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Does Adenoid Hypertrophy Affect Hemoglobin and Erythropoietin Levels in Children?

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Abstract

Objective: *Adenoid hypertrophy restricts the nasal airflow by obstructing the choanae posteriorly and may lead to chronic hypoxia. The present study mainly aims to compare pre- and postoperative erythropoietin (EPO) and hemoglobin (Hgb) levels in children undergoing adenoidectomy.*

Methods: *Between 2021 September and 2022 August, 61 children who performed adenoidectomy in the ENT clinic included in this prospective clinical trial. The pre- and postoperative third months EPO and Hgb values of children were compared.*

Results: *The mean age of the children undergoing adenoidectomy was 5.7±3.4 (range, 3-9 years). Twenty-seven of the subjects were men and 34 were women. The mean EPO values of the adenoid hypertrophy patients preoperatively and at postoperative third months were 13.7±2.4 Mu/mL and 10.8±1.6 Mu/mL, respectively. The decrease in mean EPO value was significant (p = 0.031). The mean Hgb levels of the subjects preoperatively and at postoperative 3rd months were 12.1±2.4 g/dL and 11.9±1.6 g/dL, respectively. When pre- and postoperative 3rd month mean Hgb values compared, the difference was not significant (p = 0.721).*

Conclusions: *According to these outcomes, grade 4 adenoid hypertrophy is associated with significantly increased EPO values compared to post-operative values in children. To validate these results further prospective studies with larger sample sizes are required.*

Key words: *Adenoid hypertrophy; Adenoidectomy; Erythropoietin; Hemoglobin; Hypoxia.*

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Introduction

The most important outcome of adenoid hypertrophy (AH) is Obstructive Sleep Apnea syndrome (OSAS), which is among the most common reason for nocturnal hypoxia in children. Erythropoietin (EPO), a hormone in the glycoprotein structure, the physiological regulator of erythrocyte production, is synthesized mainly in the kidney in response to hypoxia (1). In circulation, EPO has a half-life of 6-9 hours and EPO shows activity by binding to specific receptors at the level of marrow erythroid precursors. The EPO directly stimulates the bone marrow precursors to increase red blood cells (RBC) and its components, including hemoglobin (Hgb) (2). Hgb is a protein comprising iron found in red blood cells (RBC) that transfers oxygen (O2) from the alveoli to the tissues and the carbon dioxide (CO2) from the tissues back to the alveoli where the O2 and CO2 exchange occurs. Therefore, the chronic hypoxic condition leads to reduced arterial O2 saturation that results in decreased O2 transport to the peripheral tissues. As a physiological response, under the chronic hypoxemic condition, first EPO levels increases then there will be an increase in both the Hbg level and hematocrit value (3). If not cured, in the long term, severe AH -the most common reason for snoring, open-mouth breathing, and OSAS in children- may result in chronic nocturnal hypoxia (4). Neutrophil/lymphocyte ratio (NLR) and Mean platelet volume (MPV) are inflammatory markers linked to increased inflammatory conditions in the pediatric population. An increase in MPV level may cause growth retardation or an increase in the rate of upper respiratory tract infection (5). Plateletcrit (PCT), on the other hand, is a marker that has been used recently and is calculated using hemogram parameters (6). According to our knowledge, in the current literature, no study was conducted regarding EPO level and PCT changes after adenoidectomy. Thus, in the current study, the authors intended to enquire whether adenoid hypertrophy has any relation with EPO, Hgb, NLR, MPV and PCT levels or not.

Material-Methods

Study setting

This prospective clinical trial was carried out on 61 patients between September 2021 and August 2022 at a tertiary referral centre. The ethical committee approval of the study protocol was obtained. Informed consent was acquired from the parents of children included in this clinical trial.

Patient selection

Between September 2021 and August 2022, 61 children in the ENT clinic were enrolled in the study. All subjects included in this clinical trial had paradoxical or obstructed breathing during sleep/ sleepiness, snoring/labored and/or chronic postnasal discharge. AH was diagnosed by endoscopic examination and/or X-ray imaging, and was classified with respect to the scale suggested by Clements et al (7). In grade I AH; AH fills up to 1/3 of the choana, in grade II; AH occupies 2/3 of the choana, in grade III; AH obstructs the choana almost near-total, and grade IV represents total obstruction of the choana. The Sleep Disturbance Scale for Children (SDSC) scale was utilized to survey sleep disorder. This scale was developed by Bruni et al. and validity and reliability of this scale were conducted in many studies in different languages (8). SDSC contains 26 symptom items asking about characteristics of snoring, difficulty breathing during sleep, daytime sleepiness, and other pediatric sleep disorders. The questions are answered from 'never' (1 point) to 'always' (5 points). The scores can be obtained from this scale varying between the minimum (26 points) and the maximum (130 points). High scores obtained from the scale are interpreted in favor of sleep disorder. In addition, there is a T-score table in the original scale to guide clinicians. According to this table, it is accepted that those with T-score >70 show symptoms of sleep disturbance (8,9).

Pediatric subjects who performed adenoidectomy were included in this prospective clinical study. Enrollment criterions of the study were as follows: grade 3-4 adenoid hypertrophy with T-score >70 who underwent adenoidectomy. Patients with hematologic disease, iron deficiency anemia and with grade 1-2 adenoid hypertrophy were not enrolled in this study. Furthermore, patients with any malignancy, chronic inflammatory disease, thyroid dysfunction, chronic liver disease, kidney failure or any acute-subacute infectious disease in the last 3 months were not enrolled in this study. All children participating in the study underwent adenoidectomy by the same surgical team using the same surgical technique.

Parameters

Blood samples were taken preoperatively and at the 3rd month postoperatively and compared. Mainly EPO, Hgb, NLR and MPV and PCT levels are investigated. Since EPO release has a diurnal rhythm, blood samples were taken from the antecubital vein between 08:30 and 09:00 in the morning to ensure consistency. Blood samples were gathered in tubes comprising ethylene diamine tetra acetic acid and laboratory analysis was performed within two hours on the same day. All blood samples were studied on the same device to ensure standardization.

Statistical analysis

SPSS (Statistical Package for Social Sciences, Chicago, Illinois, USA) software was utilized to analyse of the data of the current study. Descriptive analysis, Wilcoxon and Paired-Sample t tests were used to investigate the data. A p-value <0.05 was considered statistically significant.

Results

Between September 2021 and August 2022, 61 children were enrolled in this clinical trial. Of these patients, 27 (44.3%) were men and 34 (55.7%) were women. The average age of the subjects participating in the study was 5.7±3.4 (range 3-9). 24 of these patients (39.3%) had grade 3 and 37 (60.7%) had grade 4 adenoid hypertrophy (Table 1).

Table 1. Demographics of patients

		n	%
Gender			
	Male	27	44.3
	Female	34	55.7
Adenoid hypertrophy			
	Grade 3	24	39.3
	Grade 4	37	60.7

While the mean preoperative EPO values were 13.7±2.4 Mu/mL, it was 10.8±1.6 Mu/mL at the postoperative 3rd month. When the pre- and postoperative 3rd month EPO values were investigated, statistically significant difference was observed in EPO values (p=0.031). When the hemoglobin values of the patients were examined, the preoperative mean was 12.1±2.4 g/dL, while the mean at the postoperative 3rd month was 11.9±1.6 gr/dL. When the pre- and postoperative 3rd month hemoglobin levels of the subjects were investigated, changes in Hgb levels was not statistically significant (p=0.721). While the preoperative NLR of the patients was 3.12±0.4, the NLR postoperative 3rd month was 2.07±0.7. Significant difference were observed in the NLR of the patients at the pre- and postoperative 3rd month (p<0.001). While the preoperative PCT mean of the patients was 0.56±0.02, the mean at the 3rd month postoperatively was 0.39±0.01. There was a statistically significant difference (p<0.001) when the mean PCT (%) of the subjects at the preoperative and postoperative 3rd month was considered. While the mean preoperative MPV value of the patients was 7.1±3.2 fL, the mean MPV at the postoperative 3rd month was 6.4±1.9 fL. The MPV values of the patients at the pre- and postoperative 3rd month were significantly different (p<0.001). The preoperative and postoperative 3rd month blood parameters of the subjects presented in Table 2.

Table 2. Comparision of preoperative and postoperative 3rd month blood parameters of patients underwent adenoidectomy

Parameters	Preoperative	Postoperative 3rd month	P-value
EPO (Mu/mL)	13.7 ± 2.4	10.8 ± 1.6	0.031*
Hgb (gr/dL)	12.1 ± 2.4	11.9 ± 1.6	0.721
NLR	3.12 ± 0.4	2.07 ± 0.7	<0.001*
PCT (%)	0.56 ± 0.02	0.39 ± 0.01	<0.001*
MPV (fL)	7.1 ± 3.2	6.4 ± 1.9	<0.001*

EPO: Erythopoietin, Hgb: Heamoglobin, NLR: Neutrophil lymphosite ratio, PCT: Platelecrit, MPV: Mean platelet volume, * p value <0.05 is statisticaly significant

When the subjects were compared with respect to the size of the adenoid vegetation, the EPO values were divided into 2 groups. In the group with grade 3 adenoid hypertrophy, the difference in EPO between preoperative and postoperative 3rd month was 2.6±1.7, and in the group with grade 4 adenoid hypertrophy, the difference in EPO between preoperative and postoperative 3rd month was 3.1±1.9. There was a significant difference when the change in EPO value in preoperative and postoperative 3 months in grade 3 and grade 4 adenoid hypertrophy patients was compared (p=0.042 and p= 0.012, respectively) (Table 3).

When the subjects were classified with respect to the size of the adenoid vegetation, the mean preoperative Hgb value in the group with grade 3 adenoid hypertrophy was 12.4±1.9 g/dL, while the mean in the postoperative 3rd month was 12.1±1.3 g/dL: in the group with grade 4 adenoid hypertrophy, the mean preoperative Hgb value was 11.3±1.6 g/dL. It was detected as

11.9±2.1gr/dL at the postoperative 3rd month. When the change in Hgb values in preoperative and postoperative 3 months in grade 3 and grade 4 adenoid hypertrophy patients was analyzed, no significant difference was observed (p=0.843 and p=0.753, respectively) (Table 3).

Table 3. Comparision of EPO level and Hbg value changes of patients with grade 3 and 4 adenoid hypertrophy

Adenoid hypertrophy	Preoperative EPO values	Postopertaive EPO values	P value
Grade 3	13.1 ± 1.1	11.2 ± 1.9	0.042*
Grade 4	14.3 ± 2.4	10.5 ± 3.2	0.012*
	Preoperative Hgb values	**Postoperative Hgb values**	**P value**
Grade 3	12.4 ± 1.9	12.1 ± 1.3	0.843
Grade 4	11.3 ± 1.6	11.9 ± 2.1	0.753

EPO: Erythopoietin, Hgb: Heamoglobin, * p value <0.05 is statisticaly significant

Discussion

Adenoidectomy alone or combined with tonsillectomy is one of the most frequent surgical procedures performed by otorhinolaryngologists across the globe. Adenoid hypertrophy causes upper airway obstruction in children. This may result in chronic hypoxia and hypercarbia by causing alveolar hypoventilation (10). If adenoidectomy is performed in appropriate indications, it noticeably improves the patient's quality of life.

Recurrent hypoxia and chronic airway collapse also cause metabolic alterations, immune system malfunction, and inflammatory reactions. In current literature, studies advocate that OSAS may lead to systemic inflammatory response and increased oxidative stress (11). One of the most important causes of diseases such as cor pulmonale, pulmonary arterial hypertension, and decompensated heart failure is chronic nocturnal hypoxia (10). Identification of varying inflammatory mediators in OSAS patients may anticipate the nocturnal sleep disturbance degree and associated systemic inflammation and the existence of comorbid conditions including cardiovascular diseases and hypertension. Low-level chronic systemic inflammatory response and coexisting vascular detriment have been proposed as the responsible mechanism for the development of these comorbid conditions. Evaluation of systemic inflammatory mediators in OSAS subjects may be useful in predicting future risk of comorbidity. In addition, the reversibility of these devastating results with adenoidectomy has increased the importance of treatment (10,12–15).

With adenoidectomy, the enlarged adenoid is controlled. Thus, the secondary inflammatory response will be minimized and inflammatory mediators will be reduced. In long term, this may lead to a significant diminish in the risk of diseases such as coronary artery disease and chronic nocturnal ischemia (16).

In the case of chronic and/or recurrent hypoxia, the erythrocyte level increases as a physiological response. Hypoxia-inducible factors (HIFs) induce increased production of the EPO, increased iron absorption, increased iron usage, and adjustment of the bone marrow functions that facilitates erythroid cells. Particularly, HIFs-2 is a transcription factor regulating the EPO productions in the liver and kidney and acts a crucial role in the regulation of iron absorption through the gut (17). The current study is the first to ascertain the correlation between chronic hypoxia and EPO level in children with grade 3 and 4 adenoid hypertrophy. In our study, the pre- and postoperative EPO levels of subjects with AH were compared and it was concluded that the EPO level decreased significantly (Table-1). In addition, although there was a slight decrease in the hemoglobin level in the measurements taken at the 3rd month postoperatively, no statistically significant difference was found.

NLR is a defined marker for systemic inflammation and a measurable marker with ease that is influenced by both the innate (mediated by neutrophils) and adaptive (mediated by lymphocytes) immune response. There is very little research in the current literature inquiring into the correlation between NLR and OSAS (12,18). In a study by Korkmaz et al. in the adult age group, there is no significant difference was found in the diagnosis and severity of NLR in OSA (12). Yenigün's study concluded that no significant difference was found to be between pre- and postoperative NLR between adenoid hypertrophy and adenotonsillar hypertrophy (19). Derin et al. analyzed the relationship between adenoid hypertrophy and NLR in the pediatric age group. In this study, it was concluded that NLR values were not associated with upper airway obstruction and NLR was not a statistically significant inflammatory factor (16). Contrary to these publications, there is a significant difference in our study.

Mean platelet volume (MPV) is a cost-effective test used to measure platelet size and is a platelet activity indicator (5). The relationship among MPV and severity of disease in adult subjects with OSAS was investigated. According to this study, it was concluded that MPV is correlated with both disease severity and severity of inflammatory response (20,21). Varol et al., reported that MPV values increased significantly in adult patients with OSAS relative to the control group (22). In another study conducted in the same cohort, they reported that MPV values decreased after 6 months of CPAP treatment (23). In a study investigating whether MPV could be utilized as an indicator of AH severity in children, it was concluded that there was no relationship between the degree of adenoid vegetation and MPV (24). Kucur et al. concluded that MPV is increased in subjects with AH and that adenoidectomy is an efficient surgical procedure in these subjects (25).

In a study investigating the relationship between chronic tonsillitis-adenoid hypertrophy (CT-AH) and MPV in children, it was concluded that OSAS caused by CT-AH is related with low MPV values in childhood (26). Similarly, in our study, as compared to preoperative MPV levels there was a significant decrease in MPV levels at the postoperative 3rd month. Erdim et al. investigated whether MPV, NLR and platelet-lymphocyte ratio (PLR) are factors contributing to the diagnosis and severity of OSAS in obese children and concluded that there is no relationship between levels of MPV and OSAS (27).

PCT is a recently used marker that uses hemogram parameters to calculate. The formula for PCT is platelet count*MPV/10000. Looking at this formula, it is directly related to the MPV value (6,28). Current study is the first to analyze the correlation between PCT value and adenoid hypertrophy. According to our study, there was a significant decrease observed in PCT values calculated in the preoperative period compared to the PCT values calculated in the 3rd month postoperatively.

5. CONCLUSION

This study is the first in the current literature to evaluate the relationship between adenoid vegetation and EPO levels. As a result, with this study, the effect of adenoid vegetation on EPO level was revealed, avoiding high EPO levels and possible comorbidities that may occur as a result, and evaluating inflammatory mediators in subjects with OSAS may be useful in predicting the risk of future comorbidity.

The limitations of our study may be the relatively small number of patients, the inability to objectively evaluate adenoid vegetation, and the inability to objectively evaluate obstructive sleep apnea.

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