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Original article

The Association between Iron Deficiency Anaemia and Chronic Suppurative Otitis Media [Safe Type]

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ABSTRACT

Background: Acute otitis media is considered as one of the most frequent childhood inflammatory disorders.

Aim of The Work: This study aimed to investigate the possible link between iron deficiency anemia and acute episodes on top of chronic otitis media.

Patients and Methods: This prospective study is included pediatric patients who attend the ENT outpatient clinic in Mallawi Hospital, El Minia; El Azhar University _Assuit, from July 2019 to June 2020. A total of 100 patients of age Group up to 18 years old and both sexes suffering from recurrent otitis media divided into Group A: Included 34 children treated with iron supplementation three months, Group B: Included 33 children treated with iron supplementation and medical treatment three months. Group C: Included 33 children treated with medical treatment for three months.

Results: In group A the change of hemoglobin level from $[10.15 \pm 0.33]$ to $[11.41 \pm 0.43]$ decreasing occurrence rate of CSOM from 3.47 ± 0.51 to 1.41 ± 0.49 with statistically significant difference $[p < 0.001]$. In group B, the change of Hb level from $[10. \pm 0.32]$ to $[11.48 \pm 0.29]$ decreasing occurrence rate of Chronic Suppurative Otitis Media from 33.42 ± 0.92 to 1.39 ± 0.56 with statistically significant difference $[p < 0.001]$. In group C, the change of Hb level from $[10.03 \pm 0.43]$ to $[10.09 \pm 0.31]$ decreasing occurrence rate of CSOM from 3.39 ± 0.66 to 2.33 ± 0.48 with statistically significant difference $[p < 0.001]$.

Conclusions: The combination of iron and medical treatment in anemic patients can improve hemoglobin level and significantly decrease otitis media's occurrence rate.

Keywords: Acute otitis media; Iron-deficiency; Hemoglobin level; Iron supplementation; Medical treatment.

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* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Acute otitis media [AOM] is considered one of the most frequent childhood inflammatory diseases. Iron deficiency causes negative effects on the normal function of the immune system. Specifically, there are two distinct alterations of the immune system linked to iron deficiency; the first is the reduced response of T-cell lymphocytes to infectious agents, and the second is the reduced bactericidal actions of the neutrophils^[1]

Children who complained of moderate to severe iron deficiency anemia are more prone to have severe infections than children who do not ^[2]

On the extreme side, few previous trials reported that iron deficiency may have a protective role and may even enhance bacterial infection resistance. They explained their results by the unfavorable circumstances produced by iron deficiency for the infective agents, as iron is required for the normal metabolic activity of these organisms^[3]

Anemia is defined as a reduction of hemoglobin concentration due to reduced red cell count compared to age-matched normal control values^[4]. The average normal hemoglobin concentration in pediatrics between [6 months to 48 months] is 12.0g/dL [range 10.5 to 14.0]. Childhood anemia is mainly due to iron deficiency, and developing countries had a high prevalence of iron deficiency anemia [IDA], which associated with low socioeconomic status^[5]

AOM is one of the commonest bacterial infections in pediatrics. Most infective agents are inhabitants of nasopharynx [e.g., Hemophilus influenza, Streptococcus pneumonia, and Moraxella catarrhalis, adenovirus, rinovirus] ^[6]

It is important to investigate if there is a possible association between IDA and AOM on top of chronic, especially with the contradictory results in previous literature.

AIM OF THE WORK

This study aimed to investigate the relationship between IDA and the occurrence of episodes of acute on top of chronic OM.

PATIENTS AND METHODS

The current clinical study had been completed in ENT outpatient Clinic [Mallawi Hospital, El Minia and

Al-Azhar University Hospital [Assuit Branch]]. It included a total of 100 patients of age Group up to 18 years old and of both sexes suffer from recurrent otitis media.

Inclusion criteria: Age of Patients up to 18 years old and both sexes with recurrent ear infections suffering from otitis media attacks and persistent ear discharge.

Exclusion criteria: adult patients > 18 years of age, who had chronic OM or scheduled for placement of ventilation tube; children who had a cleft palate and/or cleft lip or those with immunocompromise [e.g., diabetic, under chemotherapy and/or radiotherapy, had chronic medical disease [e.g., renal and hepatic failure]].

Every patient is submitted to complete history taking to confirm the disease and chronicity. In addition, all were examined clinically by a systematic approach. This included general and ENT examination, which included ear, nose, pharynx examination to show the signs of effusion suppurative or non-suppurative. Lab investigations were in the form of serum iron profile and iron-binding capacity; complete blood count [CBC] [hemoglobin concentrations, RBCs, MCV, and MCH].

All patients with iron deficiency were advised to dietary system rich in iron and iron supplementation. We completed blood picture analysis, serum iron, and total iron-binding capacity measurements for all the study participants before giving any treatment.

Ethical issue: Approval of the Al-Azhar Assuit faculty of medicine ethical committee was obtained before starting this study. All patients or caregivers of children signed informed written consent after supplying comprehensive information about the study's aim and nature.

Statistical analysis used: Statistical analysis was done using SPSS, version 25 [IBM SPSS Inc., Chicago, Illinois, USA] for Windows 10. Data were described as mean \pm Stander deviation, frequencies, and percentage. ANOVA and Paired t-test used were used. P-value < 0.05 was set as the marginal of significance.

RESULTS

There were insignificant differences between groups regarding age and gender [p>0.05]. We found insignificant differences in pre-treatment laboratory data among the three groups [p>0.05] [Table 1].

We completed blood picture analysis, serum iron, and total iron-binding capacity measurements for all the study participants before and after giving the treatment. There were statistically significant differences between groups in all post-treatment parameters. Group A who were treated with iron supplementation had the highest mean of hemoglobin, red blood cells, mean corpuscular volume, and total iron-binding capacity than the other groups. At the same time, group B had the highest mean of mean corpuscular hemoglobin and serum iron than the other groups [p<0.001] [Table 2].

Group A treated with iron supplementation had statistically significant differences between pre and post-treatment parameters. Haemoglobin [Hb], red blood cells [RBCs], mean cell volume [MCV], mean cell hemoglobin [MCH], and serum iron showed a significant increase in post-treatment. In contrast, total

iron-binding capacity [TIBC] and rate of chronic suppurative otitis media [CSOM] showed a significant decrease in post-treatment [Table 3]. Similarly, group B, treated with iron supplementation and medical treatment, had statistically significant differences between pre and post-treatment parameters. HB, RBCs, MCV, MCH, and serum iron showed a significant increase in post-treatment, while TIBC and occurrence rate of CSOM showed a significant decrease in post-treatment [Table 4].

Furthermore, group C, treated with medical treatment, only had statistically significant differences in MCV, MCH, serum iron, and occurrence rate of [CSOM] as MCV, MCH, and serum iron showed significant post-treatment. In contrast, the occurrence rate of CSOM showed a significant decrease in post-treatment [Table 5].

Table [1]: General characteristics of study groups [N=100].

| Variable | Group A [n=34] | Group B [n=33] | Group C [n=33] | p-value |
|----------------------------|----------------|----------------|----------------|---------|
| Age [years] | 7.5± 2.97 | 7.2 ± 2.12 | 7.4±2.56 | 0.984 |
| Gender | | | | 0.931 |
| Male | 17[50%] | 16[48.5%] | 15[45.5%] | |
| Female | 17[50%] | 17[51.5%] | 18[54.5%] | |
| HB [g/dl] | 10.15 ± 0.33 | 10 ± 0.32 | 10.03 ± 0.43 | 0.20 |
| RBCs[million micron/l] | 4.49 ± 0.2 | 4.29 ± 0.5 | 4.44 ± 0.11 | 0.23 |
| MCV[Micro m ³] | 75.02 ± 0.56 | 71.18 ± 0.58 | 73.16 ± 0.95 | 0.10 |
| MCH [Pg] | 24.96 ± 0.44 | 22.23 ± 0.47 | 23.36 ± 1.2 | 0.18 |
| S.iron [mg/dl] | 42 ± 0.36 | 41.3 ± 0.8 | 41.99 ± 1.2 | 0.32 |
| T.I.B.C [mg/dl] | 454.32 ± 1.1 | 433.85 ± 5.54 | 438.53 ±4.23 | 0.24 |

Results are expressed as mean±SD for quantitative data. ANOVA test used. HB: hemoglobin, RBCs: red blood cells, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, TIBC: total iron binding capacity.

Table [2]: Post-treatment laboratory data among three groups.

| | Group A [n=34] | Group B [n=33] | Group C [n=33] | P-value |
|----------------------------|----------------|----------------|----------------|---------|
| HB [g/dl] | 11.41 ± 0.43 | 11.48 ± 0.29 | 10.09± 0.31 | <0.001* |
| RBCs[million micron/l] | 4.66 ± 0.21 | 4.64 ± 0.14 | 4.44 ± 0.09 | <0.001* |
| MCV[Micro m ³] | 83.04 ± 0.48 | 81.92 ± 3.1 | 73.45 ± 0.69 | <0.001* |
| MCH [Pg] | 27.98 ± 0.54 | 28.05 ± 0.49 | 22.75 ± 0.62 | <0.001* |
| S.iron [mg/dl] | 77.66 ± 5.45 | 80.64 ± 2.77 | 42.16 ± 1.23 | <0.001* |
| T.I.B.C [mg/dl] | 453.68 ± 1.18 | 432.53 ± 5.54 | 437.16 ±4.65 | <0.001* |

Results are expressed as mean±SD for quantitative data. ANOVA test used. *:significant relationship

Table [3]: Pre and post-treatment [Iron supplementation] parameters in group A.

| | Pre- treatment [n=34] | Post- treatment [n=34] | P-value |
|------------------------------------|--------------------------|---------------------------|---------|
| HB [g/dl] | 10.15 ± 0.33 | 11.41 ± 0.43 | <0.001* |
| RBCs [million micron/l] | 4.49 ± 0.2 | 4.66 ± 0.21 | <0.001* |
| MCV [Micro m ³] | 75.02 ± 0.56 | 83.04 ± 0.48 | <0.001* |
| MCH [Pg] | 24.96 ± 0.44 | 27.98 ± 0.54 | <0.001* |
| S.iron [mg/dl] | 42 ± 0.36 | 77.66 ± 5.45 | <0.001* |
| T.I.B.C [mg/dl] | 454.32 ± 1.1 | 453.68 ± 1.18 | 0.002* |
| Occurrence rate of [CSOM] Range | 3.47 ± 0.51 [3-4] | 1.41 ± 0.49 [1-2] | <0.001* |

Results are expressed as mean±SD for quantitative data. Paired t test used. *:significant relationship

Table [4]: Pre and post-treatment [Iron + Medical ttt] parameters in group B.

| | Pre- treatment [n=33] | Post- treatment [n=33] | P-value |
|------------------------------------|--------------------------|---------------------------|---------|
| HB [g/dl] | 10 ± 0.32 | 11.48 ± 0.29 | <0.001* |
| RBCs [million micron/l] | 4.29 ± 0.5 | 4.64 ± 0.14 | <0.001* |
| MCV [Micro m ³] | 71.18 ± 0.58 | 81.92 ± 3.1 | <0.001* |
| MCH [Pg] | 22.23 ± 0.47 | 28.05 ± 0.49 | <0.001* |
| S.iron [mg/dl] | 41.3 ± 0.8 | 80.64 ± 2.77 | <0.001* |
| T.I.B.C [mg/dl] | 433.85 ± 5.54 | 432.53 ± 5.54 | 0.007* |
| Occurrence rate of [CSOM] Range | 3.42 ± 0.92 [2-6] | 1.39 ± 0.56 [1-3] | <0.001* |

Results are expressed as mean±SD for quantitative data. Paired t test used. *:significant relationship

Table [5]: Pre and post-treatment [Medical ttt only] parameters in group C.

| | Pre- treatment [n=33] | Post- treatment [n=33] | P-value |
|------------------------------------|--------------------------|---------------------------|---------|
| HB [g/dl] | 10.03 ± 0.43 | 10.09 ± 0.31 | 0.231 |
| RBCs [million micron/l] | 4.44 ± 0.11 | 4.44 ± 0.09 | 0.886 |
| MCV [Micro m ³] | 73.16 ± 0.95 | 73.45 ± 0.69 | 0.005* |
| MCH [Pg] | 23.36 ± 1.2 | 22.75 ± 0.62 | 0.002* |
| S.iron [mg/dl] | 41.99 ± 1.2 | 42.16 ± 1.23 | 0.030* |
| T.I.B.C [mg/dl] | 438.53 ± 4.23 | 437.16 ± 4.65 | 0.89 |
| Occurrence rate of [CSOM] Range | 3.39 ± 0.66 [2-5] | 2.33 ± 0.48 [2-3] | <0.001* |

Results are expressed as mean±SD for quantitative data. Paired t test used. *:significant relationship

DISCUSSION

There were insignificant differences between groups in age, gender, pre-treatment laboratory data, which denote good matching between groups. In addition, no significant difference was found regarding the pre-treatment occurrence rate of chronic suppurative otitis media, while post-treatment, the rate showed a significant reduction among all groups. The group with the highest mean of hemoglobin had the lowest number of episodes of AOM. Akcan *et al.* study reported that children with IDA have high and more

frequent OM episodes than healthy peers with normal levels of hemoglobin concentration. Also, there was a positive correlation between the degree of anemia and the AOM number of episodes [5].

In our study, the change [increase] of hemoglobin level is associated with the decreasing occurrence rate of chronic suppurative otitis media [CSOM]. It was more evident in group B; increased hemoglobin concentration significantly correlated with CSOM episodes. Comparable results were reported in the third group. Hussain *et al.* reported that hemoglobin

concentration lower than 11 g/dL was considered low; as the control group levels were 11.6g/dl and in their study groups, the hemoglobin concentrations were 8.8 g/dl. IDA incidence was 64.5% and 28.2% in the study and the control groups, respectively. The anemic group was 4.6 times more prone [susceptible] to respiratory tract infection [6]. Mourad *et al.*[7] reported an incidence rate of 32% for IDA in their patients and 16% for healthy controls. They also found low hemoglobin concentrations to be a risk factor for respiratory tract infection. Levy *et al.*[8] also reported that IDA is an independent risk factor for many respiratory infections [e.g, tonsillitis, pneumonia, asthma, and bronchitis] and AOM events, although literature had no clear data about hemoglobin level at which infection could occur.

Golz *et al.*[9] found that 83.8% of patients with hemoglobin concentrations < 9.5 g/ml had more frequent episodes of AOM, and they recommended the use of iron supplementation at hemoglobin levels <10 g/dL. In our study. Another work confirms these results found a significant correlation between low hemoglobin levels and high frequency of upper respiratory tract infections and AOM.

On the other side, other researchers identified many risk factors for otitis media, but IDA was never considered to be one of these risk factors [10-12].

The heterogeneity of studies and different sample sizes. Besides the levels at which iron deficiency was recognized, all are possible explanations for these differences.

The prospective nature and iron supplementation effect are strength points of the current study, especially in our location, where iron deficiency is prevalent due to low socioeconomic level. Fortification and iron supplementation are mandatory. However, future studies on large sample sizes are required to address the problem in more detail and consider other possible risk factors for middle ear infection.

Financial and Non-financial Relationships and Activities of Interest

None

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