in the Integrated Child Development Service (ICDS) by Varma *et al.* over children aged 3–5.5 year who received a non-fortified or a fortified "premix" with VA (500 IU as retinyl acetate), Fe (14 mg as ferrous fumarate), and folic acid (50 µg) added to prepare *khichdi* (rice and lentils mixture), to decrease the prevalence of Fe and VA deficiencies. After a subgroup analysis with anemic children at baseline, Hb concentrations increased significantly in the fortified group compared with the non-fortified group, from weeks 0 to 24 (from 99.9 to 116.9 g/L *vs.* 98.9 to 109.9 g/L, respectively; $p < 0.04$[16].

Gebremedhin et al found consistent results with our study as increase in hemoglobin and decrease in risk of anemia observed among Ethiopian children 6-59 months of age who were given single high dose Vitamin A Supplementation(VAS)[17].

Finally, the results of our study in agreement with other studies justify the hypothesis that "Vitamin A supplementation along with iron supplementation is better than iron alone in treatment of iron deficiency anemia in terms of mean Hb increase".

CONCLUSION

Addition of Vitamin A along with iron supplementations significantly improve hemoglobin levels in iron deficiency anemia patient in pediatric age group less than 5 years.

AUTHOR'S CONTRIBUTION

Ghazi SS: Conceived idea, Designed research methodology, Data collection, Manuscript writing.
Shah M: Designed research methodology, data collection, Literature review, manuscript writing.
Riaz N: Data analysis, Data interpretation, manuscript writing, Statistical analysis, Final approval of manuscript
Hashmi F: Data collection, Data analysis, Manuscript writing
Krishin J: Designed research methodology, Critical review, Final approval of manuscript
Khan A: Data collection, Data analysis, Critical review.

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