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Effect of tonsillectomy on humoral immunity in children with obstructive sleep apnea below the age of 3 years

Ayman A. Mohamdy
Department of Otorhinolaryngology, Faculty of Medicine, Benha University, Benha, Egypt

Mohammed F. , Shendy
Department of Otorhinolaryngology, Faculty of Medicine, Benha University, Benha, Egypt

Nahed F. Khater
Department of Otorhinolaryngology, Faculty of Medicine, Benha University, Benha, Egypt, hazemramadan2020@yahoo.com

Mostafa Gomaa Sobhy
Department of otorhinolaryngology,faculty of medicine ,Benha university,Egypt, mostafaent.mg1@gmail.com

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ORIGINAL STUDY

Effect of Tonsillectomy on Humoral Immunity in Children with Obstructive Sleep Apnea Below the Age of 3 Years

Ayman A. Mohamdy, Mohamed F. Shendy, Nahed F. Khater*, Mustafa G. Sobhy

Department of Otorhinolaryngology, Faculty of Medicine, Benha University, Benha, Egypt

Abstract

Background: **Tonsils are one of the most significant secondary lymphoid organs in immune system. They contain B and T lymphocytes. B cells produce all five classes of immunoglobulins. The tonsillectomy's effect on the immune system is still up for debate.**

Objective: **The study was done to observe the effect of tonsillectomy on humoral immunity parameters (IgA, IgM, and IgG) in children with obstructive sleep apnea before and after tonsillectomy.**

Patients and methods: **A total of 60 patients who were scheduled for tonsillectomy because of obstructive sleep apnea, with ages below 3 years, and diagnosed by clinical findings of adenotonsillar hypertrophy by otorhinolaryngology surgeons were included. Serum levels of immunoglobulins (IgA, IgG, and IgM) were measured in all patients before tonsillectomy after 1 and 3 months of the operation.**

Results: **There was a decrease in IgG levels 1 month after surgery ($P = 0.005$) but they were still within the normal range. At 3 months of follow-up, there were no significant differences between the postoperative and preoperative levels ($P = 0.16$). At 1 month and at 3 months of follow-up, IgA and IgM serum levels were considerably lower than their levels before the operation ($P < 0.001$), although they were still within the normal range.**

Conclusions: **After tonsillectomy, humoral parameters (IgA and IgM) were found to be reduced, but there was no effect on immune status. IgG level was not affected after 3 months of tonsillectomy.**

Keywords: Humoral immunity, Obstructive sleep apnea, Tonsillectomy

1. Introduction

Palatine tonsils known as the tonsils are a lymphoid tissue that can often be seen as flesh colored, pinkish lumps on the left and right sides of the back of the throat [1]. Palatine tonsils are part of Waldeyer's ring, which also contains adenoids and tubal and lingual tonsils [2].

The palatine tonsil is a mucosa-associated lymphoid tissue that is present near the entrance to the aerodigestive tract and serves to guard the body against foreign substances entering via the mucosa there [3].

The tonsils have a vital role in humoral as well as cellular immunity. They have B and T lymphocytes. B cells have the capacity to mature and create a wide variety of immunoglobulins (IgA, IgM, IgD, IgG, and IgE). The inner surface of the tonsil forms of about 15 crypts that lead to increase in the surface area [4].

Tonsillar hypertrophy is increase in the size of the tonsils but without inflammation. Adenotonsillar hypertrophy may lead to snoring, sleep apnea, restlessness, anorexia, and health problems that affect the child's growth and development [5].

Obstructive tonsillar hypertrophy is one of the most common causes for tonsillectomy. Several research studies have shown that the upper airway obstruction and the obstructive sleep apnea in children with adenotonsillar hypertrophy may be improved by adenotonsillectomy [6].

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* Corresponding author.
E-mail address: Hazemramadan2020@yahoo.com (N.F. Khater).

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Owing to the importance of tonsils in the humoral and cellular immunity, tonsillectomy may reduce the immune status. However, whether tonsillectomy affect the immunity or not is still debatable [7].

2. Patients and methods

This is a prospective single-armed study conducted on 60 children complaining of obstructive sleep apnea owing to adenotonsillar hypertrophy. Patients were recruited from Otorhinolaryngology Department, Benha University, and outpatient clinic of Ashmoun General Hospital. The period of study was from February 2021 to December 2021.

2.1. Patient group

A total of 60 children who had tonsillectomy because of obstructive sleep apnea were included. There were 27 male and 33 female, all under the age of 3 years, diagnosed by clinical findings of adenotonsillar hypertrophy by an otorhinolaryngology surgeon. Inclusion criteria were children with obstructive sleep apnea under the age of 3 years. Exclusion criteria were children above 3 years, an immunodeficiency condition or any autoimmune disease, bleeding disorder, and a systemic disease. The ethical committee of the ENT Department of Benha University approved the study. In addition, informed consent was taken from the parents.

2.1.1. Preoperative assessment

Full history taking, general examination, clinical otorhinolaryngology examination, laboratory tests (CBC, ESR, BT, CT, PT, INR), and immunological assays (IgM, IgG, and IgA) of serum levels as well as plain radiograph soft tissue lateral view nasopharynx were done.

2.1.2. Operative procedure (cold dissection)

The operation was done under general anesthesia. The patient was placed in the rose position when adenoidectomy was being conducted. The adenoids were removed first followed by removal of the tonsils. Observation was done of the pharynx and the tonsillar bed to detect any primary bleeding (Figs. 1 and 2).

2.1.3. Postoperative follow-up

Antibiotics for 10 days, as well as analgesics and antipyretics were given to all patients.

Follow-up was done on first day to monitor nutrition, respiration, and bleeding; on first and second weeks, for healing and complications as wound infection; and after 1 and 3 months of surgery, for laboratory studies (IgA, IgM, and IgG).

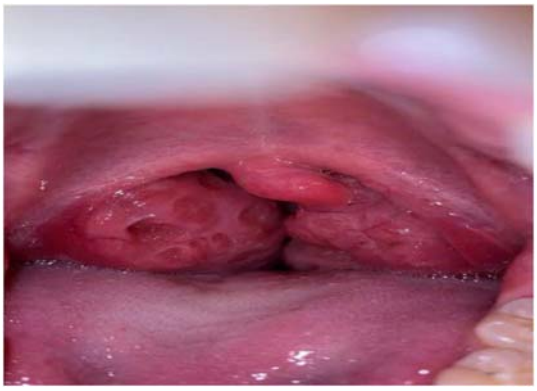

Fig. 1. Throat before tonsillectomy.

Fig. 2. Throat after tonsillectomy.

2.2. Sample collection

IgA, IgG, and IgM levels in the serum of 3 ml of venous blood were determined by centrifugation at 5000 rpm for 10 min after taking the blood from the patients under full aseptic conditions and stored at room temperature for 10 min.

2.3. Determination of IgG, IgM, and IgA levels in serum

The standard sandwich enzyme-linked immunosorbent assay kit was used.

Anti-IgA, anti-IgM, and anti-IgG antibodies had been prepared and then coated onto 96-well plates. IgA, IgG, and IgM can be detected in the samples when they react with the anti-IgA, anti-IgG, and anti- IgM antibodies that were adsorbed to the surface of polystyrene microtiter wells. As a detecting antibody, the anti-IgG antibodies conjugated with the horseradish peroxidase (HRP) were used. The samples and the HRP conjugated detection antibodies were added to the wells and then mixed and incubated. Washing was done to remove the unbound conjugates. Tetramethylebenzidine

was added as achromogenic substrates that help in visualization of HRP enzymatic activity. Tetramethylebenzidine was catalyzed by HRP to create a blue color product that turned to yellow when acidic stop solution was added. The density of yellow coloration detected the amount of the IgG, IgM, and IgA sample captured in the plate. The concentrations of IgG, IgM, and IgA were determined by measuring the absorbance at 450 nm in a microplate reader.

2.4. Statistical analysis

The data were recorded on an 'investigation report form.' These data were tabulated, coded, and analyzed using SPSS (Statistical Package for the Social Sciences Armonk, NY:IBM Corp), version 26 to get descriptive statistics such as mean, SD, numbers, and percentages. In the statistical comparison between the different groups, the significance of difference was tested using paired *t* test, which was used to compare between mean of variable of numerical data in the two different points. To be statistically significant, the *P* value was set to be below 0.05.

3. Results

A total of 60 children were included in this study; 21 of them lost 3 months postoperatively and only 39 children who complete the study. There were 21 (53.8%) females and 18 (46.2%) males, with age up to 3 years (Table 1).

One month after surgery, the IgG serum level was decreased from the preoperative level ($P = 0.005$) (Table 2). Three months postoperatively, IgG levels were not significantly different from the preoperative level ($P = 0.16$) (Table 3). The IgG level was higher after 3 months postoperatively than 1 month postoperatively in follow-up assessment ($P < 0.001$) (Table 4).

The IgM level was lower in 1 and 3 months postoperative follow-up assessments than the preoperative level ($P < 0.001$) (Tables 5 and 6). The level of IgM was statistically significant higher after 3 months postoperatively than 1 month postoperatively in follow-up assessment ($P = 0.03$) (Table 7).

The IgA level was lower in 1 and 3 months postoperative follow-up assessments than the preoperative level ($P < 0.001$) (Tables 8 and 9). The level of IgA 3 months postoperatively was not significantly different from its level 1 month postoperatively ($P = 0.14$) (Table 10).

Table 1. The study group regarding age and sex.

	n (%)
Age	
<3	12 (30.8)
3	27 (69.2)
Sex	
Female	21 (53.8)
Male	18 (46.2)

Table 2. Comparison of preoperative and 1-month postoperative IgG levels.

	Mean	SD	Paired *t* test	*P* value
IgG				
Preoperative	1159.49	182.26	2.69	0.005
After 1 month	1112.18	162.06		

Table 3. Comparison of preoperative and 3-month postoperative IgG levels.

	Mean	SD	Paired *t* test	*P* value
IgG				
Preoperative	1159.49	182.26	1.02	0.16
After 3 months	1185.97	202.26		

Table 4. Comparison of after 1-month postoperative and 3-month postoperative IgG level.

	Mean	SD	Paired *t* test	*P* value
IgG				
After 1 month	1112.18	162.06	4.71	<0.001
After 3 months	1185.97	202.26		

Table 5. Comparison of preoperative and 1-month postoperative IgM level.

	Mean	SD	Paired *t* test	*P* value
IgM				
Preoperative	149.21	43.40	5.77	<0.001
After 1 month	124.00	48.12		

Table 6. Comparison of preoperative and 3-month postoperative IgM levels.

	Mean	SD	Paired *t* test	*P* value
IgM				
Preoperative	149.21	43.40	4.57	<0.001
After 3 months	131.38	49.52		

Table 7. Comparison of 1-month postoperative and 3-month postoperative IgM levels.

	Mean	SD	Paired *t* test	*P* value
IgM				
After 1 month	124.00	48.12	1.91	0.03
After 3 months	131.38	49.52		

Table 8. Comparison of preoperative and 1-month postoperative IgA levels.

	Mean	SD	Paired *t* test	*P* value
IgA				
Preoperative	180.74	90.49	6.79	<0.001
After 1 month	148.31	90.27		

Table 9. Comparison of preoperative and 3-month postoperative IgA levels.

	Mean	SD	Paired *t* test	*P* value
IgA				
Preoperative	180.74	90.49	7.44	<0.001
After 3 months	144.82	97.90		

Table 10. Comparison of 1-month postoperative and 3-month postoperative IgA levels.

	Mean	SD	Paired *t* test	*P* value
IgA				
After 1 month	148.31	90.27	1.11	0.14
After 3 months	144.82	97.90		

4. Discussion

The palatine tonsils are two cores of lymphoid tissue that present in the oropharynx palatine tonsils; adenoids, tubal tonsil, and lingual tonsil form the Waldeyer's ring [8].

Located near the entry of the aerodigestive tract, they come in direct touch with numerous pathogens entering the body via mouth contact [4].

The palatine tonsils have a vital role in humoral as well as cellular immunity. They have B and T lymphocytes. B cells can mature and create a wide variety of immunoglobulins [4].

Upper airway obstruction and obstructive sleep apnea syndrome are the most common adverse effects of the enlargement of the tonsils and the adenoids in pediatric, and the most common treatment is adenotonsillectomy [9].

The prevalence of sleep apnea in children related to adenoid and tonsillar hypertrophy has grown in recent years as a result of the pollution of the environment and an increase in allergic responses. Surgery is still the choice of treatment.

The possible effects of adenotonsillectomy are still debatable. The absence of long-term follow-up assessment after tonsillectomy may be a contributing factor [5].

Therefore, our aim was to study the tonsillectomy effects on humoral immunity markers in children with obstructive sleep apnea until the age of 3 years. The study was a prospective single-armed study done on 60 patients from the outpatient clinic of Ashmoun General Hospital and Otorhinolaryngology Department of Faculty of Medicine, Benha University.

The present study revealed that IgG reduced after tonsillectomy in the short-term follow-up (after 1 month) but returned to its preoperative level after 3-month follow-up. IgM was reduced after 1 and 3 months of follow-up, although it was higher in 3-month follow-up than in 1-month follow-up. IgA was reduced after 1 and 3-month follow-ups. Although there was reduction of the immunoglobulin levels after surgery, all levels were within the normal range.

In agreement with our results, Yan and colleagues in China in 2019 performed a cohort study to detect the effect of adenoidectomy or adenotonsillectomy on humoral and cellular immunity. They performed a study on 40 children below 3 years who needed adenotonsillectomy owing to adenotonsillar hypertrophy that causes upper airway obstruction. Serum IgG, IgM, IgA, and complements (C3 and C4) for humoral immunity and the cellular immunity markers were tested preoperatively and 1 and 3 months following adenotonsillectomy. They stated that IgA level was reduced after 1 month but other indicators did not alter significantly. Three months postoperatively, all parameters had no significant alternation from their preoperative levels.

They were concluded that adenoidectomy with or without tonsillectomy could diminish the level of IgA in the short period after surgery but not raise the recurrent infection or lower the immunity [5].

Several studies were done to detect the adenotonsillectomy effects on the immune system of children.

In 1994, Böck et al. [10] performed a study on 160 children with adenotonsillar hypertrophy. After surgery, they found a decrease in IgA level but no alternation in the levels of IgM and IgG from their levels before surgery.

In 2002, İkincioğullarõ et al. [11] performed a study on 15 children 4–10 years old and reported that IgA, IgM, and IgG levels in serum were reduced slightly postoperatively than their levels before surgery.

In 2004, Amorós Sebastiá et al. [12] performed a research on 89 children with adenotonsillectomy. They reported that IgG level was reduced after surgery, but returned to normal levels after 4 months. IgA level was slightly reduced, and IgM level was not affected.

In 2006, Faramarzi et al. [13] performed a study on 102 children with adenotonsillectomy. They noticed that after short period (few weeks) of the operation,

the IgA level was raised but the IgM and IgG levels and B lymphocyte count were not affected.

In 2009, Kaygusuz et al. [14] observed that after 1 month of tonsillectomy, the IgM, IgA, and IgG levels were lower than the preoperative levels. However, after 54 months of operation, the IgM, IgG, and IgA levels had no statistically significant differences with the levels of the healthy controls.

In 2012, Nasrin and colleagues performed an observational study on children with chronic tonsillitis. IgG, IgM, and IgA levels were measured. The patient group (group A) had tonsillectomy, and the control group (group B) included age-matched children who never had tonsillectomy. After 1 month of tonsillectomy, they noticed that the level of IgG had a minimal decrease but IgM and IgA had slightly higher levels than their preoperative levels. IgG, IgM, or IgA levels in group A were not significantly different from their levels in group B.

Three months postoperatively, the IgG level was reduced ($P < 0.01$); otherwise, IgA and IgM were not affected when compared with their preoperative levels in group B [15].

In 2013, Pires Santos et al. [16] founded that adenotonsillectomy did not adversely affect children's cellular and humoral immunity in short or long term.

In 2014, Dai and colleagues performed a study on 57 children who had obstructive sleep apnea with tonsil hypertrophy, divided into partial tonsillectomy group and other tonsillectomy group. They noticed that in the tonsillectomy group, the IgG, IgA, and IgM levels were reduced after 1 month of the operation but returned to normal levels after 3 months. However, in the partial tonsillectomy group, they minimally decreased but with no significant difference [17].

In 2018, Cassano et al. [18] performed a study on 28 children with obstructive sleep apnea syndrome as a result of adenotonsillar hypertrophy and stated that IgG, IgA, and IgM levels were not significantly affected after adenotonsillectomy.

In 2020, Radman et al. [19] found that children with tonsillectomy had lower levels of IgA, IgM and IgG in serum.

The size of the study sample was small and the follow-up period was short. These factors may affect the study.

5. Conclusion

One month after surgery, the IgG level was reduced but still in the normal range. No significant changes at 3 months postoperatively when compared with the preoperative level. At 1 and at 3 months after the surgery, the IgM and IgA levels were lower than their preoperative levels but they were still in the normal range.

Tonsillectomy lowers humoral parameters but does not affect immune function.

5.1. Recommendations

Long-term follow-up and further large-size studies are needed to monitor the immunological status on children with tonsillectomy.

Conflict of interest

There are no conflicts of interest.

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