

The effect of medical treatment of sinusitis upon concomitant asthma

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Introduction

Sinusitis, the inflammation of one or more of the membranes of the sinus cavities, should really be termed rhinosinusitis because the membranes of the nose and sinuses are contiguous and sinusitis rarely occurs without an underlying rhinitis. Rhinosinusitis is at the more severe end of the spectrum of nasal disease and tends to be recalcitrant to treatment partly because of the inaccessibility of the sinus mucosa to local therapy.

Association of sinusitis and asthma

The relationship between sinusitis and asthma has been described for many years. At the beginning of this century, the reported incidence of sinusitis in asthma varied from 12% {1} to 43% {2} to 90% {3}. Many authors have demonstrated a high incidence of abnormal sinus radiographs in asthmatic children (4, 5). However, there is controversy as to the reliability of radiographic sinus abnormalities being diagnostic for sinus disease because of the frequent findings of similar abnormal radiographs in healthy children (6). The X-ray must always be interpreted in collaboration with the clinical findings, especially the presence of a purulent nasal discharge (7). In a recent study, sinusitis was only a risk factor for asthma in univariate analysis, not after adjustment for covariates (8).

Medical treatment of sinusitis and its effect on asthma

Cooke and coworkers, in 1947, believed that subacute and chronic upper respiratory tract infections, appendicitis and

Date:

Accepted for publication 13 August 1998

To cite this article:

Scadding G. The effect of medical treatment of sinusitis upon concomitant asthma.
Allergy 1999, 54, Suppl 57, 136–140.

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ISSN 0105-4538

tonsillitis were important factors in the aetiology of asthma and advocated aggressive surgical management together with bacterial vaccines (9). However, a controlled trial by Frankland in 1955 (10) failed to show benefit of bacterial vaccines in the treatment of asthma. Similar results were reported subsequently by Johnstone (11) and Helander (12) and the use of bacterial vaccines decreased.

Interest in the sinusitis/asthma link also decreased until in 1976 Rachelefsky (13) undertook a prospective study of the prevalence of sinus disease in allergic children and attempted to establish criteria for the diagnosis of sinusitis. He and his coworkers studied 70 children between 3 and 16 years of age with a mean duration of respiratory symptoms of 23 weeks. They found abnormal sinus X-rays in 37 (53%); 15 had opacification of one or both maxillary sinuses. The presence of a sore throat, postnasal drip, purulent nasal discharge or night-and-day cough was highly suggestive of sinus disease. The only helpful laboratory test was a nasal smear showing high levels of neutrophils and low numbers of eosinophils. Rachelefsky (14) also reported in 1984 on a cohort of 48 children (mean age 8.2 years) with sinusitis who initially had characteristics of asthma (Table 1). In 79% of these, after treatment of their sinusitis, their lower respiratory tract symptoms disappeared. Continued follow-up of these patients showed that when the sinusitis recurred, so did their asthma.

Other workers have studied medical treatment of sinusitis and its effect on asthma in children. Businco et al. (15) studied 80 asthmatic children aged 4–14 years, and found sinus X-ray abnormalities (a 2-mm thickening of one or both maxillary sinuses) in 55. The children were treated either with topical nasal corticosteroid, plus an antihistamine-decongestant, or ampicillin plus antihistamine-decongestant. After 30 days' treatment, the asthma severity decreased and the sinus X-ray films improved in both groups. Cummings et al. (16) studied the effects of active treatment (topical corticosteroids, antibiotics and oral decongestants), versus placebo, in children with marked thickening or opacification of the maxillary sinuses. Active treatment resulted in decreased asthmatic symptoms and reduced the need for inhaled bronchodilator or oral corticosteroid therapy. However, pulmonary function tests

and measures of bronchial reactivity were not changed significantly. In a retrospective study, Richards et al. (17) found that 12 of 15 of their asthmatic children noted an increase in asthma following an episode of sinusitis and that their symptoms responded well to antibiotics. Freedman (18) found similar results.

A more recent study by Oliveira (19) on 46 atopic children without sinusitis and 20 normal controls showed that bronchial hyperreactivity and FEV₁ improved only in the eight children in whom X-ray evidence of sinusitis had resolved by the end of the treatment. Treatment in this study involved not only 21 days of sulphamethoxazole-trimethoprim but also antihistamines, decongestants, douching and 5 days of oral prednisolone. Although it is possible that the asthma was affected directly by the prednisolone the fact that six children whose sinusitis did not improve also did not show an improvement in their asthma would argue against this.

Shapiro (20) has shown that in children with rhinosinusitis nasal smears revealed neutrophils and bacteria initially, but following antibiotic therapy a nasal eosinophilia was demonstrated.

Allergy is probably a prominent predisposing factor to sinusitis in children because the inflamed mucosa provides a good site for bacterial growth and blocks the ostiomeatal complex. In addition, eosinophil damage to the sinus mucosa is a possibility and our studies have shown that the allergic reaction decreases ciliary beat frequency (21). The raised expression of ICAM-1 in the allergic mucosa (22) has been suggested as a possible cause of increased infection of the upper respiratory tract since ICAM-1 is the receptor for rhinovirus (23), but the clinical significance of this remains unproven. Diagnosis of allergy may be missed, especially in small children where skin-prick tests are negative while local nasal allergy is evolving. It is now our practice in children with a history suggestive of allergic rhinitis and blue oedematous turbinates with negative skin-prick tests to repeat the skin-prick tests after a year. The results are then often positive. Allergy is also involved in most asthma in childhood, thus allergen avoidance and immunotherapy could benefit asthma directly as well as via an improvement in sinusitis.

Table 1. Pulmonary symptoms, function and need for medication in asthma children before and after sinusitis treatment (Ref. 14)

	Cough (%)	Wheeze (%)	Normal PEF (%)	Bronchodilator use (%)
Pretreatment	100	100	0	100
Post-treatment	29	15	67	21

Type of medical treatment

Antibiotics have been found efficacious in the treatment of acute and subacute sinusitis (24), where the common organisms are *Streptococcus pneumonia*, *Moraxella catarrhalis* and *Haemophilus influenzae* (25, 26). The use of antimicrobials in chronic sinusitis where inflammation, rather than infection, supervenes is usually limited to acute infective exacerbations (24). Other treatment modalities include attention to underlying allergy by allergen avoidance and/or pharmacotherapy with topical anti-inflammatories such as corticosteroids or sodium cromoglycate, antihistamines, decongestants and douching. In some countries immunotherapy may be considered for patients who do not respond to these and who have good evidence of monoallergy.

Nasal polyposis

Nasal polyposis is associated with sinus inflammation and in some patients with recurrent infection. The majority of patients have negative skin-prick tests and the associated asthma (intrinsic) is frequently severe, requiring high doses of inhaled corticosteroids plus recourse to oral steroids. The combination of oral steroids and intranasal betamethasone phosphate drops (available in UK only) form the basis of a medical polypectomy. Treatment of this type usually improves both the nasal airway and FEV₁; however, this is probably a direct effect of betamethasone phosphate on the bronchial inflammation rather than a response to the improved nasal airway, since asthmatics without rhinitis also improve with oral steroids. In contrast to modern nasal corticosteroids, betamethasone phosphate is readily absorbed and exerts systemic activity because it is not first-pass metabolized in the liver.

Lamblin (27) has shown that nasal polyposis patients can be divided into two groups based on their responsiveness to inhaled beclomethasone dipropionate. In the nonresponders who went on to have surgical intervention there was a decrease in PD₂₀ methacholine and FEV₁ whereas in the steroid-responsive group these values remained unchanged. In neither group were there any significant symptomatic changes. Further follow-up of these patients is needed to determine the clinical significance of this observation.

Sensitivity to aspirin and nonsteroidal anti-inflammatory drugs is common in nasal polyposis (23); oral desensitization to aspirin can be associated with improvement in asthma and polyposis (29), but again the effect is probably direct. We

are undertaking a double-blind, placebo-controlled cross-over study of local desensitization using 2 mg lysine aspirin on alternate days in the nose for 6 months compared to saline for 6 months, with an intervening washout period of 1 month on betamethasone phosphate nose drops. Some patients in this study are experiencing relief of nasal and lower respiratory tract symptoms together with improved peakflow recordings, others note a concomitant worsening of both. The dose used is unlikely to have a major systemic effect and suggests local application is affecting the nose which is then having secondary effects upon the chest.

Chronic rhinosinusitis

Systemic treatments which benefit sinusitis and asthma exist, such as oral corticosteroids. However, these cannot provide evidence for a sinusitis/asthma link. We have recently undertaken two studies of local treatment in chronic rhinosinusitis, one with the topical corticosteroid fluticasone propionate aqueous nasal spray, which showed a trend towards improvement in diary card symptoms ($P=0.054$) in both active and placebo groups, but no objective improvement (30). Our suspicion was that placebo helped symptom relief via a douching action and a subsequent trial has compared alkaline nasal douche made from a powder to a sterile seawater spray and to no douching (31). The powder improved endoscopic appearances ($P=0.038$), as scored by an observer blinded to the patient's therapy, whereas the spray improved quality of life ($P=0.023$), measured by a modified Juniper Rhinitis Quality of Life questionnaire.

In order to assess the effects of this treatment upon the lower respiratory tract a questionnaire was sent to patients enrolled in these two studies. The questionnaire was sent to 60 patients with chronic rhinosinusitis, of whom 40 responded, 10 of whom had physician-diagnosed asthma. Eight of these 10 asthmatics noted that their chest worsened when their sinuses were affected, but so did 14 of the 26 non-asthmatics who answered the question. However, there were significant differences with respect to sinusitis treatment, where the asthmatics were more likely to find benefit as far as their lower airways were concerned ($P=0.018$), and they were more likely to notice decreased shortness of breath on exertion during sinusitis treatment compared to those in the nonasthmatic group ($P=0.02$) (Table 2). There was no difference between the two groups with respect to changes in day cough, night cough or wheeze. Two asthmatics noticed less use of bronchodilator

Table 2. Results of questionnaire sent to patients with chronic sinusitis, with and without asthma. In both asthmatic and nonasthmatics the majority noted a worsening of chest symptoms when their sinuses were affected. However, asthmatics fared better than nonasthmatics with respect to chest symptoms and decrease in shortness of breath on sinusitis treatment

	Do your chest symptoms get worse when your sinus symptoms get worse?		How does sinusitis treatment change your chest symptoms?			How does sinusitis treatment change your shortness of breath on exertion?		
	Yes	No	Better	Same	Worse	Better	Same	Worse
Nonasthmatics	14	11	3	18	2	3	15	0
Asthmatics	8	1	6	4	0	0	6	3
	$P=0.17$		$P=0.018$			$P=0.02$		

and two noticed less use of inhaled corticosteroid during the trial; in the remainder these values were unchanged. Nobody reported an increased need for asthma therapy.

This study obviously suffers from small numbers and incomplete sampling, but does suggest that there is a difference between asthmatics and nonasthmatics in the response of the lower airway to simple medical treatment of sinusitis with asthmatics experiencing more benefit.

Conclusions

The coexistence of sinusitis and asthma has been recognized for many years, but sinusitis itself does not appear to be an independent risk factor for asthma. Worsening of asthma symptoms during episodes of sinusitis is well recognized.

Some paediatric studies demonstrate an improvement in chest symptoms and decreased need for medication after sinusitis treatment. Using the Oliveira study (19), only those children with X-ray resolution of sinusitis showed a decrease in bronchial hyperreactivity. There has been no attempt to test which particular form of treatment is responsible, since

in most studies combined or multiple therapy involving corticosteroids, antihistamines, decongestants and antibiotics have been used. One problem is that systemic treatment could act directly on the chest, rather than causing secondary effects via decreased sinus inflammation.

There are a few studies of topical treatment in adults. Lamblin (27) observed that nasal polyp patients not responding to topical beclomethasone dipropionate showed increased bronchial hyperreactivity 12 months later following ethmoidectomy, in contrast to those whose polyps were beclomethasone-responsive. Our own chronic rhinosinusitis topical corticosteroid and nasal douching trials reveal a difference between asthmatics and nonasthmatics, with the former gaining more benefit with respect to chest symptoms during topical sinusitis treatment.

There is an obvious need for well-controlled prospective randomized trials examining the effects of medical or surgical treatments of rhinosinusitis on asthmatic symptoms and pulmonary function. None the less, the evidence to date suggests that in poorly controlled asthmatics sinusitis should be actively sought and, if present, treated, since this is likely to improve asthma control.

References

1. Bullen SS. Incidence of asthma in 400 cases of chronic sinusitis. *J Allergy* 1932;4:402-407.
2. Chobot R. The incidence of sinusitis in asthmatic children. *Am J Dis Child* 1930;39:25764.
3. Gottlieb MJ. Intranasal disease and asthma. *JAMA* 1925;85:105-108.
4. Schwartz HJ, Thompson JS, Sher TH, Ross RJ. Occult sinus abnormalities in the asthmatic patient. *Arch Intern Med* 1987;147:2194-2196.
5. Iwens P, Clement PAR. Sinusitis in allergic patients. *Rhinology* 1994;32:65-67.
6. Siegel SC. Diagnosis and medical management of recurrent and chronic sinusitis in children. In: Gershwin ME, Incaudo GA, editors. *Diseases of the sinuses*. Totowa NJ: Humana Press Inc., 1996:197.
7. Gordts F, Clement PAR, Destryker A, Desprechins B, Kaufman L. Prevalence of sinusitis signs on MRI in a non-ENT paediatric population. *Rhinology* 1997;35:154-157.
8. Moussa MA, Skaik MB, Yaghy OY, Salwanes SB, Bin-Othman SA. Factors associated with asthma in schoolchildren. *Eur J Epidemiol* 1996;12:583-588.
9. Cooke RA. Infective asthma with pharmacopeia. In: Cooke RA, editor. *Allergy in theory and practice*. Philadelphia: WB Saunders & Co., 1947:151.
10. Frankland AW, Hughes WH, Garrill RH. Autogenous bacterial vaccines in the treatment of asthma. *Br Med J* 1955;2:941-944.

11. Johnstone DE. Study of the role of antigen doses in treatment of pollinosis and bronchial asthma. *Am J Dis Child* 1957;**94**:1–5.
12. Helander E. Bacterial vaccines in the treatment of bronchial asthma. *Acta Allerg (Kbh)* 1959;**13**:47–66.
13. Rachelefsky GS, Goldberg M, Katz RM, et al. Sinus disease in children with respiratory allergy. *J Allergy Clin Immunol* 1978;**61**:310–314.
14. Rachelefsky GS, Katz RM, Siegel SC. Chronic sinus disease with associated reactive airway disease in children. *Pediatrics* 1984;**73**:526–529.
15. Businco L, Fiore L, Frediani T, Artuso A, Difazio A, Bellioni P. Clinical and therapeutic aspects of sinusitis in children with bronchial asthma. *Int J Paediatr Otorhinolaryngol* 1981;**3**:287–294.
16. Cummings NP, Wood R, Lere JL, Adinoff AD. Effects of treatment of rhinitis/sinusitis on asthma: results of a double-blind study. *Paediatr Res* 1983;**17**:373–378.
17. Richards W, Roth RM, Church JA. Underdiagnosis and undertreatment of chronic sinusitis in children. *Clin Ped* 1991;**30**:88–92.
18. Freedman R, Ackerman M, Wald E, et al. Asthma and bacterial sinusitis in children. *J Allergy Clin Immunol* 1984;**74**:185–189.
19. Oliveira CAA, Sole D, Naspitz CK, Rachelefsky GS. Improvement of bronchial hyper-responsiveness in asthmatic children treated for concomitant sinusitis. *Ann Allergy Asthma Immunol* 1997;**79**:70–74.
20. Shapiro G. Sinusitis in children. *J Allergy Clin Immunol* 1988;**81**:1025–1027.
21. Holmström M, Scadding GK, Darby YC, Lund V. Ciliary beat frequency before and after nasal allergen challenge. *Am J Rhinol* 1992;**6**:101–105.
22. Montefort S, Feather IH, Wilson SJ, Haskard DO, Holgate ST, Howarth PH. The expression of leukocyte-endothelial adhesion molecules is increased in perennial allergic rhinitis. *Am J Respir Cell Mol Biol* 1992;**7**:393–398.
23. Staunton DE, Merluzzi VJ, Rothlein R, et al. A cell adhesion molecule, ICAM-1, is the major surface receptor for rhinoviruses. *Cell* 1989;**56**:849–853.
24. Wald ER. Chronic sinusitis in children. *J Paediatr* 1995;**127**:339–347.
25. Wald ER, Milmoë GJ, Bowen A'd, Ledesma-Medina J, Salamon N, Bluestone CD. Acute maxillary sinusitis in children. *N Engl J Med* 1981;**304**:749–754.
26. Wald ER, Byers C, Guerran C, Casselbrandt M, Beste D. Subacute sinusitis in children. *J Paediatr* 1989;**115**:28–32.
27. Lamblin C, Tillie-Leblond I, Darras J, et al. Sequential evaluation of pulmonary function and bronchial hyper-responsiveness in patients with nasal polyposis. *Am J Respir Crit Care Med* 1997;**155**:99–103.
28. Szczeklik A. Aspirin-induced asthma. In: Vane JR, Botting RM, editors. *Aspirin and other salicylates*. London: Chapman & Hall Medical, 1992:548–575.
29. Sweet JM, Stevenson DD, Simon RA, Mathison DA. Long term effects of aspirin desensitisation. Treatment for aspirin-sensitive rhinosinusitis and asthma. *J Allergy Clin Immunol* 1990;**85**:59–69.
30. Scadding GK, Parikh A, Baker RC, Richards DH. A double blind placebo controlled study of topical fluticasone propionate in chronic rhinosinusitis (abstract). *J Allergy Clin Immunol* 1998;**101**:S252.
31. Scadding GK, Taccariello M, Parikh A, Darby Y. Alkaline nasal douche compared to Sterimar saline spray in chronic rhinosinusitis. *Rhinology* 1999 [in press].