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Arch Dis Child 2009 94: 366-370 originally published online January 8, 2009
doi: 10.1136/adc.2008.145664

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Effect of adenoidectomy on respiratory function: a randomised prospective study

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Accepted 9 December 2008
Published Online First
8 January 2009

ABSTRACT

Objective: Risk of childhood asthma is increased in children with recurrent otitis media. This may be associated with recurrent respiratory tract infections in these children, but the role of adenoidectomy, a frequent operation during childhood, is unknown. Therefore, the role of adenoidectomy in the development of atopy and respiratory function changes characteristic of asthma was evaluated.

Design: Randomised controlled study.

Setting: Tertiary care centre.

Patients: 166 children aged 12–48 months who had recurrent or persistent otitis media and who were followed-up for 3 years after randomisation.

Intervention: Randomisation to undergo insertion of tympanostomy tubes with or without adenoidectomy.

Main outcome measures: The primary outcome measure was exercise-induced bronchoconstriction as evaluated by impulse oscillometry. The secondary outcome measures were bronchial inflammation as evaluated by exhaled nitric oxide and atopy as evaluated by skin prick tests. During the 3-year follow-up period otitis media episodes were documented in patient diaries.

Results: Adenoidectomy did not significantly influence baseline lung function, exercise-induced bronchoconstriction, exhaled nitric oxide concentration, the development of positive skin prick tests, or doctor-diagnosed asthma. Adenoidectomy did not significantly prevent otitis media. Recurrent otitis media (≥ 4 episodes) during the first follow-up year was associated with an abnormal exercise-induced bronchoconstriction (OR 6.62, 95% CI 1.27 to 34) and an elevated exhaled nitric oxide concentration (OR 3.26, 95% CI 0.98 to 10.8) regardless of adenoidectomy.

Conclusions: Adenoidectomy did not promote asthma or allergy. Recurrent respiratory tract infections during early childhood are associated with the risk of bronchial hyper-reactivity.

There is a strong connection between childhood asthma and infections, as respiratory tract infections are associated with childhood asthma^{1–4} and asthma symptoms are exacerbated by respiratory infections.^{5–8} Although, according to the so-called hygiene hypothesis, moderate exposure to pathogens during early childhood may protect against subsequent development of atopic symptoms and asthma,⁹ there is evidence that excessive respiratory tract infections, especially in the lower respiratory tract, early in life are associated with childhood asthma.¹⁰

Children with recurrent otitis media are repeatedly exposed to respiratory infections. This may occur during day care outside the home, which is a well-characterised risk factor for acute otitis media.¹¹ The common scenario is a preceding viral

What is already known on this topic

- ▶ The risk of childhood asthma is increased in children with recurrent otitis media who have undergone adenoidectomy.
- ▶ This may be associated with frequent respiratory tract infections in these children, but the role of adenoidectomy itself is unknown.

What this study adds

- ▶ Adenoidectomy does not appear to promote asthma or allergy.
- ▶ Recurrent respiratory tract infections during early childhood seem to be connected to the risk of subsequent bronchial hyper-reactivity.

nasopharyngeal infection that can lead to Eustachian tube dysfunction and secondary bacterial otitis media.¹² It has previously been shown that children with recurrent otitis media who have undergone adenoidectomy have a more than threefold increased risk of childhood asthma.¹³ The above survey showed that the risk of asthma was increased even before adenoidectomy was actually performed. This suggested that adenoidectomy per se may not influence the onset of asthma, but that the increased risk of asthma may be associated with recurrent respiratory infections.

We have recently conducted a randomised prospective study that addressed the effect of adenoidectomy.¹⁴ We have already reported the results regarding the effect of adenoidectomy on otitis media during the first year of follow-up.¹⁴ We have now followed the children up to 3 years in order to assess the effect of adenoidectomy on lung function. Exercise-induced bronchoconstriction was chosen as a measure of bronchial hyper-reactivity as it suggests asthma.¹⁵ It was assessed by a previously validated protocol using impulse oscillometry.¹⁶ Exhaled nitric oxide was also measured, since it is considered a surrogate for eosinophilic airway inflammation¹⁷ and is usually increased in young children with probable asthma.¹⁸ In addition, the development of allergy was assessed by skin prick tests against common allergens. As adenoidectomy is among the most common surgical procedures in children, we felt that its possible harmful effects on lung function or on the development of atopy, which have not previously been assessed, needed to be investigated.

METHODS

Participants

The study children were recruited from patients who were referred to the Department of Otorhinolaryngology, Helsinki University Central Hospital between March 2001 and December 2002.¹⁴ The inclusion criteria were age 1–4 years and ≥ 3 episodes of otitis media during the past 6 months or ≥ 5 during the past 12 months, or persistent middle ear effusion as judged by examination with a pneumatic otoscope 2–3 months before tympanostomy and at the time of recruitment. The exclusion criteria were previous adenotonsillar surgery or placement of tympanostomy tubes, asthma, cleft palate, diabetes, or children judged to require removal of the adenoids because of obstructive symptoms. The Ethics Review Committee of the Helsinki University Central Hospital approved the study.

Randomisation

Altogether, 296 children met the eligibility criteria. The parents of 217 children gave written consent. These children were randomised to undergo adenoidectomy or not to undergo adenoidectomy. All the children received tympanostomy tubes. The results of the randomisation were not revealed until just before the operation.

Follow-up

Whenever a child had symptoms of acute respiratory infection or the parents suspected otitis media, they were advised to visit a doctor at a primary care centre. During these visits acute otitis media episodes were prospectively documented in patient diaries.¹⁴ The diaries were collected during scheduled visits at our clinic after the first, second and third year of follow-up. At the end of the 3-year follow-up period, lung function and skin prick tests were performed.

Impulse oscillometry

We evaluated baseline lung function and exercise-induced bronchoconstriction by impulse oscillometry (IOS, Jaeger, Wurzburg, Germany).¹⁹ Three measurements were taken in order to calculate the mean value for baseline respiratory resistance.²⁰ The children then completed an outdoor running exercise test for 6–7 min and respiratory resistance was measured again to assess exercise-induced bronchoconstriction. This was estimated as the percentage of maximum change in respiratory resistance (Rrs) at 5 Hz oscillating pressure (ΔRrs_5).¹⁶ An increase of 35% in ΔRrs_5 was defined as an abnormal response and corresponds to the 95th percentile in healthy non-atopic children and has been found to reliably discriminate children with probable asthma from asymptomatic children.¹⁶

Exhaled nitric oxide

The fractional concentration of exhaled nitric oxide (FE_{NO}) was measured using a chemiluminescence analyser (Niox, Aerocrine, Solna, Sweden). The child was seated, without a nose clip, and asked to inhale deeply and then to exhale at a steady flow of 50 ± 5 ml/s for at least 6 s.²¹ The exhalations were repeated until two to three values within a 10% range of each other were obtained. The mean of the FE_{NO} values was recorded. We had previously determined the normal values for FE_{NO} which depended on the height of the child.¹⁸ The FE_{NO} concentration was regarded as abnormal when it was more than two standard deviations greater than that predicted.

Skin prick tests

Skin prick testing was carried out with the following allergens: birch, alder, grass, mugwort, cat, dog, horse, dust mite *Dermatophagoides pteronyssinus*, fish, hen's egg, wheat, cow's milk, peanut and hazel nut (Soluprick SQ, ALK, Horsholm, Denmark). The skin prick test was considered positive when the wheal diameter was 3 mm or greater and when the positive control (histamine dihydrochloride 10 mg/ml) and negative control (solvent) gave expected results.

Sample size analysis

Given that the frequency of asthma in young children is possibly 5%, we extrapolated that the frequency of asthma, and thus an abnormal ΔRrs_5 , might reach 10% in those with recurrent respiratory infections, for instance in children with a history of recurrent or persistent otitis media. We based our sample size calculations on the assumption that 10% ($p_1 = 0.10$) of the study children would have an abnormal ΔRrs_5 response. As our previous analysis suggested that adenoidectomy might be associated with a three- to fourfold increase in asthma,¹³ adenoidectomy would result in a threefold increase in the prevalence of an abnormal

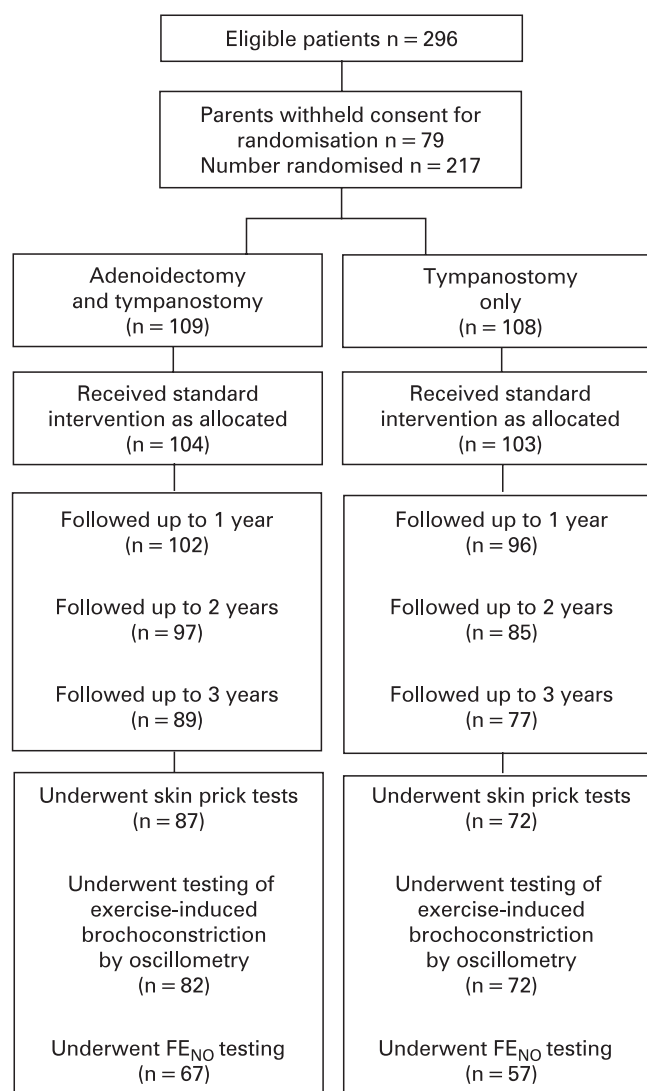


Figure 1 Randomisation of participants to the two treatment groups: adenoidectomy and the insertion of tympanostomy tubes, or the insertion of tympanostomy tubes only.

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Table 1 Characteristics of the 166 children who completed the 3-year follow-up

	Adenoidectomy with tympanostomy (n = 89)*	Tympanostomy only (n = 77)*	Mean difference or odds ratio (95% CI)	p Value
Number of girls	42 (47%)	34 (44%)	1.13 (0.61 to 2.09)†	0.76
Mean age (SD)	4.9 (0.7)	4.9 (0.7)	0.01 (−0.21 to 0.23)	0.95
Age distribution				
4.0–4.9 years	59 (66%)	49 (64%)	1.12 (0.59 to 2.13)†	0.75
5.0–5.9 years	20 (22%)	21 (27%)	0.77 (0.38 to 1.57)†	0.59
6.0–6.9 years	10 (11%)	7 (9%)	1.27 (0.46 to 3.50)†	0.80
Persistent middle ear effusion at the start of the trial	27 (30%)	21 (27%)	1.16 (0.59 to 2.28)†	0.73
Mother smokes tobacco at the end of the follow-up	32 (36%)	17 (22%)	1.98 (0.98 to 3.95)†	0.06
Mean number of otitis media episodes during				
the first year of follow-up (SD)	1.8 (1.8)	1.4 (1.5)	0.42 (−0.08 to 0.93)	0.10
the second year of follow-up (SD)	1.5 (1.5)	1.1 (1.7)	0.39 (−0.11 to 0.88)	0.14
the third year of follow-up (SD)	0.7 (1.1)	0.8 (1.5)	−0.05 (−0.45 to 0.35)	0.84

*Values are numbers with percentages in parenthesis, unless otherwise stated; †odds ratio.

$\Delta Rrs5$ ($p_2 = 0.30$). Based on these assumed frequencies and on the limits of risks of false-positive and false-negative results of $\alpha = 0.05$ and $\beta = 0.10$, respectively, we estimated that approximately 79 children were needed in each treatment group. We initially recruited 217 children. Altogether, 166 children completed the follow-up and 154 children successfully underwent testing with impulse oscillometry.

Statistical methods

Fisher's exact test was used to assess the statistical significance of two-way tables. Student's *t* test was used to compare continuous variables between groups. Logistic regression analysis was performed to assess the relationship of abnormal $\Delta Rrs5$ and elevated FE_{NO} to recurrent otitis media. The analysis was adjusted for the age of the child, gender, adenoidectomy status and maternal tobacco smoking (yes/no). Maternal smoking was used as an independent variable as it is strongly associated with recurrent otitis media.²²

RESULTS

Of the 217 children recruited, 166 (76%) completed the trial and attended the yearly follow-up visits at our clinic. Altogether, 159 children underwent skin prick testing, 154 children underwent impulse oscillometry following the exercise test ($\Delta Rrs5$), and FE_{NO} was measured in 124 children (fig 1). Lack of co-operation precluded the measurement of $\Delta Rrs5$ in 12 children and the measurement of FE_{NO} in 42 children.

There were no significant differences between the randomisation groups regarding sex distribution, age or maternal tobacco smoking habits (table 1). During the first, second and third years of follow-up there were no evident differences in the mean numbers of otitis media episodes between the groups (table 1).

Analysis of the lung function tests revealed that there were no significant differences in baseline respiratory resistance ($Rrs5$), exercise-induced changes in respiratory resistance ($\Delta Rrs5$) or FE_{NO} between children who underwent adenoidectomy and those who did not (table 2). Also, the numbers of children who had abnormal exercise-induced bronchoconstriction ($\Delta Rrs5$ more than 35%) or increased FE_{NO} (more than 2 SD above that predicted) were similar between the groups (table 2).

There appeared to be no marked differences between the randomisation groups regarding the results of skin prick tests. Of the 87 children who had undergone adenoidectomy, 13 (15%) had at least one positive skin prick test to the 19 allergens tested compared to 16 (22%) of the 72 children who did not undergo adenoidectomy (OR 0.61, 95% CI 0.27 to 1.38, $p = 0.30$). Three children developed clinical asthma as defined by repeated need for inhaled sympathomimetic and anti-inflammatory medication for episodic attacks of bronchoconstriction; none of them had undergone adenoidectomy.

We then tested whether recurrent episodes of otitis media in early childhood were associated with an abnormal lung function test. We evaluated recurrent episodes during the first follow-up year, when otitis media was most prevalent. If having recurrent episodes of otitis media was defined as having ≥ 4 episodes a year, children with recurrent otitis media seemed to have higher values of $\Delta Rrs5$ and FE_{NO} (table 3). When recurrent otitis media was defined as having ≥ 5 episodes a year, recurrent otitis media was associated with an even higher mean value of $\Delta Rrs5$ (21.8%, $n = 11$ vs 13.9%, $n = 143$; mean difference 8.0%, 95% CI 15.5% to 0.4%, $p = 0.04$) and a higher geometric mean value of FE_{NO} (8.9 ppb, $n = 11$ vs 6.6 ppb, $n = 113$; fold difference 1.35, 95% CI 0.97 to 1.87, $p = 0.07$). This suggested a dose-response effect between the number of otitis media events and abnormal

Table 2 Lung function in children randomised to undergo adenoidectomy or not to undergo adenoidectomy 3 years after surgery

	Adenoidectomy with tympanostomy		Tympanostomy only		Mean difference or odds ratio (95% CI)	p Value
	n	Mean or proportion	n	Mean or proportion		
Mean $Rrs5$ ($kPa^{-1}s^{-1}$)	82	0.89	72	0.88	0.01 (−0.05 to 0.07)	0.72
Mean $\Delta Rrs5$ (%)	82	13.0	72	16.1	−3.2 (−7.1 to 0.7)	0.11
Children with increased $\Delta Rrs5$ †	82	4%	72	10%	0.35 (0.09 to 1.42)*	0.19
Geometric mean FE_{NO} (ppb)	67	6.9	57	6.6	1.03 (0.86 to 1.25)‡	0.71
Children with increased FE_{NO} †	67	21%	57	11%	2.16 (0.77 to 6.06)*	0.15

FE_{NO} , fractional concentration of exhaled nitric oxide; $Rrs5$, baseline respiratory resistance; $\Delta Rrs5$, exercise-induced change in respiratory resistance.

*Odds ratio; †see text; ‡fold difference.

Table 3 Exercise-induced respiratory resistance and fractional concentration of exhaled nitric oxide at the end of the follow-up period according to recurrent otitis media during the first follow-up year

	Recurrent otitis media		No recurrent otitis media		Mean difference or odds ratio (95% CI)	p Value
	n	Mean or proportion	n	Mean or proportion		
Mean Δ Rrs5 (%)	19	19.1	135	13.8	5.3 (−0.7 to 11.2)	0.08
Children with increased Δ Rrs5 (%)*	19	16	135	5	3.42 (0.81 to 14.6)†	0.11
Geometric mean FE _{NO} (ppb)	18	8.3	106	6.5	1.28 (0.98 to 1.66)‡	0.07
Children with increased FE _{NO} (%)*	18	33	106	13	3.29 (1.06 to 10.2)†	0.08

FE_{NO}, fractional concentration of exhaled nitric oxide; Δ Rrs5, exercise-induced change in respiratory resistance.

*See text; †odds ratio; ‡fold-difference.

lung function tests. During the second and third follow-up years, there were fewer otitis media episodes and there was no association between the number of episodes and subsequent development of abnormal Δ Rrs5 (data not shown).

We then performed logistic regression analysis using the more conservative definition of recurrent otitis media as ≥ 4 episodes of otitis media during the first follow-up year. The dependent variables were an elevated Δ Rrs5 defined as being increased by more than 35%, and increased FE_{NO} defined as being more than 2 SD above that predicted. These cut-off values were selected based on our previous assessment to define abnormal values as explained in the Methods section. The analyses showed that recurrent otitis media during the first follow-up year was associated with an increased risk of developing abnormal Δ Rrs5 and FE_{NO} (table 4). Adenoidectomy was not associated with the development of abnormal Δ Rrs5 or FE_{NO} (table 4). Thus, regardless of adenoidectomy status, recurrent infections during the first follow-up year were associated with an increased risk of abnormal Δ Rrs5 and FE_{NO}.

DISCUSSION

Our results showed that adenoidectomy did not appear to promote exercise-induced bronchoconstriction. Nor did adenoidectomy appear to influence bronchial inflammation as measured by exhaled nitric oxide or the development of allergy. Collectively, our results imply that adenoidectomy does not increase the risk of asthma or the development of allergy to respiratory allergens. This is conceptually important, as the adenoids are located in the nasopharynx confronting inhaled antigens and potentially have a role not only in the development of immunity to microbes but also in the development of tolerance to inhaled particles.

A major reason for dropping out of the study was that parents felt that their children were healthy and did not need scheduled visits with the study doctors. As there were slightly more dropouts in the no adenoidectomy arm, healthy children dropping out preferentially from this group might have resulted in a bias, which would have dampened the potential harmful effects of adenoidectomy. Although there were more abnormal FE_{NO} observations in the adenoidectomy arm, there were more abnormal exercise-induced respiratory resistance observations in

the no adenoidectomy arm. Even further, all three children who were eventually diagnosed with asthma were in the no adenoidectomy arm. This suggests that the dropouts did not apparently hide a potential harmful effect of adenoidectomy. In addition, some dropouts occurred in both study arms immediately before the lung function tests because they require considerable co-operation. It is unlikely that these dropouts caused any systematic bias in the results.

Our analysis showed that recurrent otitis media during the first follow-up year, when the children were on average 2–3 years old, was associated with an increased risk of abnormal exercise-induced bronchoconstriction and elevated exhaled nitric oxide at preschool age. Potentially, a selection bias caused by children who dropped out might have affected this finding. However, such a bias appeared not to strongly influence the proportion of children who had recurrent otitis media as the frequency of these children was 12.1% in those who were followed up for 1 year and 12.7% in those followed up for 3 years. Even further, if we assume that all the children who dropped out were healthy with normal respiratory function and impute data to the missing observations, the odds ratio of the correlation between recurrent otitis media and abnormal respiratory function would be increased rather than decreased.

Our results may explain why the risk of asthma is greatly increased in children with recurrent otitis media who have undergone adenoidectomy.¹³ As otitis media is most frequent during the first 3 years of life, exposure to recurrent respiratory tract infections at this age may predispose not only to otitis media but possibly also to childhood asthma. On the other hand, children who are susceptible to childhood asthma are also susceptible to colonisation with respiratory pathogens at a young age.²³ Thus, children who are susceptible to childhood asthma may also be susceptible to respiratory tract infections.

We have previously reported that adenoidectomy was not efficient in preventing otitis media during the first follow-up year.¹⁴ The present report demonstrates that adenoidectomy did not prevent otitis media during the second and third follow-up years either. Our results together with previously published reports^{24–26} suggest that adenoidectomy is not warranted as the first line of treatment for the prevention of otitis media in children less than 4 years of age. However, there are subgroups

Table 4 Logistic regression analysis of the risk of increased exercise-induced change in respiratory resistance and increased fractional concentration of exhaled nitric oxide

	Risk of increased Δ Rrs5* (n = 154)		Risk of increased FE _{NO} * (n = 124)	
	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value
Recurrent otitis media during the first follow-up year (yes/no)	6.62 (1.27 to 34)	0.02	3.26 (0.98 to 10.8)	0.06
Adenoidectomy (yes/no)	0.30 (0.07 to 1.33)	0.13	2.07 (0.72 to 6.00)	0.18

FE_{NO}, fractional concentration of exhaled nitric oxide; Δ Rrs5, exercise-induced change in respiratory resistance.

*See text.

Original article

of children who may benefit from adenoidectomy. These include children more than 4 years of age with persistent effusion in the middle ear,^{27–29} who may have a chronic infection in the adenoids,³⁰ and those who have an evident adenoid hyperplasia causing obstructive symptoms.³¹

As there are still indications for adenoidectomy such as gross adenoid enlargement and/or chronic adenoid infection,³² the possible harmful effects of adenoidectomy need to be assessed. Although our study did not involve children with adenoid hyperplasia, the results suggest that adenoidectomy itself does not increase the risk of childhood asthma or atopy.

Funding: This work received financial support from the Helsinki University Central Hospital Research Funds, Allergy Research Foundation and Sigrid Juselius Foundation.

Competing interests: None.

Ethics approval: The Ethics Review Committee of Helsinki University Central Hospital approved the study.

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