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Nasal symptoms and signs in children suffering from asthma

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Summary

Objective: A link between the upper and lower airways has been convincingly demonstrated both in health and disease. To what extent the nose may be involved in children's asthma, has so far not been thoroughly investigated. In this study, we compared symptoms and signs from the upper airways in children with asthma and in children without to find out more about this.
Methods: The study group included 27 asthmatic children, the control group 29 age and sex-matched healthy volunteers. The children were investigated by a senior ENT-specialist. Their parents completed questionnaires about symptoms and signs of upper airway disorders. Skin prick tests, total IgE, acoustic rhinometry, and an X-ray of the epipharynx were performed. The data from the groups were compared.
Results: Nasal blockage, mouth breathing, day time sleepiness, apnoeas, itching, sneezing, and hearing impairment were more prevalent in asthmatics compared with controls ($p < 0.05$). For nasal blockage the mean VAS-scores were 52.4 and 30.6 for asthmatics and controls, respectively. For daytime sleepiness the corresponding figures were 34.6 and 23.1. The adenoid-nasopahrynx-index was larger, indicating reduced palatal airway in the former compared with the latter ($p < 0.05$).
Conclusions: As the site of upper airway obstruction in asthmatic children appears to be the epipharynx, the adenoids may play a key-role.

1. Introduction

The upper and lower airways may both anatomically, physiologically, epidemiologically pathophysiologically and therapeutically be considered as one

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entity [1]. They are transluminally connected, influenced by some of the same exogenous and endogenous factors and their mucosal lining is similar. The nose is important as an air conditioner for the lungs, as it tempers, humidifies, cleans and adds NO to the inspired air. The nose also preserves some of the temperature and humidity before the exhaled air leaves the body. Furthermore, 50% of the total airway resistance is situated in the most anterior 1—2 cm of the nose, a fact that may be important in preventing formation of atlectasis in the lungs. The close collaboration between the upper and lower airways is essential for normal nose- and lung-function and thus for good health.

Correspondingly, it is well documented that diseases in the upper and lower airways often co-exist [2,3]. A large number of patients suffering from rhinitis also suffer from asthma, and the majority of patients suffering from asthma also have rhinitis [4]. Approximately, one-third of patients with nasal polyps also have asthma [5]. Sinusitis and asthma are frequently seen in the same patient [6]. If there is a causal relationship is still a matter of controversy [7]. Furthermore, treatment of the nasal disorders may have positive impact on the lower airways [8].

So far little attention has been paid to childhood asthma in this one-airway-one-disease perspective [9]. It is well known that a number of children are mouth breathers for a period of time due to enlarged adenoids. The problem frequently subsides spontaneously due to an absolute and relative decrease in the size of the epipharyngeal adenoids. It is equally well known that children's asthma shows a strong tendency for spontaneous regression with increasing age. An association between the two phenomena has so far not been documented.

In this study, we aimed to investigate whether symptoms and signs from the upper airways were more prevalent in children suffering from asthma compared to age and sex-matched healthy controls, and, if so, to consider the background which may be important both for pathophysiological and therapeutical understanding of children's asthma.

2. Materials and methods

2.1. Material

Twenty seven children with doctor diagnosed asthma (13 males and 14 females) from the Department of Pediatrics, Haukeland University Hospital, Bergen, Norway, and 28 healthy volunteers (11 males and 17 females) recruited from kindergartens in the Bergen area, were included. The average age was 4.2 years and the age distribution 2—5 years in both groups. The children were included and investigated between September 2001 and March 2002.

2.2. Methods

2.2.1. Diagnostic criteria for asthma

The criteria given in the Global Initiative for Asthma (GINA)-report from 2004 were used to define asthma [10]. The asthmatic children were characterised by episodes of airflow limitations, accompanied by breathlessness and wheezing. The controls were also evaluated for asthma. None of them complied with the diagnostic criteria in the GINA-report.

2.2.2. Ear-nose-throat (ENT)-examination

The patients underwent a standard clinical ENT-examination with special attention to secretory otitis media (SOM) and signs of nasal blockage such as mouth breathing and nasal running. All children were investigated by the same senior ENT-specialist who was not aware of whether the child under investigation suffered from asthma or not.

2.2.3. Questionnaires

The parents of both patients and controls completed questionnaires about numbers of otitis media, tonsillitis, common colds, and sinusitis during the last 12 months. They also completed Visual Analogue Scales (VAS) indicating the extent of mouth breathing, snoring, apnoeas, daytime tiredness, nasal blockage, nasal running, nasal itching and sneezing.

2.2.4. Diagnosis of allergy

2.2.4.1. Skin prick test (SPT). All children underwent skin prick tests with a standard airway panel including house dust mite, birch, hazel, cat, dog, timothy, and mugworth. It was performed and scored according to the guidelines of the European Academy of Allergology and Clinical Immunology [11]. Soluprick extracts (ALK-Abello, Hørsholm, Denmark), were used.

2.2.4.2. Total IgE. Total IgE tests were performed using the CAP-FEIA system (Pharmacia Diagnostics AB, Uppsala, Sweden).

2.2.5. Acoustic rhinometry (AR)

An impulse acoustic rhinometer (*RhinoMetrics SRE2100*, *Rhinoscan Version 2.5*, *build 3.2.5.*), was used for separate measurements of the anterior 0, 0—3, 0 and the posterior 3, 0—5, 4 cm of the nasal cavity. The rhinometer was handled by the same well-trained operator throughout the study. Calibration was performed daily as recommended and a standard operating procedure was followed for all patients. Care was taken to avoid distortion of the nostrils. The minimum cross-sectional areas and the nasal cavity volumes in the anterior (MCA1 and NCV1) and posterior (MCA2 and NCV2) sections of the nose are given as a mean of three consecutive measurements [12].

2.2.6. Radiologic assessment of the epipharynx

Lateral cephalographs were obtained with the child sitting in an erect position. The mouth was closed and the teeth in occlusion during film exposure. The tube-head distance and the head-cassette distance were 1.5 and 12 cm, respectively. The exposure was made at 65—70 kV and the exposure time was 0.6 s. By using reference points and lines as described by Fujioka et al. [13], the adenoidal—nasopharyngeal ratio (ANR) was calculated and used as a parameter for comparison of the epipharyngeal status of asthmatics and controls. The roentgenograms were interpreted blindly by a senior specialist in radiology which means that he was not aware whether the pictures belonged to an asthmatic or a control subject.

2.2.7. Statistics

Statistical analyses were performed in SPSS 10.0 for Windows NT 4.0 (SPSS, Chicago, Illinois 60606). Grouped, summary measures were compared by *t*-tests for independent samples, and supplemented by Mann—Whitney *U* test when necessary. A *p*-value less than 0.05 were considered significant. With the included number of individuals and $\acute{\alpha} = 0.05$, a standardised difference of 0.75 could be found with a power of 80%.

2.2.8. Ethics

The study was approved by the Regional Ethics Committee and informed written consent was obtained from all parents.

3. Results

3.1. ENT examination

There were no consistent differences in signs of upper airway disorders between asthmatics and controls. The incidence of SOM was 3 and 2, respectively. Five children with asthma and four controls appeared to be solely mouth breathers during the approximately 20 min of clinical observation. There were no obvious group differences as to the size of the tonsils and their extent of obstruction. A rapid posterior rhinoscopy was not a valid method to compare the size of the adenoids in the two groups.

3.2. Questionnaires

The incidence of colds was close to statistically significant higher in the group of asthmatics compared to controls (Table 1). Otitis, tonsillitis and sinusitis, however, did not appear to be more prevalent among those suffering from asthma than among those without.

Children with asthma had significantly more nasal blockage, mouth breathing, day time sleepiness, apnoeas, itching, sneezing, and hearing impairment compared to healthy controls (Table 2). For snoring and nasal running there was a numerical difference, but this was not statistically significant.

Table 1 Mean number of upper airway infections the last 12 months

Diagnoses	Asthmatic	Control	95% confidence interval of the differences	*p*-Value
Otitis	1.65	0.93	−1.899 to 0.453	0.22
Cold	5.54	3.97	−1.906 to 0.461	0.06
Tonsillittis	1.27	0.76	−1.314 to 0.292	0.21
Sinusitis	0.03	0.08	−0.206 to 0.121	0.61

Table 2 Mean VAS-scores for upper airway symptoms

Symptom	Asthmatic	Control	95% confidence interval of the differences	*p*-Value
Nasal blockage	52.4	30.6	−37.919 to −5,713	0.00
Mouth breathing	42.8	25.6	−34.103 to −0.932	0.04
Day time sleepiness	34.6	23.1	−0.597 to −0.127	0.00
Snoring	36.0	26.6	0.134 to −438	0.21
Apnoeas	21.1	8.9	−0.594 to −0.152	0.00
Nasal running	41.1	27.3	−28.292 to 0.704	0.06
Nasal itching	32.6	10.5	−34.901 to −9.324	0.00
Sneezing	32.1	13.6	−30.194 to −6.823	0.00
Hearing impairment	16.2	13.3	−0.504 to −0.005	0.04

Table 3 Mean previous surgical treatment for upper airway disorders

Surgery	Asthmatic	Control	95% confidence interval of the differences	*p*-Value
Adenoidectomias	0.4	0.7	−0.950 to 0.156	0.63
Paracentesis	0.4	0.7	−0.950 to 0.556	0.63
Tonsillectomias	0.3	0.4	−0.107 to 0.990	0.94

Table 4 SIT. Number of positive individuals

Allergen	Asthmatic	Control	95% confidence interval of the differences	*p*-Value
House dust mite	4	1	−0.035 to −0.264	0.13
Birch	5	0	−0.015 to −0.280	0.03
Hazel	1	0	−0.330 to 0.107	0.21
Cat	2	1	−0.796 to 0.161	0.50
Dog	2	2	−0.130 to 0.145	0.92
Timothy	2	2	−0.130 to 0.145	0.92
Mug worth	0	0		1.00

The history of previously undergone adenoidectomies, paracentesis, and tonsillectomies were similar for both groups (Table 3).

3.3. Allergy

Mean total IgE in asthmatics and controls were 78.5, and 73.8, respectively. Birch allergy was significantly more prevalent among asthmatics than controls, but otherwise there was no difference in incidence of upper airway allergy between groups (Table 4).

3.4. AR

The minimum cross-sectional areas and the volumes in the anterior and posterior sections of the nose were comparable between groups (Table 5).

3.5. X-ray

Children with asthma had an average ANR of 0.57 which was significantly higher than the corresponding figure, 0.43 among controls (Table 6).

4. Discussion

In this study, children suffering from asthma, had more obstructive symptoms and signs from the upper airways than age and sex-matched healthy controls. The site of obstruction appeared to be the epipharynx.

It may be discussed to what extent the asthmatic children really suffered from genuine asthma or actually suffered from airway hyperreactivity secondary to rhinitis. We tried to avoid this source of error by sticking closely to the diagnostic criteria recommended in the GINA-report [10].

To get as reliable information about the situation in the upper airways as possible, we used supplementary symptom scores and objective measures to evaluate the status.

As to VAS, there are obvious limitations with the method as the transfer functions are unknown. Nevertheless, it has been established as valid and reliable in a range of clinical and research applications [14]. Simple VAS appears appropriate, especially when they are used in conjunction with other

Table 5 AR

Parameter	Asthmatic	Control	95% confidence interval of the differences	*p*-Value
MCA1	0.19	0.18	−0.051 to 0.018	0.85
Vol 1	0.82	0.81	−0.177 to 0.048	0.35
MCA2	0.50	0.52	−0.088 to 0.120	0.62
Vol 2	2.63	2.65	−0.729 to 0.560	0.79

Table 6 Mean A-N-index

	Astmatics	Control	95% confidence interval of the differences	*p*-Value
Mean ANR	0.568	0.434	−0.125 to 0.001	0.04

instruments that reflect the multidimensionality of the parameter to be measured.

The applicability and validity of X-ray as a tool to evaluate the status of epipharynx, including the size of the adenoids is debated, and different methods have been applied [15]. In the present study, the ANR was used to assess the palatal airway as a supplement to the clinical investigation. It estimates the size of the adenoid tissue and the size of the nasopharyngeal space together. This method has been found to correlate in a highly significant manner with clinical symptoms of nasal obstruction [16].

AR is accepted as a valuable technique for evaluation of nasal patency. As a method to measure essential nasal parameters in children, it has been investigated by Djupesland [17]. The reliability of AR depends on optimal cooperation from the subject, correct instructions from the investigator, and standardised techniques. In this study, close attention was paid to all these elements. To make the interpretation of the data statistically correct, we used the mean of three reproducible and acceptable readings instead of the single best recording, frequently employed in clinical practice. Acoustic rhinometry did not indicate any differences in volumes and minimal cross-sectional areas in the anterior part of the nose. Clinical investigations supported this finding as there were no obvious group differences as to mucosal oedema, septal deviations or enlarged turbinates as evaluated by anterior rhinoscopy. Increased nasal mucosal swelling in adults with asthma compared to healthy controls has previously been reported [18]. It may be objected that this possibility cannot be excluded in the asthmatic group of children as acoustic rhinometry in our study was performed without comparing the status before and after decongestion. Such an objection is hardly valid, as the baseline data in the asthmatic children and the controls were at comparable levels which was not the case in the reported group of adult patients. Subjects with asthma had significantly lower volumes and lower MCA than the healthy controls before decongestion.

Small airways have previously been ascribed as an important feature and an important therapeutical target in asthma [19]. According to the present study the term ''small airways'' may also apply for the upper airways. The X-ray investigations indicate that asthmatic children had a reduced palatal airway. It may be due to an enlarged adenoid, a small epipharynx, or a combination of these [20]. This aspect is presently under investigation and will be published separately.

A reduced palatal airway in children suffering from asthma should be considered in a ''united airways'' perspective. The co-existence may be merely coincidental and simply reflect an underlying disorder affecting both the upper and lower airways. There are several examples of co-existing upper and lower airway disorders [21]. Abnormal sinus X-rays have been found in 76% of children with serious asthma [22]. Furthermore, as many as 80% of asthmatics have symptoms of allergic rhinitis [6]. Pathophysiologically, the association appears to be based on inflammation [23] triggered either by allergic reactions and/or infections. However, it is generally accepted that disorders of the upper airways, including allergic rhinitis, chronic sinusitis and nasal polyposis, may influence the lower airways by inducing or deterioration of asthma [8,24]. Treatment of upper airway inflammatory disorders, infectious or not, may control asthmatic symptoms [24]. This includes conservative treatment with antibiotics, decongestants, and topical or oral steroids or surgery [25]. It also includes cases of allergic rhinitis treated with anti-histamines, topical steroids and allergen immunotherapy [21].

To what extent a reduced palatal airway, for which absolutely or relatively enlarged adenoids may be a key factor, is a condition with pathophysiological impact on the lower airways in general and in children's asthma in particular, has so far not been sufficiently studied. Such an association may be based both on mechanical and inflammatory mechanisms [21]. The mechanical consequence of a reduced palatal airway is increased tendency for mouth breathing. This is a common feature in asthmatics [26]. The inspired and expired air by-pass the nose and accordingly it is not warmed and humidified as intended. Excessive cold and dry air may penetrate the bronchi which may contribute to asthma [6]. Reduced pulmonary NO and reduced resistance during exhalation are other consequences of mouth breathing with potential negative impact on the lower airways. The nasal filter function also fails, both for particulate and gaseous matters, with increased exposure of the lower airways to both allergens and irritants. As to inflammation, products of inflammation from the nasal mucosa may enter the lower airways through the larynx and trachea or through systemic pathways. They may induce or increase lower airway inflammation or responsiveness. Inflammatory product may be released from the adenoids [19] and neural reflexes may be elicited [27].

An increased prevalence of symptoms of rhinitis, upper airway obstruction and their well-known pulmonary consequences, support a potential link between a reduced palatal airway and the development and/or deterioration of asthma. So does the apparent age relation between childhood wheezing and presence of enlarged adenoids. Wheezing of infancy and childhood frequently resolves spontaneously with growth of the child [10]. Clinically, the volume of adenoid tissue in relation to volume of the epipharynx is largest in children between 2 and 5 years of age [20]. This is also documented by X-rays [28]. The previously described positive impact of adenotonsillectomy on the course of asthma adds to this [29]. In this perspective, it is also interesting that the condition most commonly associated with wheezing in infants and children is thought to be respiratory viral infections since such infections may reduce the palatal airways [10,20]. Viral infections may also upgrade the role of the upper airways as a source of inflammatory products for the lower airways. Accordingly, the effects of the infections on the lower airways may be both direct and indirect. Atopy appears to be related to wheezing and asthma later in childhood. This is in line with the observations in the present study. There was no difference in total IgE between patients and controls. The increased incidence of birch senzitisation among the asthmatics cannot explain the differences in symptoms and X-ray findings between the two groups in our study as all patients were investigated outside the pollen season.

Therapeutically, this study does suggest that measures should be taken to open the palatal airway in asthmatics with obstructive symptoms and signs of upper airways. Favourable effects of adenotonsillectomy on asthma have previously been described [29]. To what extent adenoidectomy alone, a simpler surgical procedure with lower rate of morbidity than adenotonsillectomy, has the same positive impact on children's asthma remains to be shown. A study on this is in progress.

5. Conclusion

Children suffering from asthma have more obstructive signs and symptoms from upper airway disorders than healthy controls. This appears to be a consequence of a reduced palatal airway in the former.

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