The Journal of Laryngology and Otology
December 1995, Vol. **109,** pp. 1159–1162

Antimicrobial management of chronic sinusitis in children

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Abstract

This study retrospectively investigated the microbiology and management of 40 children who suffered from chronic sinusitis.

The sinuses infected were the maxillary (15 cases), ethmoid (13), and frontal (seven). Pansinusitis was present in five patients. All aspirates were cultured for aerobic and anaerobic bacteria. A total of 121 isolates (97 anaerobic and 24 aerobic) were recovered. Anaerobes were recovered from all 37 culture-positive specimens, and in 14 cases (38 per cent) they were mixed with aerobes. Twenty-three β-lactamase-producing bacteria were isolated from 16 (43 per cent) patients. The 15 patients who received clindamycin had the most rapid response to therapy and a change of therapy and surgical drainage was required in one case. Of the 16 patients who received amoxycillin or ampicillin, 16 responded to therapy, six needed a change of therapy, including four who also had surgical drainage. Of the six who were treated with erythromycin, three needed antibiotic change, two with surgical drainage. Of the three that received cefaclor, two were cured, and one had an antibiotic change. Resistant organisms were recovered in all the cases that required therapeutic change.

These findings support the important role of anaerobic bacteria in the polymicrobial cause of chronic sinusitis in children, and the superiority of therapy effective against these organisms.

Key words: Sinusitis, chronic; Child; Clindamycin

Introduction

Chronic sinusitis can be a serious infection with potential local and systemic sequelae. The polymicrobial nature of the infection has been demonstrated in several studies that utilized adequate techniques for recovery of both aerobic and anaerobic bacteria (Frederick and Braude, 1974; Evans *et al.*, 1975; Carenfelt *et al.*, 1978; Brook, 1981). However, few data are available regarding the efficacy of various antimicrobial agents in the management of this infection in children. This retrospective review of the 37 children who suffered from chronic sinusitis, evaluates the efficacy of antimicrobial agents and correlates the therapy with the bacteria recovered from the infected sinuses.

Patients and methods

The study included 40 patients (23 male) whose ages ranged from six to 16 years (median 12 years). Twelve of the children had a history of allergic conditions, five had local intranasal problems, and one had cystic fibrosis. The sinuses involved were the maxillary (15 cases), ethmoid (13), and frontal (seven). Pansinusitis was present in five instances.

Specimens were obtained from children seen at the Children's Hospital National Medical Center, Washington DC. The children suffered from chronic sinusitis of at least three weeks' duration, and none had received antibiotic therapy for at least two weeks prior to sample collection.

Chronic sinusitis was diagnosed after reviewing the clinical and roentgenographic findings. Chronic sinusitis was judged to be present if the roentgenographic studies showed mucosal thickening and either an air-fluid level or complete opacification of the maxillary sinus. Occipitomental (Waters' view), lateral, oblique, and verticomental views were obtained. The degree of mucosal thickening was evaluated by noting the nearest distance between the air-mucosal interface and the lateral part of the sinus wall. Mucosal thickening was defined as a mucosal width of 5 mm or more. Patients had at least two of these complaints: facial pain, frontal headache, cough, purulent nasal discharge, or fever.

Specimens were obtained either through external puncture of the sinuses or during surgery, employing strict asepsis to avoid any contamination. In cases involving direct puncture of a sinus, the nasal mucosa or skin was thoroughly cleaned with povidone-iodine (Betadine) solution and the area allowed to dry. The mucosa of the planned puncture site was then swabbed with a sterile applicator, which was sent

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Accepted for publication: 20 May 1995.

https://doi.org/10.1017/S0022215100132323 Published online by Cambridge University Press

for culture in a pre-reduced anaerobic transport medium. The material was aspirated with a syringe and needle, then transported to the microbiology laboratory where it was inoculated into media supportive for aerobic and anaerobic organisms. The time between specimen collection and inoculation never exceeded 30 minutes. The specimens were inoculated into sheep blood, chocolate, and MacConkey's agar plates for aerobes, incubated at 37°C aerobically (MacConkey's) or under 5% CO_2, and examined at 24 and 48 hours. For anaerobes, the material was plated onto pre-reduced vitamin K_1-enriched *Brucella* blood agar, and an anaerobic blood agar plate containing kanamycin sulphate (75 μg/ml) and vancomycin hydrochloride (7.5 μg/ml), an anaerobic blood plate containing phenylethyl alcohol, and into enriched thioglycolate broth (containing haemin, sodium bicarbonate, and vitamin K_1) (Sutter *et al.*, 1985). The plates were incubated in anaerobic jars and examined at 48 and 96 hours. The thioglycolate broth was incubated for 14 days. Aerobic and anaerobic bacteria were identified using conventional methods (Lennette *et al.*, 1985; Sutter *et al.*, 1985). β-lactamase activity was determined by use of the chromogenic cephalosporin analogue 87/312 method (O'Callaghan *et al.*, 1972).

The choice of antimicrobial agents was made by the residents and the attending physicians from the Departments of Paediatrics, Infectious Diseases or Otolaryngology. It was made immediately following collection of the specimen and therefore was not influenced by the microbiology of the infected sinus. Although gram stains were performed on all the specimens, they were not routinely reviewed by the treating physicians. The antimicrobials prescribed to the patients were clindamycin (150–450 mg q. six hours) in 15 patients, amoxycillin (250–500 mg q. eight hours) or ampicillin (250–500 mg q. six hours) in 16, erythromycin (500 mg q. eight hours) in six, and cefaclor (250–500 mg q. eight hours) in three. Statistical analysis was carried out using X^2 and the Student's *t* test.

Evaluation of patients' response was made on a daily basis during their time of hospitalization (ranging from four to 19 days) and on subsequent weekly or bi-weekly clinic visits for at least six weeks. Patients' response to therapy was judged on these days as either cure or failure. Clinical cure was defined as elimination of all the signs and symptoms of chronic sinusitis. These included complete absence of fever (above 37°C), headache, cough, and nasal discharge or congestion. Patients whose charts did not contain all the information needed to determine cure were excluded from analysis of time elapsed prior to cure. If there was no clinical improvement after therapy, patients were considered treatment failures and were considered for change in antimicrobial therapy and/or surgical intervention. Patients who had repeat surgery were followed up for at least two months with clinic visits every one or two weeks.

Antimicrobials were administered for 10–28 days (mean 15). No difference was noted in the age, sex, nor duration of illness prior to diagnosis among the four groups of patients that received the different antimicrobials. The antimicrobials were well tolerated, and the only side-effect noted was diarrhoea in two cases who received amoxycillin.

Results

Bacterial growth was present in 37 specimens and anaerobic bacteria were recovered from all of these specimens. They were the only bacterial isolates in 23 cases (62 per cent), and in 14 (38 per cent) they were mixed with aerobes. Three specimens showed no bacterial growth.

There were 121 bacterial isolates recovered from the 37 culture-positive specimens. Twenty-four of the isolates were aerobes, and they included: α-haemolytic streptococci, *Staphylococcus aureus,* and *Haemophilus* species.

Ninety-seven anaerobes (including 8 microaerophilic) were isolated. The predominant anaerobes recovered were *Peptostreptococcus* species (28 isolates); pigmented *Prevotella* species (14), *Fusobacterium* species (13), and *Bacteroides* species (12). The microbiological data have been presented in detail in a previous publication (Brook *et al.*, 1981). The organisms recovered from the four therapeutic groups are presented in Table I. No differences were noted in the number of isolates per patient and types of bacteria recovered in each of the groups.

Twenty-three β-lactamase-producing bacteria (BLPB) were isolated in 16 of 37 patients (43 per cent) (Table I). These included all isolates of *S. aureus*, 10 of 24 *Prevotella* species, and five of 12 *Bacteroides* species.

The patients who received clindamycin had the most rapid response to therapy ($p<0.05$ compared to amoxycillin/ampicillin) (Table II). One patient who had not responded to antimicrobial therapy had surgical drainage on the seventh day of therapy. He continued to improve completely while receiving metronidazole and amoxycillin.

Of the 16 patients who received amoxycillin or ampicillin, 10 responded to therapy. Six deteriorated and required a change in therapy (four to clindamycin, and one each to erythromycin or cefaclor). Surgical drainage was required in four of these instances. Organisms resistant to amoxycillin were present in all of these cases. They included one *S. aureus*, three pigmented *Prevotella* species and two *Prevotella oris-buccae* (all *Prevotella* isolates produced β-lactamase).

Of the six children who were treated with erythromycin, three needed an antibiotic change (two to amoxycillin, and one to metronidazole). Surgical drainage was performed in two cases. Organisms resistant to erythromycin were present in all of the three cases. They included one isolate each of *Haemophilus influenzae*, *Bacteroides* sp. and pigmented *Privotella.* Of the three patients who received cefaclor, two were cured (one after five days and one at nine days). One patient had the drug changed to clindamycin on the fifth day and had

https://doi.org/10.1017/S0022215100132323 Published online by Cambridge University Press

TABLE I
BACTERIOLOGY AND THERAPY OF 40 CHILDREN WITH CHRONIC SINUSITIS*

Microorganisms	Organisms in antimicrobial therapy groups				
	Clindamycin n = 15	Amoxycillin/ ampicillin n = 16	Erythromycin n = 6	Cefaclor n = 3	Total number bacteria
α-haemolytic streptococci	2	3	2		7
Streptococcus pyogenes	1	2			3
Group F *Streptococcus*			1		1
Staphylococcus aureus	3 (3)	2 (2)	1 (1)	1 (1)	7 (7)
Staphylococcus epidermidis	1				1
Escherichia coli		1			1
Haemophilus influenzae		1	1 (1)		2 (1)
Haemophilus parainfluenzae	1			1	2
Microaerophilic streptococci	3	2	2	1	8
Peptostreptococcus sp.	9	8	2	1	20
Veillonella pasvulla	2	3	1		6
Eubacterium sp.		1		1	2
Propionibacterium acnes	4	3	1		8
Propionibacterium avidum		1			1
Clostridium sp.	1	2			3
Fusobacterium sp.	4	3	1		8
Fusobacterium nucleatum		2	1	2	5
Bacteroides sp.	6 (2)	4 (1)	1 (1)	1 (1)	12 (5)
Pigmented *Prevotella* sp.	7 (3)	6 (3)	1 (1)		14 (7)
Prevotella oralis	2	2		1 (1)	5 (1)
Prevotella oris-buccae	2	3 (2)			5 (2)
Total	48 (8)	49 (8)	15 (4)	9 (3)	121 (23)
Average number organisms/patient	3.2	3.1	2.5	3.0	3.02

*Number within parentheses indicate β-lactamase producers.

recovered completely by Day 12. *P. oralis* (β-lactamase producer) was recovered from this child's infected sinus.

Discussion

The results of this retrospective study illustrate the efficacy of clindamycin therapy over other therapies that do not provide adequate coverage against aerobic and anaerobic BLPB. Aerobic and anaerobic BLPB were recovered from 43 per cent of our patients. Many of the anaerobic bacteria that can be recovered from patients with chronic sinusitis – are resistant to β-lactam antibiotics through the production of β-lactamase. Over 40 per cent of the isolates of pigmented *Prevotella* (previously named *Bacteroides melaninogenicus* group), and *Fusobacterium* species, can produce β-lactamase, and are also not inhibited by erythromycin (Sutter and Finegold, 1976).

This study illustrates that failure to respond to β-lactam or macrolides is often associated with the presence of resistant anaerobic organisms. Previous studies illustrated the increased recovery rate of BLPB in upper respiratory infections in children (Brook, 1988). The number of BLPB was shown to increase following administration of β-lactam antimicrobial therapy (Brook and Gober, 1984).

The recovery of these BLPB requires the administration of appropriate antimicrobial agents such as

TABLE II
OUTCOME AND RESPONSE OF CHILDREN WITH CHRONIC SINUSITIS TO THERAPY

	No. (%)			
	Clindamycin n = 15	Amoxycillin/ Ampicillin n = 16	Erythromycin n = 6	Cefaclor n = 3
Antimicrobial change due to clinical failure	1/15 (7)*	6/16 (37)	3/6 (50)	1/3 (33)
Surgical drainage following therapy needed	1/15 (7)	4/16 (25)	2/6 (33)	0/3 (0)
Day of therapy when patient considered clinically cured†	6.8 ± 2.4*	10.6 ± 1.8	10.7 ± 1.4	12.3 ± 0.8

*$p<0.05$ compared with amoxycillin/ampicillin group.

https://doi.org/10.1017/S0022215100132323 Published online by Cambridge University Press

clindamycin, lincomycin, metronidazole plus a macrolide or some of the newer agents that were not available during this study such as the combination of a penicillin and a β-lactamase inhibitor or imipenem.

Clindamycin, an analogue of lincomycin, is distributed rapidly in body fluid and was found to have good bone penetration (Rodriguez *et al.*, 1977) and to be very effective in the treatment of anaerobic infections (Chow *et al.*, 1974; Bartlett and Gorbach, 1975). It is also a very effective drug in the treatment of many aerobic organisms especially *S. aureus* (Rodriguez *et al.*, 1977), which is one of the pathogens frequently isolated from cases of chronic sinusitis. Usually the drug is very well tolerated; however, diarrhoea and colitis (Cohen *et al.*, 1973) have been reported rarely in adults. Diarrhoea or colitis are, however, extremely rare in paediatric patients (Randolph and Morris, 1977).

Although judicious selection of the antimicrobial agent is essential for the treatment of chronic sinusitis and its complications, surgical intervention for evacuation of pus is frequently required. Surgical drainage is therefore an integral part of the management of these cases. The early detection and initiation of appropriate antimicrobial therapy in sinusitis, with consideration of the probable presence of anaerobic organisms, is of utmost importance. Appropriate medical therapy during the initial phase of infection will reduce the likelihood of the complications of sinusitis and thereby decrease the morbidity and mortality of this potentially life-threatening infection (Brook *et al.*, 1980).

Antimicrobials effective for the therapy of chronic sinusitis should be effective against aerobic and anaerobic BLPB. These agents include, in addition to clindamycin, the combination of metronidazole and a macrolide or a β-lactam agent, or the combination of penicillin and a β-lactamase inhibitor. All these agents are available in oral and parenteral forms but some agents that are available only in parenteral form (e.g. cefoxitin, cefotetan, cefmetazole, and imipenem) are also effective.

Although this retrospective study illustrates the superiority of clindamycin over agents less effective against BLPB, prospective studies are needed to further investigate the management of chronic sinusitis in children.

Acknowledgements

The authors acknowledge the assistance and co-operation of the hospital and clinical microbiology staff at Children's Hospital National Medical Center and the secretarial assistance of Sally Eckert and Susan Renema.

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https://doi.org/10.1017/S0022215100132323 Published online by Cambridge University Press