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Adenoidectomy and/or tonsillectomy in childhood is not associated with atopic disease later in life

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Summary

Objective To investigate the association between adenoidectomy and/or tonsillectomy in childhood and asthma, allergic rhinitis (AR), and eczema in adolescence.

Methods Longitudinal birth cohort study of 1328 members born in the city of Nijmegen. Information on ear–nose–throat surgery was documented at 2, 4, and 8 years of age. In 1055 cohort members the incidence of asthma, AR, and eczema at 21 years of age was determined using the International Study of Asthma and Allergic disease in Childhood Core Questionnaire. To analyse the association between adenoidectomy and/or tonsillectomy in childhood and asthma, AR, and eczema at age 21 years, relative risks (RR) were calculated.

Results Six hundred and ninety-three (66%) members completed the questionnaire at age 21 years, of whom 104 (15%) had undergone adenoidectomy and/or tonsillectomy and 262 (38%) reported atopic disease. Children who underwent adenoidectomy and/or tonsillectomy before the age of 8 years were not more likely to develop asthma, AR, or eczema at the age of 21 years than children who did not; RR 0.93 (95% confidence limits (CL) 0.52–1.64), RR 0.94 (CL 0.68–1.30), and RR 1.00 (CL 0.59–1.68), respectively.

Conclusions Our data show no association between adenoidectomy and/or tonsillectomy in childhood and the incidence of atopic disease in young adults.

Keywords adenotonsillectomy, allergic rhinitis, asthma, atopic disease, eczema

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Introduction

The prevalence of asthma and other atopic diseases like allergic rhinitis (AR) and eczema is increasing, especially in Western societies [1, 2]. Both genetic predisposition and environmental factors play a role in the pathogenesis of atopy [3]. In 1989, Strachan hypothesized that an improved hygienic lifestyle enhances the risk of the development of atopic diseases, the so-called 'hygiene hypothesis' [4]. Exposure to allergens and viral or bacterial infections during childhood is proposed to skew the immune system from a T-helper type 2 (Th2) cell into a T-helper type 1 (Th1) cell regulated immune response [5, 6]. It has been speculated that disturbances of the immune system, particularly in the Th1–Th2 balance, play an important role in the development of atopic diseases [7–9].

Adenoidectomy and tonsillectomy are common surgical procedures in young children with recurrent upper respiratory tract infections [10, 11]. Only scarce data are available on their long-term effects. Tonsils and adenoids are part of Waldeyer's ring and as such involved in the defence against airborne and alimentary micro-organisms [12, 13]. Therefore, one might speculate that surgical removal of adenoid and/or tonsil tissue results in reduced humoral and cellular responses and thus reduces stimulation of the immune system in young children [14]. In line with the 'hygiene hypothesis' this decrease of stimulation might result in an increasing risk of atopic disease in later life.

We therefore tested the hypothesis that adenoidectomy and tonsillectomy at an early age are associated with an increased risk of asthma, AR, and eczema at adolescence in a large prospective birth cohort study followed from ages 2 to 21 years.

¹Equally contributed.

Methods

Study population and ear–nose–throat interventions

A birth cohort of 1328 Dutch children born between 1 September 1982, and 31 August 1983, living in the city of Nijmegen (the Netherlands) has been followed prospectively from ages 2 to 8 years. At 2 years of age, baseline characteristics such as duration of pregnancy, birth weight, breastfeeding, parental smoking, number of siblings, day care attendance, and educational level of the parents were collected. All ear–nose–throat (ENT) interventions including adenoidectomy and tonsillectomy during the first 2 years were recorded. Between 2 and 4 years of age, all children were followed prospectively by 3-monthly interviews regarding ENT interventions. At the age of 8 years the children were re-evaluated by means of a standardized questionnaire regarding ENT interventions that occurred between the ages of 4 and 8 years [15].

Atopic disease at age 21 years

At the age of 21 years all cohort members were invited for re-assessment; via the City Council of Nijmegen, their home addresses were traced.

They were sent the International Study of Asthma and Allergic disease in Childhood (ISAAC) Core Questionnaire, which has been validated to obtain data on asthma, AR, and eczema [16]. Furthermore, information on parental history of atopic diseases was obtained. The latter was defined as asthma, AR, or eczema present in at least one of the parents. The study was approved by the medical ethics committee of the University Medical Centre Utrecht.

Asthma was defined as the occurrence of wheezing in the last 12 months and/or a doctor's diagnosis of asthma in that same period and/or current use of asthma medication.

AR was defined as the presence of a runny or blocked nose without having a cold or flu in the last 12 months, accompanied by itchy-watery eyes and/or some interference of this nose problem with daily activities.

Eczema was defined as itchy skin rash that has been coming and going for at least 6 months and affecting particular skin sites (i.e. folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes) in the last 12 months.

Statistical analysis

We estimated the relative risks to analyse the association between adenoidectomy and/or tonsillectomy in childhood on asthma, AR, and eczema at age 21 years. Mantel–Haenszel analyses were performed to adjust for potential confounders as well as to study effect modifiers, e.g. parental smoking, parental history of atopy, parental educational level, breastfeeding, birth weight, and gesta-

tional age. The final rate ratios were adjusted for maternal smoking and parental history of atopy as these factors were indeed found to be confounders. SAS software (version 8.0) was used for all statistical analyses.

Results

Response

Addresses of 1055 subjects (79%) of the 1328 original cohort members could be traced; 693 subjects (66%) responded by returning the questionnaire.

Baseline characteristics and ear–nose–throat interventions

Of the 693 respondents, 374 (54%) were females, 299 (44%) had a mother who smoked, and 315 (46%) had a parental history of atopy (Table 1).

A total of 104 participants (15%) had undergone adenoidectomy and/or tonsillectomy before the age of 8 years (Table 1).

Responding and non-responding cohort members were comparable according to the baseline characteristics and ENT interventions.

Outcome measures

At age 21 years, 86 (12%) of the 693 subjects who participated in the follow-up had asthma according to our definition; 214 subjects (31%) met the criteria for AR

Table 1. Characteristics of the study population (693 responders)

	N (%)
Female gender	374 (54)
Family size	
Any brother(s)/sister(s)	647 (94)
More than one brother/sister	378 (55)
Breast fed more than 3 months	222 (34)
Smoking mother	299 (44)
Educational level mother:	
Low	278 (40)
Medium	257 (37)
High	158 (23)
Parental atopy of at least one parent	315 (46)
Adenoidectomy and/or tonsillectomy	
0–2 years	10 (1)
2–4 years	50 (7)
4–8 years	72 (50)
0–8 years	104 (15)
Atopic disease at age 21 years	
Asthma	86 (12)
Allergic rhinitis	214 (31)
Eczema	98 (14)
At least one atopic disease	262 (38)

Table 2. Relative risks (95% confidence limits (CL)) of asthma, allergic rhinitis and eczema in 693 subjects at age 21 years who had undergone adenoidectomy and/or tonsillectomy during childhood

	Asthma (95% CL)	Allergic rhinitis (95% CL)	Eczema (95% CL)
Adenoidectomy and/or tonsillectomy			
0–2 years	0.78 (0.12–5.21)	0.97 (0.31–2.58)	1.24 (0.35–4.44)
2–4 years	0.94 (0.43–2.04)	1.03 (0.68–1.58)	1.23 (0.64–2.38)
4–8 years	0.90 (0.46–1.78)	1.03 (0.71–1.48)	1.05 (0.58–1.89)
0–4 years	0.93 (0.45–1.92)	1.05 (0.71–1.56)	1.03 (0.53–2.01)
4–8 years	0.93 (0.52–1.54)	0.94 (0.68–1.30)	1.00 (0.59–1.69)

Adjusted for maternal smoking and parental atopy.

and 98 (14%) for eczema. A total of 262 (38%) subjects had at least one of the atopic diseases.

Association between ear–nose–throat interventions in childhood and atopic disease at age 21 years

Table 2 shows the relative risks (RR) of asthma, AR, and eczema at age 21 years adjusted for confounding factors, i.e. maternal smoking and parental history of atopy. There was no significant association between adenoidectomy and/or tonsillectomy and asthma, AR, or eczema: RR 0.93 (95% confidence limits (CL) 0.52–1.64), RR 0.94 (CL 0.68–1.30) and RR 1.00 (CL 0.59–1.68), respectively. The age at which surgery was performed did not affect this association.

Discussion

In the present study, documented ENT interventions until the age of 8 years were compared with the incidence of asthma, AR, and eczema at 21 years of age in 693 participants. Adenoidectomy and tonsillectomy performed in childhood are not associated with atopic disease in later life. This contradicts our hypothesis that removing immunological competent tissue at young age increases the risk of developing atopic disease.

The ring of Waldeyer is an important part of the general immune system. Several studies showed slightly decreased serum Ig levels after adenoidectomy and tonsillectomy. Cantani *et al.* [17] studied 65 children aged 2–11 years with normal levels of serum IgA, IgM, and IgG before surgery. At 1 and 4 months after tonsillectomy, serum Igs were significantly lower. Jeschke and Ströder [18] observed a cohort of 106 children who underwent tonsillectomy at the age of 3–15 years; serum IgG, IgA, and IgM and secretory IgA gradually fell during follow-up to 38 months. Other studies reported the same changes in Ig levels after adenoidectomy and tonsillectomy compared with a control group [19–21]. Beside changes in humoral immune responses, changes in the cellular immune system have also been described after adenoidectomy and tonsillectomy. Several authors reported changes in B and T cells, as well as in different T cell subsets [20, 22, 23].

The short-term effects on humoral and cellular immune responses might argue for a more reserved attitude towards performing adenoidectomy and tonsillectomy in children. Although one can speculate that short-term changes might proceed into immunological imbalance on the longrun, long-term data are lacking. In view of these immunological observations and the 'hygiene hypothesis' we studied the long-term clinical consequences of adenoidectomy and tonsillectomy in childhood on the development of atopic disease.

Our findings are in contrast with those from the British National Child Development Study (NCDS) [24]. In this latter national cohort study, children who had adenoidectomy or tonsillectomy before the age of 7 years had a 1.4-fold risk of developing asthma at age 12–16 years. Differences in asthma phenotypes at different ages might explain the difference between both studies. Moreover, the association that was found in the NCDS was based on univariate analysis, and lack of potential confounding factors might also explain part of the discrepancy. Associations with other atopic diseases, such as AR and eczema, were not studied in the NCDS.

In our cohort, we had the unique opportunity to study the effects of adenoidectomy and tonsillectomy over a prolonged period of time. The large birth cohort provided an excellent basis to study interaction without introduction of selection bias. A potential limitation of our study is the use of a questionnaire to define the outcome parameters of atopic disease. A more objective measure for atopic disease, like pulmonary function testing, might have improved the validity of the outcome. The ISAAC questionnaire has, however, been validated in many settings [16].

Another potential limitation is the fact that only 693 (52%) of the original 1328 study members could be evaluated in the final analysis. This might introduce selection bias as study members with atopic disease could have been more motivated to participate. The most important reason for loss to follow-up, however, was that study members could not be traced because they had moved. Moreover, a comparison of the baseline characteristics of the study members with complete data and the original cohort showed no differences between

both groups. We therefore, believe that selection bias can be considered minimal.

The debate about performing adenoidectomy and tonsillectomy is still ongoing. A recent study by van Staaïj *et al.* [25] showed that children having repetitive upper respiratory tract infections find relief within the first 6 months following adenoidectomy and/or tonsillectomy. However, in comparison with the so-called watchful waiting treatment all differences between the two groups had disappeared by the period of 24 months. In addition to the question about long-term adverse effects, long-term effectiveness should be weighted in the indication for adenoidectomy and tonsillectomy in children. Our data do not support the idea that adenoidectomy and/or tonsillectomy in childhood is harmful in terms of atopic development, but in the absence of noticeable long-term benefits, a more conservative attitude is indicated.

Conclusion

No relationship has been found between adenoidectomy and tonsillectomy in childhood and the incidence of atopic diseases at adolescence.

Acknowledgements

Conflicts of interest: none.

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