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Review article

The effect of tonsillectomy on the immune system: A systematic review and meta-analysis

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ABSTRACT

Importance: The immunological sequelae of tonsillectomy in children have been a source of debate among physicians and a continuous concern for parents. Contradictory pertinent results exist in the literature.
Objective: To understand the real effect of tonsillectomy on the immune system.
Data sources: MEDLINE, EMBASE and COCHRANE.
Study selection: Articles addressing the effect of tonsillectomy on the immune system, up to Dec 2014. Related keywords and medical subject headings were used during the search. The abstracts were reviewed to determine suitability for inclusion based on a set of criteria. Manual crosscheck of references was performed.
Data extraction: We checked the tests results and the conclusion of each study to classify it as supporting or refuting the hypothesis of a negative effect of tonsillectomy on the immune system.
Results: We reviewed 35 articles, published between 1971 and 2014, including 1997 patients. Only Four studies (11.4%), including 406 patients (20.3%) found that tonsillectomy negatively affects the immune system. We performed a separate meta-analysis on various reviewed humoral and cellular immunological parameters (e.g. total and specific serum Ig's, SecIgA, cellular immunity, and Ag specific Ig). There is more evidence to suggest that tonsillectomy has no negative clinical or immunological sequalae on the immune system. Study limitations included heterogeneity in the diagnostic tools, timing of testing, indication for tonsillectomy and patients' age.
Conclusion: It is reasonable to say that there is enough evidence to conclude that tonsillectomy has no clinically significant negative effect on the immune system. It will be important for future studies to uniformly use both preoperative and control laboratory tests' levels to compare the postoperative levels with, to have short and long term follow-up levels, and to include both humoral and cellular immunity in their measurements.
Relevance: The results should reassure both surgeons and parents that tonsillectomy has no proven clinical sequalae. If more research is to be done in the future, it should be performed in a standardized way to avoid the heterogeneity seen in the literature.

Contents

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1. Introduction

Palatine tonsils produce antibodies via their B cells. Maximum tonsillar growth occurs between 4 and 7 years of age [1], while involution begins by the age of 14 years resulting in little lymphoid tissue remaining at the age of 60 years [2].

The immunological sequalae of tonsillectomy in children has long been a source of debate among physicians and a continuous concern for the parents. Many studies tried to understand the real effect of this common procedure on the various components of the immune system whether on the short or long term. This resulted in a heterogeneous pool of information sometimes creating confusion or uncertainty regarding this issue.

For that reason, we found it important to conduct a systematic review to carefully look at all the available studies and try to analyze the effect of tonsillectomy on each component of the immune system, hoping to answer the following questions: "does tonsillectomy negatively affect the immune system?","if it does, to what extent?", and "which components are mostly affected?"

2. Materials & methods

A MEDLINE, EMBASE and COCHRANE search was conducted to include all articles addressing the effect of tonsillectomy on the immune system, up to Dec 2014. Various related keywords and medical subject headings were used during the search; such as, (tonsillectomy AND humoral immunity) OR (tonsillectomy AND cellular immunity) OR (tonsillectomy AND immunity) OR (tonsillectomy AND Immune system).

The obtained titles and abstracts were reviewed to determine suitability for inclusion based on set criteria. Manual crosscheck of the included articles' references was performed. We excluded descriptive articles and narrative reviews, and patients duplicated in studies.

Inclusion criteria included: (1) aim of the study should be the effect of tonsillectomy with or without adenoidectomy on the immune system; (2) the study should measure quantitatively or qualitatively immunological factors; (3) the study should compare the obtained results to preoperative values and/or controls; (4) the study should be published in the English language.

A study was considered supporting the hypothesis that tonsillectomy has a negative effect on the immune system when the lab results confirmed that and the conclusion of the authors suggested that tonsillectomy has a negative impact on immunity or at least raised a significant concern regarding its negative effect on the immune system.

2.1. Statistical analysis

The reviewed studies addressed different parameters, so a meta-analysis could only be done on individual parameters, taking into consideration the different interpretations used among various studies. We tried, within the limitations of the information in each study, to classify the results as: no significant change (when no noticeable change in the level of the studied immunological factor is reported); decrease or increase to normal (when a noticeable change is reported); a significant decrease or increase (when statistically significant change is reported); below or above normal (when the level is reported as below or above the control levels and or a normal values' reference). We also looked at the effect of using controls vs. only using preoperative values to compare and report results.

The result of each individual meta-analysis was reported as a percentage of studies (including percentage of enrolled patients) showing negative vs. no effect (or positive) on the particular immunological factor. Comparison was made between both groups within the same meta-analysis with respect to age range, duration of follow-up and presence of control group.

3. Results

The process of articles' screening and selection is summarized in Fig. 1. We searched the articles that were written in the English literature, with available abstract and including only studies conducted on humans.

We reviewed 35 articles, published between 1971 and 2014 [3–37]. These included 1997 patients, aged 1.5 to 55 years. Seven studies included patients older than 18 years in conjunction with pediatric patients. We could not isolate the data of the pediatric patients from those of adults within each of these articles, so we kept them combined and pointed to any reported difference in results within each article, where applicable. Another reason we did not exclude these studies is the fact that some included different age groups for comparison which was quite useful [8,10,25], while others looked at the sequalae of tonsillectomy in young adults who had tonsillectomy in the past [11]. The timing of postoperative testing varied from 10 days to 11 years, with 2 studies not specifying the timing. This variation in timing provided information about the short and long-term immunological consequences of tonsillectomy. The indication for tonsillectomy was recurrent or chronic tonsillitis in 14 studies, adenotonsillar hypertrophy in 5, both indications in 11 and unspecified in 5. The distribution of the various studied parameters among the reviewed manuscripts is summarized in Fig. 2.

Based on the conclusion of each study and taking into consideration the tests' values and their clinical significance where applicable, we could classify 4 studies as implying a negative impact of tonsillectomy on the immune system or at least raising a significant concern regarding its negative effect on immunity. Table 1 summarizes the various tests performed, and the conclusion of each study. The results were divided into 2 groups: one studying the effect of tonsillectomy on the humoral immunity (Table 2) and another studying the effect of tonsillectomy on the cellular immunity (Table 3).