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Title: Is Adenoidectomy and/or Tonsillectomy a Risk Factor for Allergic Diseases and Asthma in Adulthood?

Running Head: Is Adenotonsillectomy Risky for Allergy and Asthma?

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ABSTRACT

Objective: To investigate the relationship between adenoidectomy and/or tonsillectomy in childhood and allergic diseases in adulthood.

Materials and Methods: A case-control study of 510 patients (F/M: 379/131) who were followed by our department between January-June 2014 with diagnosis of asthma (248), allergic rhinitis (205), urticaria-angioedema (73), drug allergy (82), food allergy (24) and venom allergy (14) and agreed to participate in the study was conducted using a survey and clinical data. 65 (%12.7) of these patients had

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adenoidectomy and/or tonsillectomy. Out of 65 patients; 41 had asthma, 33 had allergic rhinitis and 28 had other allergic diseases. Patients were evaluated as “above 15 years of age” and “below 15 years of age”.

Results: No relation between history of atopy and adenoidectomy and/or tonsillectomy ($p=0.129$) was detected in both groups, however there was a positive relationship between asthma and patients under the age of 15 with history of tonsillectomy and/or adenoidectomy ($p=0.020$). The risk of asthma was determined to be increased by 1.96 fold among our patients if the patient had been adenoidectomized and/or tonsillectomized (CI:1.14-3.36). No connection was found between atopic and non-atopic asthmatic patients in relation to adenoidectomy and/or tonsillectomy ($p=0.46$). There was no relationship between allergic rhinitis and adenoidectomy and/or tonsillectomy.

Conclusion: Adenoidectomy and/or tonsillectomy in childhood increases the risk of asthma in adulthood while it doesn't increase the risk of atopy. This result can signify the importance of adenoidectomy or tonsillectomy in the pathogenesis of asthma.

Keywords: Asthma, chest diseases, pulmonology, allergy, dermatology, immunology, internal medicine

Introduction

Adenoids and tonsils have significant roles in cellular and humoral immune system. They are also among the essential organs of mucosal immune defense which balances Th1 and Th2 cells. [1] Adenoidectomy and tonsillectomy are common surgical procedures in childhood. However removal of tonsils and adenoids might cause an immunologic imbalance and a rise in atopy or allergic diseases [2]. How adenoidectomy and tonsillectomy affects allergic responses is unknown and different studies show contradictory results. In the review by Kohli et al, the compilation of data suggests a definitive association [3]. On the other hand in the database analysis by Bhattacharjee et al, children had relief from asthma after adenotonsillectomy [4]. None of the studies report long term outcomes and

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acknowledge about the progress of asthma in adulthood. It's crucial to determine if there's a relationship between removal of these organs in childhood and gradual increase in allergy in adulthood.

The aim of the present study was to find out whether previous adenoidectomy and/or tonsillectomy is associated with allergic diseases later in life.

Materials and Methods

Study subjects

Our study was planned as a retrospective cohort study. We recruited 510 patients who were admitted into the xxxx, between January and June 2014. All patients were asked to fill out a formed questionnaire.

Questionnaire

This questionnaire consisted of following questions: age; occupation (officer, housewife, student, other); existence of allergic diseases (asthma, allergic rhinitis, drug hypersensitivity, food allergy, urticaria-angioedema, venom allergy) and age of diagnosis; if had tonsils removed, at what age, reason of removal; if had adenoids removed, at what age, reason of removal; presence of other diseases (nasal polyp, sinusitis, upper respiratory tract infection); history of atopy; any relative with any allergic diseases. The last part of the questionnaire was completed by a physician; asthma severity (using Global Initiative for Asthma Management and Prevention [5]), rhinitis severity (using Allergic Rhinitis and its Impact on Asthma [6]) and skin prick test results.

All subjects gave their written consent and the Local Ethics Committee at xxx, approved the protocol.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences for Windows (SPSS version 16; SPSS, Chicago, Ill., USA). Descriptive statistics were expressed as mean±SD and numbers with percentages. Categorical data was analyzed by Chi-square and Fisher's exact tests and $p < 0.05$ was

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considered to be significant. The relationship analyzed between adenotonsillectomy and asthma and allergic rhinitis using univariate analysis with chi-square tests and univariate odds ratio (uORs) and their 95% confidence intervals (CIs).

Results

Characteristic of the study population

There were total of 510 patients. Mean age was 42.5 ± 13.8 (age range 17-85 years). Male to female ratio was 131:379. Occupations were as following: 30 officer (5.9%), 141 housewife (27.6%), 45 student (8.8%), 294 other (57.6%). 57.5% of patients had positive history of atopy. According to skin prick test results, 46.2% of patients had positive results; 31.1% of them were monosensitized and 25.1% of them were polysensitized. Among the 510 subjects 65 (12.7%) had history of adenoidectomy and/or tonsillectomy (Table 1).

Allergic and other diseases

The most common allergic disease was asthma with a rate of 48.6%, and the following were allergic rhinitis (40.2%). Number of patients with other allergic diseases was lower than asthma and allergic rhinitis. The prevalence of accompanying upper airway diseases 7.3%, 22.2% and 43.5%. for nasal polip, chronic sinusitis, frequent upper respiratory tract infection, respectively. (Table 1)

Patients with adenotonsillectomy

There were 65 patients with adenoidectomy and/or tonsillectomy. Mean age was 44.4 ± 14.7 . Twenty-four patients had operation before age of 15 and thirty-five had operation after age of 15. Six patients didn't remember the age of operation. 66.2% of patients mentioned history of atopy. Distribution of allergic

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diseases of patients with adenoidectomy and/or tonsillectomy can be seen in Table 2.

There is no statistical significance between history of atopy and adenoidectomy and/or tonsillectomy ($p=0.129$).

Asthmatic patients with adenotonsillectomy

There were 41 patients with adenoidectomy and/or tonsillectomy. Mean age was 21.6 ± 16.5 . Eleven patients had operation before age of 15 and twenty-five had operation after age of 15. Five patients didn't remember the age of operation. Twenty-nine (70.7%) patients mentioned history of atopy. In 39.0% of the subjects skin prick test results were positive. The most common group in terms of severity was mild persistent asthma (24.4%) (Table 3).

There was a significant relationship between asthma and adenoidectomy and/or tonsillectomy ($p=0.013$). We also found an important relationship between removal of tonsils or adenoids before the age of 15 and development of asthma.

No relationship has been detected between asthma severity and adenoidectomy and/or tonsillectomy ($p=0.91$). We didn't find a significant difference between atopic and non-atopic patients in terms of adenoidectomy and/or tonsillectomy ($p=0.46$). There was not a significant relationship between the age of operation and the age asthma was diagnosed in patients who had had adenoidectomy and/or tonsillectomy before the age of 15 ($p=0.05$).

The risk of asthma was determined to be increased by 1.96fold in adenoidectomized and/or tonsillectomized among our allergic patients (CI:1.14-3.36).

Allergic rhinitis patients with adenotonsillectomy

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Thirty three patients with a mean age of 44.1 ± 15.5 had adenoidectomy and/or tonsillectomy. Eleven patients had operation before age of 15 and nineteen had operation after age of 15. Three patients didn't remember the age of operation. Thirty (69.7%) patients had a history of atopy. Skin prick tests were positive in 54.5% of the patients. Mild intermittent rhinitis was the most frequent severity form (42.4%). (Table 4)

No relationship was found between allergic rhinitis and adenoidectomy and/or tonsillectomy ($p=0.063$). Relationship between other allergic diseases and adenoidectomy and/or tonsillectomy couldn't be evaluated due to inadequate number of patients.

Discussion

In the present study, we found a significant relationship between asthma and history of adenoidectomy and/or tonsillectomy, especially if the surgery had been performed before the age of 15 years. Patient with a history of adenoidectomy and/or tonsillectomy had a 1.96 fold risk of developing asthma among our allergic patients.

There has been an increase worldwide in the prevalence of atopic diseases such as asthma and allergic rhinitis. Both genetic predisposition and environmental factors play a role in the pathogenesis of allergic diseases. Especially changes in Th1-Th2 balance establish an important cause in the immune system for the development of atopic diseases.[7]

Waldeyer ring is a significant part of the immune system. [1] Adenotonsillectomy is one of the most common pediatric operations. [8] Removal of adenoid and/or tonsillar tissue may cause a decrease in the humoral or cellular immune response. In correlation with the hygiene hypothesis, a decrease in this immune response may cause an increase in the risk of atopic diseases in the long term. [1] In some studies, a

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minor decrease of serum Ig levels after adenoidectomy and tonsillectomy has been shown.[9,10] After adenoidectomy and tonsillectomy, a change in the response has been reported in not only humoral but also cellular immune system. A couple of authors stated changes in B and T cells specifically in different T cell subtypes. [10-13] Do such short term changes in immune system continue in the long term? Data on this subject is limited. Today, immunologic consequences of surgical removal of Waldeyer ring and relationship with allergic diseases has been studied and contradictory results has been found. [3, 4, 7, 14]There is no data related to the defect of the immune system in the long-term. In a longitudinal cohort study, adenotonsillectomy operation performed in childhood was found not to be a cause for an increase in the atopy frequency in the early adulthood. [7] In the study of Suvilehto and friends, allergy and asthma diagnosis was determined to be more for patients who had recurrent respiratory infections before the age of 7 and had adenoidectomy. [9] In a cross sectional study in Turkey, history of tonsillectomy was proven to increase eczema risk 2.10 fold.[14]In similar study by Akcay et al. adenoidectomy and tonsillectomy was associated with increased risk of asthma [15].

In 1989, Strachan proposed a hypothesis called “hygiene hypothesis” stating that hygienic environment increases the development of atopic diseases. Facing allergens, viral and bacterial infections in childhood shifts immune system from Th2 to Th1.[16] Moreover, lower respiratory infections in early childhood such as RSV and measles increase the risk of asthma.[17-19] What if the increase in the asthma risk is arises from frequent upper respiratory infections and not the adenoidectomy? Mattila and friends looked for the answer in their study and detected the risk of asthma to be higher in children who were operated due to recurrent otitis media. [14] In a survey study that was done with 209 children between the ages 3 and 8 who had history of chronic or recurrent otitis media, asthma frequency, nasal eosinophilia and skin test positivity was found to be increased.[20] In another study, development of atopy and sensitivity was found to be positively correlated with adenoidectomy or tonsillectomy, history of recurrent upper respiratory infection and frequent use of antibiotics.[21] We planned and encouraged further studies in larger patient populations to reveal the predicted results on the effect of especially adenoidectomy on atopy.

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Considering these results, children must be evaluated attentively before deciding to remove tonsils or adenoids, because there are some arguments in literature on whether adenoidectomy or tonsillectomy is necessary. In Van Staaïj and friends' study, despite healing within six months after removal of adenoidectomy and/or tonsillectomy done due to recurrent upper respiratory infections, no difference was found in the control group in twenty four month period in recovery. [22] Moreover, long term effects of these operations are unknown.

Our study, contrary to studies in literature, is a retrospective cohort study. For this reason, the most important limitation in our study is the lack of a control group and questioning the ratio of adenotonsillectomy retrospectively in patients who were admitted to our allergy clinic. But, our goal in planning this study was to determine the ratio of patients with adenotonsillectomy in the population of allergic patients. Moreover, we detected that having had adenoidectomy and/or tonsillectomy increased the risk for development of asthma 1.96 fold. We detected a marginally significant relationship between having had adenoidectomy and/or tonsillectomy before age of 15 and the age that asthma developed. Does adenotonsillectomy at early age increase the risk of asthma? We believe, in order to find out an answer to our question, multicenter prospective cohort studies in larger patient groups are needed.

Conclusion

Our findings reveal the ratio of adenoidectomy and/or tonsillectomy to be higher in allergic patient populations, especially in asthmatic patients, and show that if these surgeries are performed at early ages they increase the risk of developing asthma. Underlying mechanisms must be studied to enlighten the relationship.

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Table 1: Characteristics of all patients

N	510
Age (Mean±SD)	42.5±13.8
Female/Male n (%)	379/131 (74.3-25.7)
History of atopy n (%)	293 (57.5)
Prick test positivity n (%)	192 (46.2)
Monosensitized/Polisensitized n (%)	129/63 (31.1/25.1)
Familial history of atopy n (%)	245 (48)
Adenoidectomy and/or tonsillectomy n (%)	65 (12.7)
Allergic diseases	
Asthma	248 (48.6)
Allergic rhinitis	205 (40.2)
Drug allergy	82 (16.1)
Food allergy	24 (4.7)
Venom allergy	14 (2.7)
Chronic urticaria and angioedema	73 (14.3)
Others	
Nasal polip	37(7.3)
Chronic sinusitis	113(22.2)
Frequent upper respiratory tract infection	222(43.5)

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Table 2: Demographic characteristics of patients with or without history of adenoidectomy and/or tonsillectomy

	Previous tonsillectomy and/or adenoidectomy	No previous tonsillectomy and/or adenoidectomy
N	65	445
Age (Mean±SD)	44.4±14.7	42.7±13.7
Age of adenoidectomy and/or tonsillectomy (Mean±SD)	21.6 ±16.5	
0-15 years (n,%)	24 (36.9)	
Age (mean±SD)	9.2±3.8	
>15 years(n,%)	35 (53.8)	
Age (mean±SD)	31±16.3	
Female/Male, n (%) (min-max)	53/12 (81.5-18.5)	326/119 (73.3-26.7)
History of atopy, n (%)	43 (66.2)	250 (56.2)
Prick test positivity, n (%)	22 (33.8)	170 (38.2)
Monosensitized/Polisensitized, n (%)	14/8 (63.6-36.4)	115/55 (25.8-12.4)
Familial history of atopy, n (%)	36 (55.4)	209 (47)
Allergic disease		
Asthma	41 (63.1)	207 (46.5)
Allergic rhinitis	33 (50.8)	172 (38.7)
Drug allergy	14 (21.5)	68 (15.3)
Food allergy	3 (4.6)	21 (4.7)
Venom allergy	1 (1.5)	13 (2.9)
Chronic urticaria/angioedema	10 (15.4)	104 (23.4)
Others		
Nasal polip	5 (7.7)	32 (7.2)
Chronic sinusitis	22 (33.8)	91 (20.4)

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Table 3: Demographic characteristics of asthmatic patients with or without history of adenoidectomy and/or tonsillectomy

	Previous adenoidectomy and/or tonsillectomy	No previous adenoidectomy and/or tonsillectomy
N (%)	41 (63.1)	207 (46.5)
Age (Mean±SD)	21.6±16.5	44.9±13.2
Age of adenoidectomy and/or tonsillectomy (Mean±SD)	21.6±16.5	
0-15 years (n,%)	11 (26.8)	
Age (mean±SD)	8.9±3.7	
>15 years (n,%)	25 (61)	
Age (mean±SD)	32.6±17.7	
Female/Male n (%)	35/6 (85.4-14.6)	166/41 (80.2-19.8)
Atopic/Nonatopic (%)	29/12 (70.7-29.3)	134/73 (64.7-35.3)
Prick test positivity, n (%)	16 (39)	73 (35.3)
Monosensitized/Polisensitized, n (%)	10/6 (62.5-37.5)	48/25 (23.2-12.1)
Asthma severity n (%)		
Mild intermittent	8 (19.5)	46 (22.2)
Mild persistent	16 (39)	86 (41.5)
Moderate persistent	10 (24.4)	41 (19.8)
Severe persistent	7 (17.1)	34 (16.4)

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Table 4: Demographic characteristics of allergic rhinitis patients with or without history of adenoidectomy and/or tonsillectomy

	Previous adenoidectomy and/or tonsillectomy	No previous adenoidectomy and/or tonsillectomy
N	33	172
Age (Mean±SD)	44.1±15.5	38.06±12.2
Age of adenoidectomy and/or tonsillectomy (Mean±SD)	21.7±15.2	
0-15 years (n,%)	11(45.8)	
Age (mean±SD)	9.2±4.0	
>15 years(n,%)	19(54.3)	
Age (mean±SD)	29.7±14.3	
Female/Male n (%)	23/10 (69.7-30.3)	127/45 (73.8-26.2)
History of atopy (%)	30 (90.9)	158 (91.9)
Prick test pozitivitiy, n (%)	18 (54.5)	112 (65.1)
Monosensitized/Polisensitized, n (%)	11/7 (61.1-38.9)	77/35 (44.8-20.3)
Rhinitis severity n (%)		
Mild intermittent	14 (42.4)	79 (45.9)
Severe intermittent	10 (30.3)	35 (20.3)
Mild persistent	5 (15.2)	33 (19.2)
Severe persistent	4 (12.1)	25 (14.5)

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