

The effect of long-term antibiotic therapy upon ciliary beat frequency in chronic rhinosinusitis

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Abstract

The mucociliary escalator is the first line of defence of the upper and lower respiratory tracts (Greenstone and Cole, 1985; Sleigh *et al.*, 1988). Failure of mucociliary clearance is associated with chronic or recurrent respiratory tract infection. Ten patients with chronic rhinosinusitis underwent nasal brushings for the assessment of ciliary beat frequency. In two no beating cilia were seen; in the remainder the mean value was $9.3 \text{ Hz} \pm 2.3$; range 6.1–12.8 Hz ($n = 8$).

Following three months continuous oral antibiotic therapy repeat nasal brushings demonstrated increased ciliary beat frequencies in all patients, mean value $13.7 \text{ Hz} \pm 1.6$; range 11.5–16.3 Hz ($n = 10$); ($p < 0.01$; paired *t*-test).

Depression of mucociliary clearance can occur secondarily to chronic infection and is improved by prolonged antibiotics.

Key words: Cilia; Mucociliary clearance; Rhinitis; Sinusitis; Antibiotics

Introduction

Primary defects of ciliary function are rare (Afzelius, 1976; Greenstone *et al.*, 1985; Greenstone *et al.*, 1988), but secondary adverse effects upon cilia are more common. Viral infections can decrease the number of cilia present (Wilson *et al.*, 1987a), pollution, and allergic reactions (Holmstrom *et al.*, 1992) can slow ciliary beating. Certain bacteria which are frequently associated with chronic respiratory infection, such as *Haemophilus influenzae* (Wilson and Cole, 1988), *Streptococcus pneumoniae* (Steinfort *et al.*, 1989; Feldman *et al.*, 1990) and *Pseudomonas aeruginosa* (Wilson *et al.*, 1988) have recently been shown to release compounds which slow and disorganize ciliary beating *in vitro* (Wilson *et al.*, 1987b), affect mucus transport (Munro *et al.*, 1989) and may disrupt the ciliated epithelium (Wilson *et al.*, 1988). It is likely that these microbe-mediated effects on mucociliary clearance assist the bacteria to colonize the respiratory tract. This in turn leads to a chronic inflammatory response which causes further mucosal damage and leads to further microbial colonization, a 'vicious circle' of events leading to chronic sinusitis and/or bronchiectasis (Cole, 1989; Cole and Wilson, 1989). Interruption of this cycle of events should aid resolution of the infection.

We report here the effect of long-term (three months) antibiotic therapy upon patients, with chronic rhinosinusitis, who had failed to respond to conventional measures which included surgery, two-week courses of antibiotics, decongestants, douching, intranasal beta-

methasone plus neomycin together with allergen avoidance where necessary.

Patients and methods

Ten patients (six female) aged from 13 to 55 years with chronic purulent or mucopurulent nasal discharge, present on most days for over a year (mean 8.7 years; range 3–30 years) were studied (Table I).

Ciliary brushings were taken from the inferior turbinate under direct vision using a bronchoscopy brush, and were placed immediately in Hank's solution. This was then transferred to a microscope slide and examined on a stage warmed to 37°C. The frequency of ciliary beating was assessed with a photometric technique as described by Rutland and Cole (1980). Between five and 10 different clumps of ciliated epithelium in each sample were studied using a Leitz Dialux 20 microscope with a Leitz MPV compact microscope photometer attached. The readings were done at $\times 320$ magnification. A rectangular light ($1.5 \times 5 \mu\text{m}$) from the photometer was positioned in the long axis of the cilia so that it was interrupted by ciliary beating. The change in light intensity was transferred into an electrical signal which was then converted to a reading of CBF (Hz) by a ciliary beat frequency (CBF) processing unit (Greenstone *et al.*, 1984). Five to ten readings were made on each specimen and the mean was calculated.

After three months therapy with an antibiotic, two weeks on full dosage and 10 weeks on half dosage (speci-

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TABLE I

Patient	Age	Sex	Length of history	Previous surgery*	Skin prick test	Long-term antibiotic
1	32	F	4 years	None	+ (H, C, A)	Amoxycillin
2	35	F	10 years	Eight operations including Caldwell-Luc	+ (F, A, C, TP, M, E)	Flucloxacillin
3	40	F	9 years	BAWO and trimming of turbinates	+ (H, CL, A, F, C)	Amoxycillin
4	29	F	8 years	Seven operations including FESS	-	Cefadroxil
5	55	F	3 years	None	+ (M, E, C, GP, TP)	Cefadroxil
6	44	M	30 years	Six operations	+ (H)	Cefadroxil
7	25	F	5 years	Tonsillectomy and trimming of turbinates	-	Amoxycillin
8	43	M	4 years	Two operations including FESS	-	Co-Trimoxazole
9	13	M	4 years	None	+ (H, CL)	Cefadroxil
10	15	M	10 years+	FESS	-	Co-Trimoxazole

*All patients had been treated with betamethasone nasal drops, douching, short courses of antibiotics and allergen avoidance where relevant. Key: BAWO = bilateral antral washout; FESS = functional endoscopic sinus surgery; H = house dust mite; C = cat; CL = *Cladosporium*; A = *Aspergillus*; GP = grass pollen; TP = tree pollen; F = feathers; M = milk; E = eggs.

fied in Table I and chosen on the basis of previous bacterial cultures from sinuses or middle meatus swabs) the ciliary brushings were repeated at the same time of day.

Ciliary brushings from normal control subjects were examined approximately every week during the course of this study in order to assess normal variation.

Results

Ciliary beat frequency from normal subjects varied from 12.5 to 16 Hz. Individuals showed characteristic frequencies with less than 10 per cent variation on a single occasion, and less than 20 per cent on different samplings.

With one exception all of the chronic rhinosinusitis patients had mean ciliary beat frequencies which were lower than those of the controls. The variability between different clumps of cilia was also greater, being 20 per cent or more at the initial assessment.

The initial mean values are shown on the left side of Figure 1, with the post-antibiotic mean values on the right. All individuals demonstrated an increase in mean ciliary beat frequency; in two, in whom no beating cilia were

initially found, normal frequencies were seen after three months of antibiotics. The variability between readings of ciliary beat frequency from a single individual was also decreased to under 10 per cent after antibiotic therapy.

Marked symptomatic improvement (>60 per cent decrease in symptom scores as judged by visual analogue scale) was seen in eight of the 10 patients.

Discussion

Chronic rhinosinusitis is a relatively common condition. Predisposing factors are probably anatomical, involving osteomeatal drainage, and immunological, involving the effectiveness of host defences including mucociliary clearance. Certain bacteria have evolved mechanisms to reduce the efficacy of the major clearance mechanism and thus allow colonization of the upper respiratory tract (Cole, 1989; Cole and Wilson, 1989). Short (up to two-week courses) of antibiotic may be insufficient to eradicate these organisms because of their relatively protected position where antibiotic penetration is poor. They are not accessible to the systemic immune system since they are colonizers rather than invaders; however they have effectively paralysed the mucosal defence mechanisms.

In this paper we have shown that a group of patients with chronic infection in nose and sinuses have lowered ciliary beat frequencies, with a variation between cilia which probably reflects their proximity to bacterial products. Long-term antimicrobial therapy was not only associated with a decrease in symptoms, but also with a significant increase in ciliary beat frequency.

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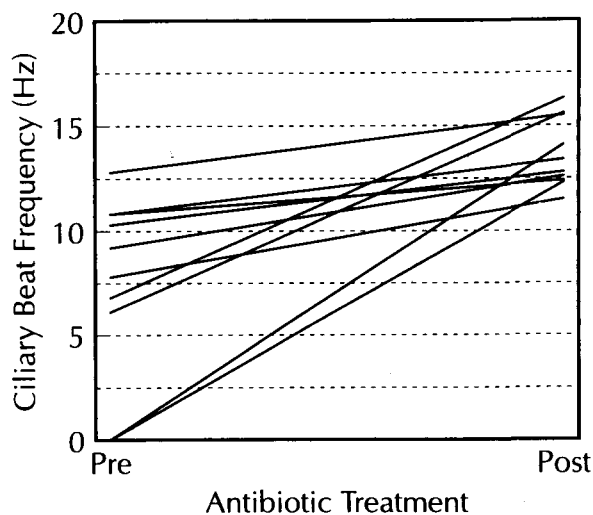


FIG. 1

The left hand figures are the mean ciliary beat frequencies of individual patients prior to long-term antibiotic therapy. The mean value in the eight patients in whom beating cilia were demonstrable was 9.3 ± 2.3 Hz. The right hand values are the post-treatment means. Lines join the values for each individual. The mean value for all ten patients post-antibiotic therapy was 13.7 ± 1.6 Hz. These changes are highly significant ($p < 0.001$, paired *t*-test).

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