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Effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy: open, randomised controlled trial

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Abstract

Objective To assess the effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy.

Design Open, randomised controlled trial.

Setting 21 general hospitals and three academic centres in the Netherlands.

Participants 300 children aged 2-8 years requiring adenotonsillectomy.

Intervention Adenotonsillectomy compared with watchful waiting.

Main outcome measures Episodes of fever, throat infections, upper respiratory tract infections, and health related quality of life.

Results During the median follow up period of 22 months, children in the adenotonsillectomy group had 2.97 episodes of fever per person year compared with 3.18 in the watchful waiting group (difference -0.21, 95% confidence interval -0.54 to 0.12), 0.56 throat infections per person year compared with 0.77 (-0.21, -0.36 to -0.06), and 5.47 upper respiratory tract infections per person year compared with 6.00 (-0.53, -0.97 to -0.08). No clinically relevant differences were found for health related quality of life. Adenotonsillectomy was more effective in children with a history of three to six throat infections than in those with none to two. 12 children had surgery related complications.

Conclusion Adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy has no major clinical benefits over watchful waiting.

Introduction

Tonsillectomy, with or without adenoidectomy, is a common procedure in children in Western countries, yet the indications for surgery remain uncertain. Although frequent throat infections and obstructive sleep apnoea are considered adequate indications for adenotonsillectomy in children,¹⁻⁶ evidence for the benefits of surgery in children with milder symptoms is lacking.⁷⁻¹¹ We carried out a randomised controlled trial to assess the effectiveness of adenotonsillectomy

in children with mild symptoms of throat infections or adenotonsillar hypertrophy.

Participants and methods

Our open, multicentre, randomised controlled trial was carried out between March 2000 and February 2003 with the help of otorhinolaryngologists from 21 general hospitals and three academic centres in the Netherlands. They completed a questionnaire on all their patients aged 2 to 8 years with indications for adenotonsillectomy according to current medical practice. They were asked to give the indication they considered most important for surgery.

We excluded children with a history of seven or more throat infections in the preceding year, with five or more in each of the previous two years, or with three or more in each of the previous three years,¹ and children with suspected obstructive sleep apnoea (Brouillette's obstructive sleep apnoea score >3.5).¹² Other exclusion criteria were Down's syndrome, craniofacial malformations, and immunodeficiency, other than that of IgA or IgG₂.

Randomisation

Children were randomly assigned to either adenotonsillectomy or watchful waiting according to a computer generated list. At entry to the study, a disease specific questionnaire was completed for information on the number of throat infections and upper respiratory tract infections experienced by the children in the previous year; obstructive symptoms during sleep¹²; eating patterns; ear, nose, and throat operations; and risk factors for upper respiratory tract infections.

The parents completed two generic health related quality of life instruments: the TNO-AZL preschool children quality of life questionnaire and the child health questionnaire parental form.^{13 14} The children

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The participating hospitals and members of the executive steering committee are on bmj.com



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Table 1 Incidence of fever, throat infections, sore throats, and upper respiratory tract infections per person year for children with mild symptoms of throat infections or adenotonsillar hypertrophy after adenotonsillectomy or watchful waiting

Variable	Adenotonsillectomy group	Watchful waiting group	Incidence rate ratio (95% CI)	Difference (95% CI)
Fever:				
No of episodes	2.97	3.18	0.94 (0.84 to 1.04)	-0.21 (-0.54 to 0.12)
No of days	5.31	5.93	0.90 (0.83 to 0.97)	-0.62 (-1.06 to -0.18)
Throat infections:				
No of episodes	0.56	0.77	0.73 (0.58 to 0.92)	-0.21 (-0.36 to -0.06)
No of days	0.83	1.36	0.61 (0.51 to 0.73)	-0.53 (-0.73 to -0.34)
Sore throat:				
No of episodes	2.25	2.85	0.79 (0.70 to 0.89)	-0.60 (-0.90 to -0.30)
No of days	9.81	15.71	0.62 (0.59 to 0.66)	-5.91 (-6.57 to -5.24)
Upper respiratory tract infections and fever:				
No of episodes	1.59	1.88	0.85 (0.73 to 0.98)	-0.29 (-0.53 to -0.04)
No of days	2.81	3.63	0.77 (0.70 to 0.86)	-0.82 (-1.16 to -0.49)
Upper respiratory tract infections:				
No of episodes	5.47	6.00	0.91 (0.84 to 0.99)	-0.53 (-0.97 to -0.08)
No of days	78.16	89.92	0.87 (0.85 to 0.89)	-11.76 (-13.47 to -10.05)

underwent an ear, nose, and throat examination and had their length and weight measured.

Follow up

The parents kept a diary of upper respiratory tract infections in their child. Absences from day care or school due to upper respiratory tract infections were also noted. The children's temperature was measured daily with a validated tympanic membrane thermometer¹⁵; an inbuilt device stored the date and first measurement of each day. The study doctors collected all data during follow up visits at 3, 6, 12, 18, and 24 months. At these visits, the questionnaires were again completed. An ear, nose, and throat examination was carried out, and length and weight were measured.

Primary and secondary outcomes

Our primary outcome was the incidence of fever ($\geq 38.0^{\circ}\text{C}$ for at least one day), measured in number of episodes and days. An episode was considered finished when at least one day was without fever. New episodes were those occurring after a fever free interval of at least seven days.

Secondary outcomes were throat infections (sore throat with fever), number of episodes and days of sore throat, upper respiratory tract infections, absence from day care or school due to upper respiratory tract infections, health related quality of life, patterns of sleep and eating, length, and weight. Throat infections, sore throats, and upper respiratory tract infections were measured in episodes and days. We also included sore throats and upper respiratory tract infections immediately after adenotonsillectomy.

Statistical analysis

Our sample size calculation was based on a clinically relevant reduction of fever episodes and throat infections after adenotonsillectomy of 25% (see [bmj.com](#)). We calculated the effects of adenotonsillectomy on fever, throat infections, and upper respiratory tract infections as differences in incidence and incidence rate ratios per person year, with 95% confidence intervals. We used χ^2 tests and Student's *t* tests to evaluate differences in percentages and mean values between the groups. We used the Bonferroni correction to adjust for multiple testing and the

Mantel-Haenzel test to adjust for potential confounders. As the estimates of effect were not influenced by these adjustments, we present the estimates of crude effect.

To detect possible modification from effects, we carried out subgroup analyses according to the burden of upper respiratory tract symptoms in the year before entry to the trial and age. We analysed interactions with Poisson regression. All analyses were performed on an intention to treat basis.

Results

Between March 2000 and August 2002 we enrolled 300 children in our study; 151 were allocated to adenotonsillectomy and 149 to watchful waiting (see [bmj.com](#)). Characteristics at baseline were similar between the groups (see [bmj.com](#)). Overall, 43 children were lost to follow up. Fifty children allocated to watchful waiting underwent adenotonsillectomy and seven allocated to adenotonsillectomy did not undergo surgery.

Children in the adenotonsillectomy group had 0.21 fewer episodes of fever (95% confidence interval -0.12 to 0.54) per person year (table 1). During the first six months of follow up, the number of episodes was lower in children in the adenotonsillectomy group (see [bmj.com](#)). From six to 24 months there was no difference between the groups.

Compared with the watchful waiting group, children in the adenotonsillectomy group had, per person year, fewer throat infections (0.21, 95% confidence interval 0.06 to 0.36), fewer sore throats (0.60, 0.30 to 0.90), fewer days with sore throat (5.91, 5.24 to 6.57), and fewer upper respiratory tract infections (0.53, 0.08 to 0.97; see table 1).

Absence from day care or school due to upper tract respiratory infections was comparable between the groups (difference 0.09, -0.27 to 0.44).

At six months, small significant differences were found for some domains of the health related quality of life questionnaires, but these were not clinically relevant (see [bmj.com](#)). We found no differences in other domains and at 24 months.

At six months, Brouillette's scores were lower for children in the adenotonsillectomy group (see [bmj.com](#)). At 24 months there was no difference between the groups. Similarly, at six months, fewer children in the adenotonsillectomy group experienced snoring and difficulties in eating, whereas there were no differences at 24 months (data not shown). Length and weight of children in both groups remained similar (data not shown).

The effects of adenotonsillectomy were more pronounced in children with three to six throat infections in the year before entry to the trial than in those with none to two throat infections: fever episodes (differences -1.07, 95% confidence interval -1.59 to -0.56 *v* 0.34, -0.08 to 0.77, $P=0.01$; table 2) and days with sore throat per person year (differences -11.33, -12.48 to -10.17 *v* -2.38, -3.19 to -1.60, $P=0.01$). Age had no effect.

Of the 195 children who underwent adenotonsillectomy (50 in the watchful waiting group), 12 (6%) had surgery related complications; 7 (4%) had a primary haemorrhage and five (3%) had postoperative nausea.

Table 2 Differences in incidence of fever, throat infections, upper respiratory tract infections, and days with sore throat in subgroups of children after adenotonsillectomy or watchful waiting for mild symptoms of throat infections or adenotonsillar hypertrophy

Variable	Fever (95% CI)	P value*	Throat infections (95% CI)	P value*	Days with sore throat (95% CI)	P value*	Upper respiratory tract infections (95% CI)	P value*
Overall	-0.21 (-0.54 to 0.12)		-0.21 (-0.36 to -0.06)		-5.91 (-6.57 to -5.24)		-0.53 (-0.97 to -0.08)	
Indication:								
Recurrent throat infections	-0.84 (-1.33 to -0.35)	0.10	-0.38 (-0.62 to -0.13)	0.12	-9.70 (-10.79 to -8.61)	0.06	-0.33 (-0.99 to 0.34)	0.79
Other	0.27 (-0.18 to 0.72)		-0.08 (-0.28 to 0.11)		-3.19 (-4.04 to -2.35)		-0.63 (-1.24 to -0.02)	
No of throat infections†:								
0-2	0.34 (-0.08 to 0.77)	0.01	-0.03 (-0.21 to 0.15)	0.05	-2.38 (-3.19 to -1.60)	0.01	-0.27 (-0.86 to 0.32)	0.18
3-6	-1.07 (-1.59 to -0.56)		-0.49 (-0.75 to -0.22)		-11.33 (-12.48 to -10.17)		-0.92 (-1.61 to -0.23)	

*Values of interaction term in Poisson regression analysis.

†In year before entry to trial.

Discussion

Adenotonsillectomy for mild symptoms of throat infections or adenotonsillar hypertrophy in children has little clinical benefit over watchful waiting. Surgery marginally reduced the number of episodes of fever, throat infections, and upper respiratory tract infections per person year. The effects of surgery were more pronounced in children who had had three to six throat infections in the year before entry to the trial than in those with none to two throat infections. No clinically relevant differences were found for health related quality of life.

During the first six months of follow up the incidence of fever was significantly lower in the adenotonsillectomy group than in the watchful waiting group, but was the same from six to 24 months. Sleep and eating patterns initially improved more in children in the adenotonsillectomy group, but by 24 months the differences had disappeared.

Possible limitations

Our trial has several limitations. Firstly, our results are generalisable only to children with mild symptoms of throat infections or adenotonsillar hypertrophy as we excluded children with frequent throat infections or obstructive sleep apnoea, which are generally considered adequate for surgery.

Secondly, 50 children (34%) changed from watchful waiting to surgery. Per protocol analyses that exclude children who change groups will underestimate the effect of treatment. Conversely, analysing children on the basis of time spent in a treatment arm might overestimate or underestimate this effect. For these reasons we chose an intention to treat analysis.

Thirdly, we measured health related quality of life with generic questionnaires because disease specific instruments for children with tonsil and adenoid disease were not available when we started our study.¹⁶ We chose the TAPQoL and TACQoL preschool children quality of life questionnaires because they include relevant domains.¹³

Finally, not all eligible children entered the trial. In an earlier study, however, we showed that there were no major differences between included children and those who were eligible but not included.¹⁷

Strengths of the study

The major strength of our study is the inclusion of the objective primary outcome of fever measured daily by a validated thermometer that automatically stored data.¹⁵ Fever is an important physical sign in many diseases of children, and most episodes of fever in children under 8 years of age are caused by upper respiratory tract infections.^{18,19} We found that adenotonsillectomy did not significantly reduce the number of fever episodes but did have a small but statistically significant effect on the number of throat infections.

The power of our study was large enough to allow for subgroup analyses, providing a tool for clinicians to identify children that are likely to benefit from adenotonsillectomy.

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Competing interests: None declared.

Ethical approval: This study was approved by the medical ethics committees of all participating hospitals.

What is already known on this topic

Frequent throat infections and obstructive sleep apnoea are adequate indications for adenotonsillectomy

Evidence of the benefits of adenotonsillectomy in children with milder symptoms is lacking

What this study adds

Adenotonsillectomy has no major clinical benefits over watchful waiting in children with mild symptoms of throat infections or adenotonsillar hypertrophy

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Commentary: Watchful waiting is useful for children with recurrent throat infections

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Van Staaik et al's study is a welcome addition to a controversial subject.¹ It shows that for children with moderately frequent throat infections (on average three in the previous year) a "wait and see" approach results in acceptable control of symptoms and avoids postoperative pain and complications (1% requiring operative surgery for haemorrhage, and 2.6% having severe nausea or dehydration). The major limitation of the study is the large number of children from the watchful waiting group who had tonsillectomy (34%). Since a per protocol analysis was not done—that is, comparing those who had tonsillectomy with those who did not, controlling for severity indices—it cannot be concluded that tonsillectomy in itself is ineffective but simply that immediate tonsillectomy is not effective. The data from this trial, however, match data from a similar trial, which reported little symptomatic benefit and a significant rate of complications (7%) among children who had tonsillectomy for more severe symptoms.²

Should children with more severe symptoms be offered surgery? With the normal caveats about subgroup analysis, there was some evidence from Van Staaik et al's trial that those more severely affected (three or more infections a year) had some benefit from immediate tonsillectomy—one less episode of sore throat. The earlier Paradise trial assessed tonsillectomy among selected children with severe symptoms³—the "Paradise" criteria of seven or more throat infections in the preceding year, or five or more a year for each of the preceding two years, or three or more a year for each of the preceding three years. This trial showed a reduction of around one episode, rated as moderate or severe (3 of 38 surgical patients *v* 41 of 35 controls); however, the trial was small and was criticised by the Cochrane review for imbalances of important baseline characteristics (the author argued that this was unlikely to affect inferences).⁴

Given the paucity of evidence and controversy about existing evidence, more data are clearly needed

on tonsillectomy among children with recurrent throat infections, and particularly data on non-surgical approaches. Until this evidence is available it would be reasonable for doctors to share with parents the probable benefits of surgery—among children with the Paradise criteria, one less episode of moderately severe or severe sore throat a year; among children with at least three infections in the past year, one less episode of sore throat a year—but also the important harms of operation—a complication rate of 4-7%. For the remaining children, doctors should probably not offer tonsillectomy.

Competing interests. PL has been paid for two consultancy sessions from Abbott Pharmaceuticals for antibiotics for complications of respiratory tract infections.

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Endpiece

My wife and my mistress

Medicine is my lawful wife, but literature is my mistress. When I'm bored with one, I spend the night with the other.

Anton Chekhov (1860-1904), Russian writer, dramatist, and doctor

Fred Charatan, retired geriatric physician, Florida