Original article

International Journal of Medical Arts 2019; 1(1): 48-

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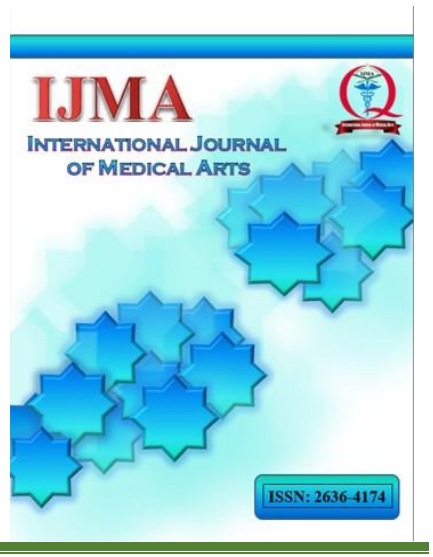

Original article

Effect of Lactoferrin Supplementation on Iron Deficiency Anemia in Primary School Children

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Received at: May 7, 2019.

Revised at: June 7, 2019

Accepted at: June 7, 2019.

Available online: June 8, 2019

Background: Many studies were done to evaluate the effect of oral lactoferrin administration on iron deficiency anemia, with controversial results.

Objective: This study was designed to assess the effects of lactoferrin supplementation on primary school children having iron deficiency anemia.

Patients and Methods: Prospective cohort study was conducted on 94 patients with iron deficiency anemia. They were 58 females and 36 males. Their ages range from 6 years to 12 years with mean age of 8.4 years. In the period between October 2018 and January 2019. Each child was submitted to full history taking, complete clinical examination and laboratory investigations including complete blood count, Serum ferritin, serum iron and total iron binding capacity.

Results: Oral administration of bovine lactoferrin (BLf) significantly increases the number of red blood cells, hemoglobin, serum ferritin and total iron after thirty days of the treatment. BLf is a more effective and safe alternative than elemental iron for treating iron deficiency and iron deficiency anemia.

Conclusions: Lactoferrin is a better substitute for elementary iron in treatment of iron deficiency.

Keywords: Iron; Anemia; Iron Deficiency; Primary school Children.

https://doi.org/10.21608/ijma.2019.12596.1003.

Please cite this article as: El-Khawaga AH, Abdelmaksoud HM. Effect of Lactoferrin Supplementation on Iron Deficiency Anemia in Primary School Children. IJMA 2019; 1(1): 48. Article in Press, https://doi.org/10.21608/ijma.2019.12596.1003.

Introduction

Iron deficiency (ID) anemia (IDA) is a challenging health problem in pediatrics. It is the most common nutritional deficiency all-over the world, mainly in developing countries. World health organization (WHO) in 2001 estimated that 30% of children aged 0-4 years and 48% of children aged 5-14 years were anemic. The etiologies of iron deficiency in children include inadequate iron intake and increased needs due to rapid growth[1]. ID and IDA had a remarkable adverse effect on children health. Negative effects include – but not limited to – stunted development, low immunity, decrease IQ values, reduced capacity of physical activity, increased fatigue, poor psychomotor, cognitive power and school achievement [2].

Children with mild IDA were usually asymptomatic. However, some of them could be presented with pica, easy fatigability, irritability, palpitation, shortness of breath, conjunctival pallor and/or pallor of palms and nail bed. In children with severe iron deficiency anemia; tachycardia and heart failure may be developed [3]. The most commonly used definitions of anemia are from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), based on hemoglobin levels (levels < 11g/dl in infants aged 0.5-5 years: and < 11.5g/dl in children aged 5-12 years. Prevention of iron deficiency anemia is an important public health issue and many strategies are available (e.g. iron supplementation, fortification of foods, proper management of parasitic infestation and dietary diversification)[4].

Recently, some researcher suggested that, lactoferrin could play a role in solving this global health issue[5]. Lactoferrin is an iron binding, non-haem protein that is structurally and chemically similar to serum transferrin, the transporter of iron in the serum. It is produced by epithelial cells of mucosa and found in secretions as saliva, tears, nasal, bronchial secretions and abundantly secreted in milk[6]. Lactoferrin has proved to have 300 times higher affinity to iron as compared to serum transferrin and an ability to retain iron over a broader PH range. Also, it was evidenced that it affects iron homeostasis by increasing iron export from gastrointestinal tract (GIT) and enhancing iron storage in ferritin. These mechanisms have proved to give better results with patients who are using lactoferrin as compared with those using ferrous sulphate in terms of red cell count, hemoglobin level, serum ferritin and total serum iron[7].

Aim of the study

This study was designed to assess the effects of oral lactoferrin administration on primary school children having iron deficiency anemia.

Patients and Methods

The current work was designed as a prospective cohort study and was conducted on 94 patients with IDA. They were 58 females and 36 males. Their ages range from 6 to 12 years with mean age of 8.4 years. This study was performed in the period between October 2018 and January 2019. Children of this study has been collected from two different primary schools in Tanta City. Letters from Pediatric Department (Al-Azhar Faculty of Medicine, Damietta) to primary schools for co-operation in this study. In our study, children were studied to evaluate the effect of oral Lf on treating IDA instead of elemental iron. They were numbered randomly from 1 to 94 (There were nine children not responding to follow up). They were classified into: Group 1: (included children with odd numbers) 47 children received lactoferrin as a treatment of anemia. Oral bovine lactoferrin (one sachet contains 100 mg of bovine lactoferrin over a quarter cup of water) was given twice daily for one month before meals. Group 2: (included children with even numbers) 47 children received iron as treatment of anemia. Elemental iron (6mgl/kg/day) was administered orally with meals, once daily for 30 days.

Inclusion criteria: the study included children of primary school age with iron deficiency anemia and both sexes were involved. **Exclusion criteria:** children with one or more of the following: chronic infections as TB, collagen diseases, renal diseases, liver diseases, malignancies and those underwent iron therapy or received blood transfusion in the last 3 months, were excluded. For all children, full history and clinical examinations were carried out. Also, blood samples were collected to measure ferritin and iron in serum, total iron binding capacity, and to do complete blood count, at baseline (Just before initiation of treatment) and after one month; after regular therapy by bovine lactoferrin or elemental iron.

Statistical analysis: Data were collected, coded, revised and analyzed by the Statistical Package for Social Science (IBM® SPSS®, Chicago, USA) version 20. Frequency and percent were calculated for the qualitative data, while mean, standard deviations and ranges were calculated for the quantitative data with parametric distribution and median with inter quartile range (IQR) for non-

parametrically distributed data. The p-value < 0.05 was considered significant.

Results

In the present study, males represented 41.2% and females 58.8% of studied children. The mean age was 8.40±1.90 years. The socioeconomic state was high in 14.1%, moderate in 42.4%, low in 27.1% and very low in 16.5%. General examination revealed that, no patients had jaundice, while 5.9% had severe pallor and 91.8% had some pallor. The mean weigh was 28.02±9.62 kg, while mean height was 124.49±13.22 cm; no patients had lymph-adenopathy, hepatomegaly or splenomegaly. However, 20.0% of studied children had tachycardia (table 1).

In the present work, there was statistically significant increase of hemoglobin, RBCs, MCHC, serum ferritin and serum iron after treatment in lactoferrin group when compared to elemental iron group (table 2).

Table (1): General characters, general and systemic examinations among studied children

			No.	%
Sex	Female		50	58.8%
	Male		35	41.2%
Age	Mean ±SD		8.40±1.90	
Socio-economic Status	High		12	14.1%
	Moderate		36	42.4%
	Low		23	27.1%
	Very low		14	16.5%
General examination	Pallor	Severe	5	5.9%
		Some	78	91.8%
	Jaundice		0	0.0%
	Weight (mean±SD)		28.02±9.62	
	Height (mean±SD)		124.49±13.22	
Systemic examination	Lymphadenopathy		0	0.0%
	Tachycardia		17	20.0%
	Hepatomegaly		0	0.0%
	Splenomegaly		0	0.0%

Table (2): Comparison between lactoferrin and elemental iron groups regarding laboratory investigation

		Lactoferrin group (No.=43)		Elemental iron group (No.=42)		Mean Difference	p value
		Mean	SD	Mean	SD		
Hemoglobin (g/dl)	Before treatment	9.7	0.49	9.6	0.66	0.1	0.429
	After treatment	10.84	0.59	10.2	0.70	0.64	0.001*
RBCs (m/cmm)	Before treatment	3.91	0.31	3.71	0.29	0.2	0.003*
	After treatment	4.40	0.34	4.15	0.31	0.25	0.001*
Hematocrit %	Before treatment	30.02	2.11	29.7	2.3	0.32	0.50
	After treatment	30.7	2.06	30.1	1.81	0.6	0.157
MCV (fl)	Before treatment	73.6	4.05	72.3	4.5	1.3	0.165
	After treatment	76.8	3.9	76.2	4.1	0.6	0.491
MCH (pg)	Before treatment	24.5	1.7	24.7	1.7	0.2	0.589
	After treatment	27.2	1.8	26.4	2.3	0.8	0.077
MCHC (g%)	Before treatment	33.4	1.20	32.9	1.4	0.5	0.082
	After treatment	35.8	2.2	34.1	1.7	1.7	0.001*
Serum ferritin	Before treatment	14.9	7.46	16.6	7.4	1.7	0.294
	After treatment	40.3	18.3	24.8	9.4	15.5	0.001*
Serum iron	Before treatment	39.2	8.8	41.9	8.9	2.7	0.163
	After treatment	69.6	14.3	63.0	14.7	6.6	0.038*
TIBC	Before treatment	3.9	0.42	3.8	0.47	0.1	0.303
	After treatment	3.16	0.46	3.2	0.47	0.04	0.692

RBCs: Red blood cells; MCV: mean cell volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentrations; TIBC: total iron binding capacity.

Discussion

This study was designed to assess the effects of Lf supplementation for primary school children with IDA. Lactoferrin is structurally and chemically comparable to serum transferrin (functions as iron transporter in the serum)[7]. Lf has 300 times higher affinity to iron than serum transferrin and an ability to retain iron over a broad PH range[8]. Monitoring of complete blood picture (CBC) and iron profile including serum iron, serum ferritin and total iron binding capacity (TIBC) before and after one month

of treatment. These mechanisms have proved to give better results with patients who are using Lf as compared with those using elemental iron in terms of red cell count, hemoglobin level, serum ferritin and total serum iron[9]**.**

Regarding clinical presentation, pallor detected in about 97% of cases. This agree with the study conducted by **Ali et al.[10]** that found that pallor was the most common sign observed in iron deficient children..

In terms of laboratory investigations, the current study noted that at the beginning of the study, both groups were comparable as regard to hemoglobin concentration. However, after one month of treatment, both groups showed significant increase of hemoglobin with significant increase in lactoferrin group. This agreed with the study of **Rezk et al.[11]** that stated that mean increase of hemoglobin level was by (2.26 ±.51 g/dl) in patients with IDA who received Lf for 8 weeks on a dose of 250 mg once daily. Another study by **Paesano et al.**[9] revealed that mean increase of hemoglobin level was (1.7 ± 0.9 g/dl) in patients with IDA who received Lf for 30 days on a dose of 100 mg twice daily**.**

The mean hematocrit count was 30.02% and increase to 30.7% in Lf group and mean value was 29.7% before treatment, increased to 30.1% in elemental iron group. This agreed with the study of **King et al.[12]**, who carried out a pilot study of Lf supplementation for infants and revealed that supplementation Lf had potentially favorable outcomes such as marked reduction of lower respiratory tract infection and increased hematocrits.

Mean serum ferritin before treatment was 14.98 ng/ml and after 1 month it increased to 40.30 ng/ml in Lf group, while in elemental iron group, it was 16.95 ng/ml before treatment and after one month, increase to 24.80 ng/ml. This agreed with the study of the serum ferritin level noted by **Paesano et al.[9]**, in which ferritin was ≤12 ng/ml initially while after one month of treatment it was 29±7 ng/ml.

Mean total serum iron before treatment was 39.2 mg/dl and after 1 month it increases to 69.6 mg/dl in Lf group compared to 41.9 mg/dl and 63.0 mg/dl before and after one month of treatment in elemental iron group. This consisted with the study of **Paesano et al.[13],** who study Lf versus iron (ferrous sulphate) in management of iron deficiency and IDA and reported that, mean iron level before treatment was ≤30 mg/dl, that elevated to 84±16 mg/dl after treatment for 30 days. Also, results coincides with the study of **Ke et al.[14]** who reported significant increase in iron absorption in exclusively breastfed infants after supplementation with Lf-fortified milk. Also, results in agreement with the study held by **Bethell and Huang[15].**

Mean TIBC before treatment was 3.9 and after one month, it decreases to 3.1 in Lf group compared to, 3.8 before and 3.2 after treatment in elemental iron group. This agreed with the study of **Rezk et al.[11]** that stated that of TIBC levels decreased in cases with IDA who received Lf for 8 weeks on a dose of 250 mg once daily.

In conclusion, oral lactoferrin represents a substitute for oral iron in the management of iron deficiency in children.

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