

Nebulization treatment with saline compared to bromhexine in treating chronic sinusitis in asthmatic children

H. P. S. VAN BEVER,¹ J. BOSMANS² and W. J. STEVENS²

¹Departments of Paediatrics and ²Clinical Immunology, University of Antwerp, Antwerp, Belgium

Twenty children aged 3 to 14 years with a history of bronchial asthma complicated by chronic sinusitis were studied in a double-blind study. Patients received, at random, over a period of 2 weeks, either 2 ml saline or 2 ml bromhexine (2 mg/ml) t.i.d. by means of a home nebulizer. A significant decline of clinical symptoms during both nebulization treatments as compared to the pretreatment symptom score was observed (mean score of 1.5 ± 0.7 and 0.5 ± 0.8 , respectively, $P < 0.01$). Both types of nebulization were equally efficient in reducing the symptom score. Radiological abnormalities were significantly more reversed after saline nebulization as compared with bromhexine ($P < 0.05$), although both treatments showed radiological improvement ($P < 0.01$). The present study indicates that nebulization with saline may have some beneficial effect on chronic sinusitis in asthmatic children. Bromhexine was not superior to saline for this purpose.

Key words: asthma; bromhexine; nebulization; saline; sinusitis.

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Reactive airway disease (asthma) in children is frequently associated with abnormal sinus radiographs (8). Although the treatment of chronic sinusitis has not been well established, it has been shown that improvement of the associated asthmatic symptoms often occurs after the sinus pathology has been resolved (6). Administration of antimicrobial agents is helpful in children with chronic sinusitis but the benefit of other medication (antihistamines, decongestants, mucolytics) remains to be determined (7). We attempted to evaluate the effect of nebulised bromhexine, by comparing it in a double-blind manner with nebulised saline in children with bronchial asthma complicated by chronic sinusitis. Bromhexine, a mucolytic agent, is known to decrease the viscosity of mucus secretions (4). Furthermore, it is advocated by its producing manufacturer as a drug of choice in the treatment of chronic sinusitis.

Saline is known to be useful in the management of upper respiratory infections (2, 3) but its effect on chronic sinusitis has not been established.

MATERIAL AND METHODS

Twenty children aged 3 to 14 years with bronchial asthma were studied. Despite a bronchodilator treatment, they all had a history of persistent rhinitis (sneezing, nasal blockade, nasal discharge) for at least 3 months, associated with bronchial asthma, according to the criteria of the American Thoracic Society (1) with daily wheezing and/or cough, and Waters sinus radiograph demonstrated a mucosal thickening equal or greater than 3 mm, or opacification in one or both maxillary sinuses. This combination of radiologic abnormalities and clinical signs was considered as "chronic sinusitis". At

the time of the study, all the patients were free of symptoms of acute upper respiratory infection. There was no preceding fever in any of the patients. Subjects were randomized in double-blind fashion, to be given either saline or bromhexine nebulization, using a portable home nebulizer with a jet nebuliser. Two ml saline or 2 ml bromhexine (2 mg/ml) were administered 3 to 4 times a day for 2 weeks. All children were maintained on their anti-asthmatic medications (betamimetics and/or oral long-acting theophylline) while receiving the nebulization treatment. After the 2 weeks treatment, the Waters radiograph was repeated.

Evaluation of the nebulization treatment was performed using a symptom score and a score

for radiographic abnormalities before and after the treatment period. Wheezing, cough and rhinitis were evaluated separately on a 0-3 scale (0 = none, 1 = occasional, 2 = frequent and 3 = severe). Each child was examined by one of us (V.B.) before and after the nebulization treatment. Maxillary sinus radiographs were scored by two observers, unaware of the treatment which was offered, using a 0-5 scale (0 = bilateral normal maxillary sinuses, 1 = unilateral mucosal thickening > 2 mm, 2 = bilateral mucosal thickening > 2 mm, 3 = unilateral opacification + normal sinus, 4 = unilateral opacification + mucosal thickening > 2 mm, 5 = bilateral opacification).

Statistical analysis of the results was accomplished with the Student's t test for paired observations. *P* values < 0.05 were considered to be significant.

Table 1
Characteristics of the two groups before nebulization treatment (mean ± SD)

	Group I (saline) <i>n</i> = 10	Group II (bromhexine) <i>n</i> = 10	Total <i>n</i> = 20
Age (years)	6.6 ± 4.3	4.5 ± 3.1	5.6 ± 3.6
Sex	6/10 ♂	6/10 ♂	12/20 ♂
Duration of asthma (months)	34 ± 24	31 ± 17	32.5 ± 20
Asthmatic medication			
No bronchodilator treatment	2/10	1/10	3/20
Betamimetics	6/10	9/10	15/20
Betamimetics + theophylline	2/10	(-)	2/20

RESULTS

Details of the two groups are given in Table 1. The differences between groups regarding to age, sex, duration of asthma and previous asthmatic medication are not statistically significant.

The evaluation of both groups before treatment is shown in Table 2. Both groups had a comparable symptom score for cough and rhinitis. Wheezing was not present in the bromhexine groups, while 4/10 children treated with saline suffered from wheezing before the nebulization treatment. The score for radiologic sinus abnormalities was comparable in both groups.

Table 2
Evaluation criteria (mean ± SD)

	Evaluation before treatment			Evaluation after treatment		
	Total <i>n</i> = 20	Saline <i>n</i> = 10	Bromhexine <i>n</i> = 10	Total <i>n</i> = 20	Saline <i>n</i> = 10	Bromhexine <i>n</i> = 10
Cough	2.2 ± 0.6	2.2 ± 0.6	2.2 ± 0.6	**0.7 ± 0.9	**0.6 ± 1.0	**0.8 ± 0.9
Rhinitis	2.0 ± 0.8	2.0 ± 0.9	1.9 ± 0.7	**0.7 ± 0.9	**0.4 ± 0.7	**1.0 ± 0.9
Wheezing	0.3 ± 0.7	0.6 ± 1.0	0 ± 0	***0 ± 0	***0 ± 0	0 ± 0
Radiology	3.4 ± 1.3	3.5 ± 1.3	3.3 ± 1.3	*1.9 ± 1.7	**1.3 ± 1.6	2.6 ± 1.7

* *P* < 0.05: compared with pretreatment status. ** *P* < 0.01: compared with pretreatment status. *** *P* < 0.001: compared with pretreatment status.

The clinical score decreased significantly in both groups without any statistically significant difference between the groups. 5/10 children treated with saline and 2/10 treated with bromhexine became free of symptoms. No patient showed deterioration.

The radiographic outcome was statistically significantly better for the saline-group ($P < 0.01$), although both treatments induced improvement on X-ray abnormalities ($P < 0.01$). 4/10 children treated with saline nebulization and 0/10 treated with bromhexine became radiologically normal. (Table 3).

DISCUSSION

In this series of patients with reactive airway disease complicated by chronic sinusitis, clinical improvement was observed after either of the nebulization treatments with saline or with bromhexine. Nebulization with bromhexine was not found to have any significant advantage over saline nebulization. On the other hand, X-ray abnormalities were significantly more

reversed after saline nebulization, although both treatments showed radiological improvement. It seems most reasonable that the beneficial effect upon clinical and radiological signs must be attributed to the nebulization aerosol treatment *per se*, resulting in an increased humidification of upper respiratory tract mucosae. Lack of humidity in the nasal, sinusal and bronchial mucosa is associated with increased mucus viscosity, depression of the ciliary activity and inhibition of the clearance of luminal collections which are well-known predisposing factors for respiratory infections (2, 5). The decrease in sinusal secretion viscosity as a result of the aerosol treatment, may be beneficial to the function of the ciliary transport system, thereby more easily evacuating secretions and preventing colonization of pathogenic viruses and bacteria.

Although it has been shown that bromhexine decreases the viscosity of mucus secretions *in vitro*, the lack of a more beneficial effect compared to saline, in this study, could be due to the more important effect of humidification upon mucus viscosity, rather than the chemical breakdown of mucus by bromhexine.

The results of this preliminary study indicate that humidification with saline, one of the safest therapeutic agents, is *probably* of value in treating chronic sinusitis in asthmatics subjects. Although antimicrobial agents are helpful in treating chronic sinusitis, we suggest that antibiotics should be instituted after failure of nebulization treatment with saline.

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Table 3
Radiologic evolution

	Score before treatment	Score after treatment
Bromhexine		
B1	4	1
B2	5	4
B3	2	2
B4	3	1
B5	5	5
B6	3	1
E7	5	5
B8	2	4
B9	2	2
B10	2	1
Saline		
S1	4	2
S2	1	1
S3	2	0
S4	5	5
S5	5	0
S6	4	2
S7	3	0
S8	4	2
S9	3	1
S10	4	0

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Address

H. P. S. Van Bever, M.D.
Immunology - Paediatrics UIA
Universiteitsplein 1
B 2610 Antwerp
Belgium

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