COMPARISON OF IRON-SUPPLEMENTATION VERSUS COMBINATION OF VITAMIN-A & IRON-SUPPLEMENTATION IN CHILDHOOD IRON DEFICIENCY ANAEMIA

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Abstract

Background and Objectives: childhood anemia is highly prevalent worldwide and its effective treatment is the cornerstone to improve health of these children. This study was conducted to compare the mean rise in haemoglobin (Hb) after iron-alone versus the combination of vitamin-A & iron supplementation in childhood iron-deficiency anemia.

Methods: This randomized controlled trial was done at Paediatrics Medicine Department, Jinnah Hospital, Lahore from January-2019 to June-2019. A total of 60 cases, as per inclusion criteria were enrolled from the Paediatric Medicine Department of Jinnah Hospital Lahore. Group-A was supplemented with a combination of vitamin-A and iron while Group-B patients were supplemented with Iron alone. Hb was checked at baseline and after 3 months of treatment as per the designated group. All information, as per predesigned proforma, was entered and interpreted using SPSS version 23.0. An Independent sample t-test was applied and a p-value < 0.05 was considered statistically significant.

Results: Sixty patients were included, keeping 30 in each group i.e. Group-A (Vitamin-A + Iron) & Group-B (Iron-alone). In both groups, most of the patients were male, i.e. 22(73.3%) and 23(76.7%) in group-A and group-B respectively. In group-A, the mean age was 1.96±1.6 years while 2.12±1.5 years in group-B. In group-A, the mean rise in Hb level after 3-months of treatment was 3.0±0.99 g/dl, on the other hand, it was 1.96±1.00 g/dl in group B, with a p-value of 0.00014.

Conclusion: Vitamin-A supplementation combined with iron replacement therapy is recommended for substantial improvement among children with iron deficiency anemia.

Keywords: Vitamin-A, Iron-Supplementation, Hemoglobin (Hb), Iron Deficiency Anemia (IDA).

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Childhood anemia is one of the prime global health issues. Iron deficiency anemia (IDA) is the leading cause of nutritional anemia among children.[1] Prematurity, low birth weight, low intake of iron-rich complementary foods, high consumption of cow's-milk, immigrants from endemic areas, and low socioeconomic status are various risk factors associated with childhood IDA.[2] A local study, conducted to assess the burden of iron deficiency anemia among 6 to 59 months, reported anemia among 62.3% of students and 33.2% of the anemic students were iron deficient.[3] That is almost like the prevalence of anemia documented in underdeveloped areas of Bangladesh.[4] As per WHO, pediatric anemia is a prime global health concern while IDA is categorized as a moderate burden. Along with its prime function in hemostasis, iron has a fundamental role in our physical and mental growth.[2,5] Besides anemia,

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iron deficiency can lead to various issues like growth retardation, low IQ, poor school performance, lethargy, restlessness, lethargy, etc.[5,6]

Like iron deficiency, vitamin-A deficiency (VAD) is also a highly prevalent nutritional deficiency. A study conducted in North Benin by Alafoe and his coworker reported the coexistence of VAD and iron deficiency among children with microcytic hypochromic anemia, particularly between 12 to 59 months of age. Apart from iron deficiency, VAD may also have a contributory role in childhood anemia.[7]

Although the direct impact of VAD on anemia or IDA is not much clear; either VAD is an independent risk factor for anemia, or it is just contributing by influencing iron metabolism. However, a study conducted in India also linked the supplementation of vitamin-A and iron together with a better rise in haemoglobin levels among anemic adolescent girls.[8] García-Casal and Layrisse in 1998 proposed a synergistic effect of low-dose vitamin-A/Beta-Carotene by enhancing the absorption of non-heme iron from staple food.[9] Arnab Biswas's study is supporting the advantages of vitamin-A supplementation in IDA regardless of the level of vitamin-A and even in the absence of clinical features suggestive of VAD. They documented the statistically significant impact of combining vitamin-A and iron supplementation as compared to isolated iron supplementation, in terms of mean rise in Hb level after treatment.[10] Another study reported the influence of vitamin-A to improve erythropoiesis in IDA by mobilizing iron from existing body stores.[11]

A meta-analysis conducted to evaluate the impact of vitamin-A supplementation on iron status and IDA among human beings reported 26% reduction in risk of anemia along with a substantial increase in Hb level, regardless of age and stage of life. Although, clinical trials included pediatric and teenage group were not showing a significant effect on the frequency of iron deficiency anemia.[12]

This study was conducted in the Pediatrics department of Jinnah hospital, Lahore to establish the impact of vitamin-A supplementation along with routine iron-supplementation in our pediatric population having iron deficiency anemia.

METHODS

This randomized controlled trial was conducted in the Pediatrics Department of Jinnah Hospital Lahore, Pakistan, for 6-months (January-2019 to June-2019). Approval has been taken from institutional ethical review board (Ref: ERB146/3/18-07-2023/S1 ERB). After Sixty patients were enrolled according to pre-defined inclusion and exclusion criteria and were randomly divided into two comparable groups by adopting the lottery method. Patients of Group-A were treated with Vitamin-A and iron supplementation while that of Group-B were managed with only iron supplementation. Iron supplementation was invariable for all the patients, in the form of ferrous sulfate (5mg/kg/day) while vitamin-A was given only to patients of group-A as a single oral dose of 100,000 IU in children ≤ 1 year of age and 200,000 IU to children aged > 1 year.

The sample size was estimated using the WHO calculator keeping 3-months post-treatment Hb levels as 22.1±1.0 g/l in vitamin-A plus iron and 17.5±1.0 g/l in the iron-alone group.6 We used 80% power of the study and 95% confidence level.

Patients of either gender from 6-months to 5-years of age with recently diagnosed iron deficiency anemia (IDA) were included in the study. Patients diagnosed with any blood disorder other than IDA, requiring blood transfusion, having coexisting chronic illnesses like asthma, diabetes mellitus, any renal or hepatic disorder, congenital malformation, and/or patients already on any mineral/vitamin supplementation were excluded from the study. Recently diagnosed IDA was labeled for the patients diagnosed within a month from the date of enrollment keeping haemoglobin (Hb) level < 11g/dL along with serum ferritin level < 40 ng/dl. Blood samples for Hb level, at baseline and after 3-months of treatment as per the assigned group, and for serum ferritin, only at the time of diagnosis, were taken under aseptic measures and sent to hospital laboratories. Change in Hb was calculated by the rise in Hb level after 3-months of assigned treatment and that at the time of diagnosis.

Data were collected on predesigned proforma after informed consent from the parents/guardians of the patient. Demographic information like age, gender, and baseline haemoglobin (Hb) as well as haemoglobin (Hb) after three months of treatment as per the assigned group, was recorded for all the patients. Change in Hb was taken as a response indicator.

All data were analyzed through SPSS-version-23.0. Mean and standard deviation was calculated for quantitative data as age, duration of anemia, baseline Hb, Hb after 3-months of treatment, and escalation in Hb in both groups. Frequency & percentage was used for qualitative data like gender. Both groups were compared by post-stratification t-test for change in Hb, taking a p-value of <0.05 as significant. Data from both groups were stratified regarding age, gender, duration of anemia, baseline Hb, and change in Hb; to determine the impact of effect modifiers like age, gender, duration of anemia, and baseline Hb.

RESULTS

During the study period out of 82 patients presented with anemia, 60 patients participated in the study as per predefined inclusion & exclusion criteria. They were randomly allocated into two almost alike groups. Group-A patients were treated with vitamin-A along with iron supplementation while group-B patients received only iron supplementation.

In group-A, 73.3% (n=22) were male and 26.7% (n=8) were female, while in group-B, 76.7% (n=23) were male and 23.3% (n=7) were female, with male predominance in both groups. In the study, most of the patients were < 1 year of age i.e. 53.3% (n=32), keeping 56.7% (n=17) and 50% (n=15) in group-A and group-B respectively. The mean age was 1.96 ± 1.6 and 2.12 ± 1.5 years in group-A and group-B correspondingly. In group-A, 16.7% (n=5) and 26.7% (n=8) were belonging to the age group of 1-3 and 3-5 years, respectively while in group-B this ratio was 30.0% (n=9) and 20.0% (n=6) accordingly. Approximately one-third of the patients 35% (n=21) included in the study were having anemia for less than 3-months, with 36.7% (n=11) and 33.3% (n=10) in group-A and group-B respectively. In group-A, 20.0% (n=6) and 43.3% (n=13) had anemia for 3-5 and >5 months respectively on the other hand in group-B, this proportion was 26.7% (n=8) and 40.0% (n=12) correspondingly (Table-1).

The baseline-Hb level was comparable in both the groups i.e. 8.13 ± 0.82 g/dl and 8.07 ± 1.1 g/dl in

Table 1: *Comparison of Demographics (n=60)*

	Group-A (Vitamin A+ Iron)	Group-B (Iron only)	Total
Gender:			
Male	22 (73.3%)	23 (76.7%)	45 (75%)
Female	08 (26.7%)	07 (23.3%)	25 (25%)
Age Group:			
<1year	17 (56.7%)	15 (50%)	32 (53.3%)
1-3 years	05 (16.7%)	09 (30%)	14 (23.3%)
3-5 years	08 (26.7%)	06 (20%)	14 (23.3%)
Mean ± Sd Deviation	1.96 ± 1.6	2.12 ± 1.5	
Duration of anemia:			
< 3 Months	11 (36.7%)	10 (33.3%)	21 (35%)
3-5 Months	06 (20%)	08 (26.7%)	14 (23.3%)
> 6 months	13 (43.3%)	12 (40%)	25 (41.7%)

Table 2: *Comparison of Hb levels (gm/dL) at baseline and after 3 months*

Groups	Hb Levels	Mean Hb ± SD	p-value
Group-A (Vitamin A+ Iron)	Hb levels at baseline	8.13 ± 0.82	0.00001
	Hb levels after 3 months	11.17±0.99	
Group-B (Iron only)	Hb levels at baseline	8.07±1.11	0.00001
	Hb levels after 3 months	10.03±0.67	

Table 3: *Stratification of comparison of mean change in Hb concerning Gender, Age & Duration of anemia*

	Group-A (Vitamin A+ Iron)	Group-B (Iron only)	P value
Gender:			
Male	3.09 ± 0.92	2.13 ± 1.10	0.003
Female	2.88 ± 1.25	1.43 ± 0.53	0.014
Age Group:			
<1year	3.24 ± 1.03	1.80 ± 1.15	0.001
1-3 years	2.60 ± 0.55	2.11 ± 1.05	0.358
3-5 years	2.88 ± 1.13	2.17 ± 0.75	0.209
Duration of anemia:			
< 3 Months	3.09 ± 0.83	1.90 ± 1.29	0.020
3-5 Months	3.00 ± 1.10	2.00 ± 1.07	0.112
> 6 months	3.00 ± 1.15	2.00 ± 0.85	0.023

group-A and group-B respectively. While notable difference among both the groups in terms of mean Hb-level and mean rise in Hb after 3-months of supplementation was documented (Table-2). Mean increase in Hb after 3 months of supplementation was 3.03 ± 1.00 g/dl in group-A while in group-B it was 1.96 ± 1.00 g/dl that is statistically significant with the p-value of 0.00014 (Table-2). Statistically, infants responded better than the children older than one year. Concerning the duration of anemia, results highlight a significant disparity in anemia duration. Anemia for less than 6 months and more than 12 months has significant impact on outcome, while no substantial effect in 6 to 12 months categories. When considering gender, there was no notable distinction observed. (Table-3).

DISCUSSION

Numerous studies are supporting the effect of VAD on iron Status leading to IDA. Studies conducted in Bangladesh and South Asia were reporting association of iron, zinc, and VAD with nutritional anemia among children under 60-months of age. Vitamin A deficient children are prone to anemia, which may be reversed with adequate vitamin-A Supplementation.[13-16]

The majority of the patients who contributed to this study were male, 75% (45 out of 60), like the study conducted in Bangladesh. In contrast to other studies as the one conducted in southern Ethiopia among children of 2-5 years, demographic health survey analysis published in Global Pediatric Health, and the study accomplished among preschool children of rural Ghana, presentation of the patient from each gender was almost equal.[6,17–19]

A major fraction of the study data was from infants/young children. Possibly nutritional anemia is more common among young children due to various reasons, as was documented in national and international studies conducted to address different aspects of childhood anemia.[5,6,18]

The current study noted a mean baseline Hb of around 8gm/dl, in both groups. While the mean rise in Hb-level, after 3-months of supplementations as per the assigned group, is reported better in group-A; with a p-value of 0.00014. Similar results were documented in other international studies among anemic school children in Tanzania and Western-Kenya.[6,20] At the same time, it is comparable to the study conducted by Arnab Biswas in Kolkata that is reporting better outcomes with iron and vitamin-A combination in terms of rise in RBC count and ferritin level rather than mean rise in Hb level.[10]

The current study reported a better response with combination therapy (vit-A and Iron) as compared to isolated iron-supplementation. As the sample size of this study was small and we do not know about the vitamin-A level of the participant of the study at baseline and after 3 months, need to conduct a similar study with a larger sample size and vitamin-A level at baseline and after 3 months of treatment to determine the relationship between response to iron supplementation and vitamin-A level among iron-deficient children.

CONCLUSION

Vitamin-A supplementation along with standard iron-replacement therapy in childhood IDA is appreciated in terms of a better rise in hemoglobin levels. Like other developing countries, iron and VAD are common nutritional deficiencies in our community as well; concomitant supplementation of vitamin-A and iron should be encouraged in microcytic hypochromic anemia, although the sign and symptoms of vitamin-A deficiency are not obvious.

Ethical Approval:

The ethical Approval was obtained from Jinnah Hospital Lahore. (Reference No. ERB146/3/18-7-2023/SL ERB)

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