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# Serum Immunoglobulin Values and Lymphocytes' Phenotypes, in Children Undergoing Adneotonsillectomy

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## Abstract

**Background:** Chronic tonsillitis in childhood is a leading cause of adneotonsillectomy and there is a question for a long time, is there any risk of immune impairment after adneotonsillectomy? So we decided to evaluate immunologic parameter in children before and after adenoidectomy.

**Methods:** In this case control study, we enrolled 25 children (14 male) who were candidate for adneotonsillectomy in Rasoul Akram Hospital. We get adequate blood samples in three intervals (before surgery and two and six months after operation) from our patients to measure immunoglobulins IgA, IgM, IgG and IgG subclasses by nephelometric assay and to count lymphocyte subsets (markers CD2, Cd3, CD4, CD8, CD19, CD23 and CD56) by flow cytometry and ELISA methods.

**Results:** IgM, IgG and IgA had no significant changes postoperatively. IgG subclasses (IgG1, IgG2, IgG3 and IgG4) had small rises after operation. According to lymphocyte phenotypes, CD4+, CD23+ and CD56+ cells and CD4/CD8 ratio were constant through the three intervals. Mean CD8+ cells had significant decrease during these intervals (P value = 0.02) especially between specimens before and two months after operation (P value = 0.03). Serum value of CD19+ significantly decrease two (P = 0.00) and six months (P = 0.00) post tonsillectomy.

**Conclusions:** Adneotonsillectomy in the short time had no effect on immune system. Next studies must be design for long term evaluation of immune system of children with chronic tonsillitis.

**Keywords:** Adneotonsillectomy; Child; Lymphocyte phenotypes; Immunoglobulin

## Introduction

Tonsil as lymphoid organ is small at child birth and enlarges until around 14 years old and will regress in the adolescent. Children with tonsilar hypertrophy had some pathologic symptoms [1, 2]. These patients had obstruction in respiratory tract and some problems in eating which lead to reduce in their appetite. Tonsilar hypertrophy might cause pharyngeal obstruction and sleep related difficulties [3]. It is known that tonsils are one of the main parts of immune system against pathogens of upper respiratory tract. Tonsil is part of Waldeyer's ring and was known as reactive lymphoid organ that present high concentration of B and T cell lymphocytes in response to pathogens [4, 5]. But In most of children who inferred to primary clinic, physician due to inflammation in their tonsils usually suggested tonsillectomy as one of suitable operations for them [6].

We know that inflammation of human tonsil cause presenting many surface crypts which are specific components of lymphoepithelial symbiosis, which play an important role in immune response [4]. Research studies showed that T and B cell lymphocyte subsets are increased in tonsillitis [7, 8]. Various investigators have reported high serum levels of IgG and IgA in patients with chronic tonsillitis [5, 9]. However, some studies reported that decreased in functions of local and systemic immunity might cause inflammation and/or hypertrophy of adenoids and tonsils [10-12]. Aim of the present study was assessment serum values of immunoglobulins and lymphocytes phenotypes after tonsillectomy operation

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**Table 1.** Mean and Standard Deviation of Serum Values of Immunoglobulins in Our Children

| | | Case | | Control | | P-value |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | |
| IgM | Prior operation | 1.52 | 1.33 | 1.26 | 1.23 | 0.35 |
| | Post operation (two months) | 1.76 | 2.09 | 1.56 | 1.89 | 0.64 |
| | Post operation (six months) | 1.62 | 2.17 | 1.45 | 2.25 | 0.73 |
| IgA | Prior operation | 1.37 | 0.78 | 1.44 | 1.02 | 0.75 |
| | Post operation (two months) | 1.27 | 0.71 | 1.32 | 0.89 | 0.79 |
| | Post operation (six months) | 1.23 | 0.61 | 1.29 | 0.79 | 0.72 |
| IgG | Prior operation | 10.37 | 2.87 | 10.15 | 2.65 | 0.72 |
| | Post operation (two months) | 10.52 | 2.16 | 10.44 | 2.12 | 0.87 |
| | Post operation (six months) | 11.05 | 2.50 | 10.89 | 1.45 | 0.68 |
| IgG1 | Prior operation | 40.51 | 19.34 | 41.44 | 19.38 | 0.83 |
| | Post operation (two months) | 40.02 | 17.11 | 42.11 | 18.12 | 0.60 |
| | Post operation (six months) | 46.29 | 16.11 | 47.32 | 17.12 | 0.77 |
| IgG2 | Prior operation | 100.66 | 37.08 | 99.86 | 35.46 | 0.92 |
| | Post operation (two months) | 105.26 | 41.13 | 103.23 | 39.12 | 0.83 |
| | Post operation (six months) | 101.59 | 30.84 | 99.87 | 29.47 | 0.80 |
| IgG3 | Prior operation | 25.80 | 9.90 | 26.34 | 10.12 | 0.81 |
| | Post operation (two months) | 22.29 | 10.56 | 24.32 | 11.65 | 0.43 |
| | Post operation (six months) | 22.80 | 8.79 | 23.78 | 9.67 | 0.65 |
| IgG4 | Prior operation | 21.67 | 16.13 | 22.87 | 17.25 | 0.18 |
| | Post operation (two months) | 23.92 | 19.24 | 24.89 | 21.34 | 0.84 |
| | Post operation (six months) | 22.66 | 16.50 | 23.76 | 17.04 | 0.77 |

in children.

## Material and Method

The present case control study was performed on a total of 25 children (14 boys and 11 girls; aged 3-16 years, median age 8 years) at the ENT Clinic, at Rasoul Akram hospital in Iran medical university. This study was confirmed in ethical committee of Iran medical university.

Twenty five children with tonsillectomy indication were included to the study as case group. A standard anesthetic protocol was applied to all included children. Our ENT specialist used standard surgical techniques and controlled physiological parameters of our patients including respiratory rate, pulse rate, blood pressure and temperature during the

**Table 2.** Comparison of Lymphocyte Phenotypes in Our Study Samples and Control Group

| Lymphocyte markers | | Case group | | Control group | | Significances |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | |
| CD2 | Prior operation | 74.54 | 4.47 | 75.15 | 5.27 | 0.60 |
| | Post infection (2 months) | 75.66 | 5.06 | 74.46 | 4.08 | 0.21 |
| | Post infection (6 months) | 69.79 | 14.01 | 71.54 | 12.46 | 0.54 |
| CD3 | Prior operation | 62.17 | 7.90 | 63.26 | 8.11 | 0.55 |
| | Post infection (2 months) | 63.90 | 6.60 | 64.36 | 7.44 | 0.78 |
| | Post infection (6 months) | 59.66 | 10.43 | 57.78 | 9.86 | 0.43 |
| CD4 | Prior operation | 33.07 | 7.39 | 36.18 | 5.32 | 0.02 |
| | Post infection (2 months) | 35.40 | 11.03 | 36.18 | 5.32 | 0.61 |
| | Post infection (6 months) | 32.88 | 12.51 | 36.18 | 5.32 | 0.05 |
| CD8 | Prior operation | 28.90 | 6.31 | 25.85 | 4.76 | 0.00 |
| | Post infection (2 months) | 28.31 | 6.08 | 25.85 | 4.76 | 0.03 |
| | Post infection (6 months) | 24.28 | 4.76 | 25.85 | 4.76 | 0.15 |
| CD4/CD8 | Prior operation | 1.25 | 0.50 | 1.41 | 1.15 | 0.51 |
| | Post infection (2 months) | 1.36 | 0.64 | 1.41 | 1.15 | 0.83 |
| | Post infection (6 months) | 1.43 | 0.64 | 1.41 | 1.15 | 0.93 |
| CD19 | Prior operation | 15.47 | 5.17 | 18.42 | 5.4 | 0.02 |
| | Post infection (2 months) | 13.70 | 3.61 | 18.42 | 5.4 | 0.00 |
| | Post infection (6 months) | 13.93 | 3.59 | 18.42 | 5.4 | 0.00 |
| CD23 | Prior operation | 4.63 | 3.02 | 4.54 | 2.12 | 0.86 |
| | Post infection (2 months) | 6.03 | 2.48 | 5.89 | 2.45 | 0.80 |
| | Post infection (6 months) | 7.18 | 3.09 | 6.35 | 4.08 | 0.34 |
| CD56 | Prior operation | 9.80 | 6.21 | 9.39 | 4.69 | 0.71 |
| | Post infection (2 months) | 10.05 | 5.63 | 9.39 | 4.69 | 0.55 |
| | Post infection (6 months) | 3.30 | 2.34 | 9.39 | 4.69 | 0.00 |

surgery. Our control group consists of 100 healthy age and sex matched children (58 boys and 42 girls; aged 4-16, median age 7 years) who inferred the clinic due to other causes.

**Immunologic measurements**

Blood samples were taken from children one day before tonsillectomy (as preoperative sample) and two and six months after tonsillectomy (as post operative samples). We obtained a volume of four milliliters of venous blood from our children. After clotting, the serum was separated and kept at −20 °C until immunological analyzing. We measured serum values of immunoglobulins M, A and G (with its subclasses) and CD2+ CD3+, CD4+ CD8+, CD19+, CD23 and CD56+ as lymphocytes phenotypes. We measured serum values of immunoglobulins via the standard nephelometric study and its kit (Nima Pooyesh Teb Co). Lymphocyte phenotypes were measured by flow cytometry study in the peripheral blood samples by using (Kavian Company) and Elisa (Nima Pooyesh Teb Co.)

**Statistical analysis**

Data were analyzed using SPSS for Windows version 16. Quantitative variables were presented in central indices (Mean and Standard deviation) and qualitative variables were presented in frequency tables (frequency and percentages). General linear model (ANOVA test from repeated measures results) was used for comparison of means of study variables. Benferroni (Post hoc test) was used for comparison between means after significant results of repeated measured ANOVA tests. Two-tailed significance level of 0.05 was used to detect difference between variables.

## Results

We did not see significant differences between pre and postoperative values of IgG, IgM and IgA in our case and control groups ($P > 0.05$). We saw only non significant decrease in postoperative serum IgA, IgG1 and IgG3 value and non significant increase in serum value of IgM, IgG, IgG2 and IgG4 subclasses (Table 1).

Serum value of CD8+, CD23+, CD56+ and CD4+/CD8+ ratio had no significant changes after tonsillectomy ($P > 0.05$). Serum values of CD8+ had significant changes after tonsillectomy ($P = 0.02$). Post hoc results showed that mean of CD8+ in six months after tonsillectomy significantly decreased in comparison with its value in two months after surgery ($P = 0.03$). Serum value of CD19+ had significant changes in our measurements ($P = 0.01$). Post hoc results showed that mean of CD19+ in two months after surgery had significant decrease in comparison with preoperative value ($P = 0.01$).

In comparison of lymphocytes phenotypes between case and control group, we observed no significant changes in most of lymphocytes phenotypes in our cases. Only serum level of CD4+ in our patients was significantly lower in preoperative ($P = 0.00$) and six months post tonsillectomy ($P = 0.01$) in comparison with control group. But this decline in two months after tonsillectomy was not significant ($P = 0.21$). Serum value of CD19+ prior ($P = 0.01$), two ($P = 0.00$) and six months ($P = 0.00$) post tonsillectomy was significantly lower than values in control group (Table 2).

## Discussion

Results of present study showed that serum value of immunoglobulins had no significant differences after adneotonsillectomy and only non significant decreases were seen in them. Previous studies showed that concentration of lymphocytes in tonsilar tissues of children had higher than adults and antigen stimulus was presented from infected tonsil and before adneotonsillectomy immunoglobulins value of sick tonsil had in high amounts [13, 14]. El-Asshmawy et al in their study found that serum values of IgG and IgA were increased in chronic tonsillitis but IgM value had not similar pattern. They added two months after tonsillectomy increased values of immunoglobulins were significantly reduced [14]. Saniz et al study, showed increase in serum values of immunoglobulins preoperatively and significantly decline after tonsillectomy [15]. Zielnik-Jurkiewicz et al in their study reported that increase in preoperative higher values of immunoglobulins including IgA and IgG was happened in patient with hypertrophic adenoid and tonsils in comparison with control group and significantly decreased one month after tonsillectomy [4]. In against our study, Moreno et al in their studies reported that higher values of immunoglobulins even after tonsillectomy. They believed that this increase in immunoglobulin values was due to lymphocytes stimulation by bacterial antigens [16]. In against of above studies, we did not have postoperatively significant decline in immunoglobulin values. We guess that ending of continues bacterial antigen stimulation of tonsilar tissue might be responsible for slightly decrease in serum values of IgG, IgA and IgM in present study after adneotonsillectomy.

Significant differences in serum values of CD8+, CD19+ and CD56+ lymphocyte CD markers after tonsillectomy were seen in our study. In comparison with control data, Serum value of CD4+ had significant changes prior and six months after tonsillectomy. Serum value of CD19+ prior, two and six months post tonsillectomy had significant differences.

The tonsils are getaway of alimentary and respiratory system and had contact with several microorganisms and antigens of food and inhaled air [17]. Tonsils due lymphatic activation might have main role in local immunity [4, 18]. Some research findings showed that CD4+ and CD25+ had

regulatory function on T lymphocytes in blood and in the tonsils and near to ten percent of T cells are represented by tonsils [19]. Previous studies indicated that preoperative increase CD8+ values was significantly postoperatively decreased and even after six months after operation reach to equal value with control group [4]. Prusek et al in their studies reported normal values of T and B lymphocytes in children 4 - 10 months after tonsillectomy [20]. Bock et al. refused inhibition of immune system development in children after tonsillectomy [21]. Sennaroglu et al. had appositive idea with other studies. They believed that tonsillectomy can improve immune system of children due to increase in abnormal neutrophyl chemotaxis [22].

According to our results and reviewing other studies on the literature serum immunoglobulin values in children with chronic tonsillitis are increased due to continues bacterial stimulation. Removal of tonsil with tonsillectomy operation can discontinued this stimulation without considerable affects on immune system of children. We suggested that adneotonsillectomy operation must be considered only for children who have chronic tonsillitis. Other next cohort studies for long term follow up of children who undergoing tonsillectomy for assessment other operation indications.

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