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BACTERIAL ETIOLOGIES AND ANTIBIOTIC RESISTANCE IN SINUSITIS: A STUDY OF 264 CASES

M. FARHADI, M.D., G. BEHZADIAN NEJAD,M. S., B. FATHOLLAHZADEH,Ph.D., N. MOAZAMI, Ph.D., AND K. HOLAKOEI, Ph.D.

Fram the Department of Otolaryngology, Shaheed Rahnamon Hospital, Iran University of Medical Sciences, and the Tarbiat Modarres University, Tehran, Islamic Republic of Iran

ABSTRACT

Although inflammatory processes involving facial sinuses rarely develop during childhood, these antrums due to their anatomic situations are exposed to a variety of biologic and nonbiologic agents after birth.

Many types of bacteria are able to initiate inflammatory responses in these antrums. Since effective management of these patients rests upon demonstration of a specific pathogen and testing the organism(s) for sensitivity to a variety of antimicrobial agents and due to the fact that there are distinct epidemiological features in certain regions with respect to the etiologies, we have randomly selected 264 patients with sinusitis from several Tehran hospitals in order to estimate the frequency with which various organisms may cause the condition and to evaluate antibiotic potency and efficacy in eradicating the condition.

In 62.12 percent of cases the causative organisms could be cultured, in 32.3% of which more than one genus of bactria were isolated. The most common bacterium in this setting was *Staphylococcus aureus* followed in order by pneumococcus, enterobacteriaceae, haemophilus, pseudomonas and branhamella. The sensitivity of these organisms to various antibiotics (suitable in each case) were studied as well.

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INTRODUCTION

Four pairs of antrums called sinuses are found within the facial bones,[1] the nomenclature of which corresponds to their relative anatomic sites: maxillary, frontal, ethmoidal and sphenoidal. In the early stages of embryogenesis (the first and second months) and at birth some are pneumatized, the growth of which continues until 15-20 years of age when they achieve their final shape [2]

Sinuses are lined with mucous membranes continuous with that of the nasal cavity through some ostia. Histologically, it resembles that of the respiratory region of the nasal cavity though somewhat thinner, less vascular (which is of significance in the management of inflammatory reactions involving the sinuses)

and loosely adherent to the underlying bony walls.

The function of sinuses is controversial. However, they appear to contribute in warming and humidifying the inspired air, adding resonance to the voice, balancing the intranasal pressure, expanding the surface of the olfactory apparatus, protecting the sensory organ from head traumas, secreting a sort of mucinous substance for keeping the meati continuously wet, functioning as a barrier against heat conduction to the neural centers, etc.[3] These remain to be proved.

The pneumatized antrums are ordinarily sterile. They are protected by the potent nonspecific immunity inherent in the mucosal continuity, secretory antibodies and mechanical sweeping-like function of the ciliary system, as well.[4] Despite this effective protection, sinuses are fairly exposed to biologic injurious agents such as viruses[5] (rhinovirus, para-influnza virus III 182, echo type 28, coxsackie A21 and respiratory syncytial virus), fungi (aspergillus,[6] etc.) and many bacteria[5] (coagulase-positive and - negative staphylococcu, pneumococcus, and hemolytic streptococcus; *Haemophilus influenzae*, enterobacteriaceae, pseudomonas,[7] *Branhamella catarrhalis*,[10] mycobacteria,[5] *Legionella pneumophilia*,[8] *Eikenella corrodens*,[9] bacteroids[13] and anaerobes) of the normal flora and exogenous agents such as barotraumatism.

Table I. Frequency and percentage distribution of infection via one genus of bacteria (simple infection) and more than one genus of bacteria (mixed infection) in 264 patients surveyed.

Species of infections	No.	Percentage
Simple (one genus of bacteria)	111	67.7
Mixed (more than one of genus of bacteria)	53	32.3
Total	164	100

Perdisposing factors[6] particularly obstructive lesions and underlying conditions[14,5] such as diabetes mellitus, multiple sclerosis, cystic fibrosis, respiratory disorders and rhinitis, etc. play important roles in the etiology of this entity.

Sinusitis manifests with variable symptoms and signs: nasal discharge, congestion, headache, fever, discomfort, facial pain, inflammation, tenderness over the involved sinus(es), postnasal drip and some other nonspecific symptoms.[2,5]

Table II. Frequency and percentage distribution of responsible organisms isolated from patients with simple and mixed infections in this survey.

Organism	simple infections		mixed infections		total	
	No	Per	No	Per	No	Per
Staphylococcus	40	36.94	32	29.63	73	33.33
a:ß-Hemolytic Streptococcus	5	4.5	6	5.56	11	5.02
b: α -Hemolytic	2	1.8	3	2.7	5	2.28
Pneumococcus	36	32.43	30	27.03	66	30.14
Haemophilus	6	5.41	8	7.41	14	6.39
E. coli	5	4.5	9	8.33	14	6.39
Klebsiella	8	7.21	5	4.63	13	5.94
Proteus	2	1.8	2	1.85	4	1.83
Enterobacter	1	.9	2	1.85	3	1.83
Hafnia	1	.9	--	--	1	.46
Citrobacter	1	.9	1	.9	2	.91
Pseudomonas	2	1.8	8	7.41	10	4.57
Branhamella catarrhalis	1	09	2	1.85	3	1.37
Total	111	100	108	100	219	100

Table III. Results of antibiogram examination of responsible organism.

Organism	Staphylococcus						Pneumococcus					
Effective / Antibiotic	S*		I**		R***		S		I		R	
							No	Per	No	Per	No	Per
AM	12	16.43	7	9.58	54	73.97	60	106	---	---	---	---
PG	2	2.73	3	4.10	67	91.78	59	98.33	1	1.67	---	---
NA	64	87.67	5	6.84	4	5.47	57	95.42	3	5	---	---
CF	64	87.67	3	4.10	6	8.21	58	96.97	2	3.03	---	---
C	73	100	--	---	--	---	59	98.33	1	1.67	---	---
E	54	73.97	4	5.47	15	20.54	57	95	3	5	---	---
GM	55	75.34	6	8.21	12	16.43	27	45.42	20	33.3	14	23.32
TE	32	42.46	9	12.32	33	45.20	40	66.15	8	13.33	12	20
SXT	71	97.26	2	2.74	--	---	43	71.66	6	10	21	35.33
CX	46	63.01	3	4.10	14	32.87	--	---	---	----	---	---
L	56	76.71	6	8.21	11	15.06	20	33.3	28	46.66	12	20.18
AMX	31	43.83	11	15.06	30	41.09	--	---	---	----	---	---

* Sensitive
** Intermediate
*** Resistant

Diagnosis is based on the clinical manifestations.[11] However, it should be supported by transillumination, radiograpic, ultrasonographic, tomographic, angiographic, magenetic resonance imaging (MRI) examination and/or culturing of the secretions of the sinuses and an antibiogram to help manage the patient.

Treatment[2,5] rests upon the administration of suitable antibiotics, analgesics, decongestants and surgical drainage of the purulent secretions trapped within the sinuses.

MATERIALS AND METHODS

1- The patients who presented with signs and symptoms clinically suggestive of sinusitis and in whom the diagnosis was confirmed by roentgenographic findings, were selected without regard to age.

2- The materials needed were obtained by aspiration from the antrum and swab sampling of the middle meatus secretions.

3- Culturing: a) Thioglycolate media were used for anaerobes and organisms which might have been treated with antibiotics before sampling.

b) Purulent secretions of the sinuses were cultured on three media of blood agar, chocolate agar, McConckey and/or EMB agar which were incubated at 37°C for four days and studied every 24 hours (chocolate agar media were treated with CO_2).

c) Differential media and diagnostic discs were used in addition to the aforementioned procedures to identify the organism(s) cultured on the above media.

d) Having been identified, the organisms were tested for sensitivity to various antibiotics using chocolate, blood and casuagur (organism specific) and commercial antibiotic-containing discs. The clear zone of bacterial growth inhibition which formed around the

Table III. Continued.

Organism	Haemophilus influenza						Branhamella Catarrhalis					
Effective / Antibiotic	S		I		R		S		I		R	
	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER
AM	10	71.4	1	7.14	3	21.43	3	100	---	---	----	----
C	1	92.86	1	7.14	--	---	3	100	---	---	----	----
CF	14	100	--	--	--	---	3	100	---	---	----	----
GM	14	100	--	--	--	---	3	100	---	---	----	----
RA	13	92.86	1	7.14	--	---	2	67	1	33	----	----
SXT	11	78.57	--	--	3	21.43	--	---	---	---	3	100
AMX	1	7.14	10	71.43	3	21.43	3	100	---	---	----	----
K	---	---	--	--	--	---	1	33	---	---	2	67
PG	---	---	--	--	--	---	3	100	---	---	----	----

Table III. Continued.

Organism	Citrobacter						Klebsiellae					
Effective / Antibiotic	S		I		R		S		I		R	
	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER
AM	--	--	--	--	2	100	3	13.07	2	15.38	8	61.53
GM	1	50	--	--	1	50	6	46.15	--	---	7	53.85
TE	1	50	1	50	--	---	10	76.92	1	7.69	2	15.38
SXT	1	50	1	50	--	---	9	69.23	--	---	4	30.76
C	2	100	--	--	--	---	10	76	1	7.19	2	15.38
K	1	50	1	50	--	---	8	61.54	2	15.38	3	23.07
CF	2	100	--	--	--	---	9	69.23	--	---	4	30.76
F.M	2	100	--	--	--	---	5	38.46	4	30.76	4	30.76
AMK	2	100	--	--	--	---	8	61.54	2	15.4	3	13.08
AMX	--	---	--	--	2	100	--	---	---	---	----	-----

discs at 37°C were compared with standard scales and tables after 24 hours.

RESULTS

Of the 264 patients who were studied for a period of 11 months, 164 cases (62.12%) had positive cultures; in a considerable percentage of which (32.3%) more than one genus of bacteria were isolated (Table I). A total of 219 species of bacteria were identified which are listed in order of frequency in Table II.

According to Table II, staphylococci isolated from 73 cases (33.33%) proved to be the most frequent cause of sinusitis in this study. Pneumococcus was isolated in 66 cases (30.14%), and ß-hemolytic streptococci in 16 cases (7.3%), haemophilus and *E.coli* each in 14 cases (6.39%), klebsiella in 13 cases (5.94%), pseudomonas in 10 cases (4.57%), proteus in four cases (1.83%), enterobacter and branhamella each in three cases (1.37%), and citrobacter in two cases (0.91%). In one case (0.46%) hafnia was proved to be the causative organism. It merits separate consideration that the staphylococci were of the coagulase-positive species and the pneumococci were encapsulated. 11 cases with streptococcal origin were of the ß-hemolytic group, two cases of group B, three of group C, and the remainder of group A. In five cases -hemolytic and nonenterococcal group D streptococci grew on the culture media. Haemophilus infections were probably due to influenza species. Klebsiellae were found in one case of rhinoscleromata, in two cases of *K. ozaenae*, in three cases of *K. oxytoca* and in seven cases of *K. pneumoniae*.

Two cases of *Enterobacter agglomerans*, one case of *Enterobacter cloacae* and two cases of *Citrobacter fruendii* were also found. In addition, *Pseudomonas aeruginosa* and *Branhamella catarrhalis* were identified. No certain species were identified in hafnia infections. Antibiogramfindings are listed (see tables).

According to Table III it is evident that coagulase-positive staphylococci were generally sensitive to

Table III. Continued.

Organism	Sterptococcus ß-Hemolytic						Streptococcus α -Hemolytic Group D					
Effect / Antibiotic	S		I		R		S		I		R	
	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER
PG	11	100	--	--	--	---	5	100	---	---	----	----
E	11	100	--	--	--	---	5	100	---	---	----	----
AM	9	81.81	1	9.09	1	9.09	4	80	---	---	1	20
GM	11	100	--	--	--	---	3	60	1	20	1	20
CF	10	90.9	1	9.1	--	---	5	100	---	---	----	----
SXT	4	36.36	3	27.27	3	27.27	2	40	1	20	2	40
C	11	100	--	--	--	---	5	100	---	---	----	----
RA	--	---	--	--	--	---	4	80	---	---	1	20
TE	10	90.9	1	9.1	--	---	4	80	1	20	---	---

Table III. Continued.

Organism	*E. coli*						Enterobacter					
Effective / Antibiotic	S		I		R		S		I		R	
	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER
AM	10	71.43	2	14.29	2	14.29	--	--	---	---	4	100
CF	9	64.3	1	7.15	4	28.55	--	--	---	---	4	100
C	6	42.85	4	28.57	4	28.57	1	33.3	---	---	2	6.7
GM	10	71.43	--	--	4	28.57	2	67	1	33	---	---
Te	5	35.71	1	7.14	8	57.14	1	33.3	1	33.3	1	33.3
SXT	6	42.84	2	14.29	6	42.86	--	--	2	67	2	33
F,M	14	100	--	--	--	--	2	67	---	---	1	33
AMK	6	27.5	2	12.5	8	50	2	67	1	33	---	---
AMX	7	50	--	--	7	50	--	--	---	---	4	100

chloramphenicol and co-trimoxazole in 97%, to cephalothin and vancomycin in more than 87%, to lincomycin or clindamycin in about 77% and to gentamicin in more than 75% of the cases. In contrast, they were resistant to penicillin in 91%, to ampicillin in 73% and to cloxacillin in 32.87% of cases.

The second most frequent organism isolated in this study, pneumococcus, was sensitive to ampicillin in all cases, to penicillin and cephalothin in about 97%, to chloramphenicol in 98% and to erythromycin in 97% of the cases. Gentamicin, tetracycline and cotrimoxazole did not have any effect on this organism in 95%, 21% and 32% of cases, respectively. Haemophilus infections in sinusitis might successfully be eradicated in all cases by using cephalothin and gentamicin or rifampin in 93%, chloramphenicol in 93%, co-trimoxazole in 79% and ampicillin in 71% of the cases. Thus as to the presence of ampicillin-resistant species, it is wise to consider ampicillin as a relatively potent (not absolute) drug against haemophilus in these settings. All cases of *Branhamella catarrhalis* were sensitive to ampicillin, cephalothin, gentamicin and chloramphenicol in contrast to their high degrees of resistance to co-trimoxazole.

ß-hemolytic and group D, α -hemolytic streptococcal infections responded to penicillin, erythromycin and chloramphenicol in 100% of the cases. It merits mentioning that streptococci of the hemolytic species were sensitive to gentamicin in 100% and to cephalothin in 91% of the cases, whereas ß-hemolytic species were found to be sensitive to cephalothin in 100% and to rifampin and tetracycline in 80% of the cases.

Of the enterobacteriacea family klebsiella had the highest degree of sensitivity to tetracycline and chloramphenicol, the drugs to which infections due to other members of this family responded 77 percent of the time. Klebsiella colony growth could be inhibited on culture media by using co-trimoxazole and cephalothin in only 70% of cases, whereas the former was resistant to ampicillin and gentamicin in 61 and 53 percent, respectively. *E.coli* had variable sensitivity to ampicillin and gentamicin in about 71%, to cephalothin in 64% and to amoxicillin in 50% of the cases. It was only nitrofurantoin which reported to exert optimum effect on this organism in 100% of the cases. *E. coli* resistance to tetracycline, cephalothin and amoxicillin was observed in 57, 40, and 50 percent, respectively. Ampicillin, cephalothin and amoxicillin did not show any effect on the growth of enterobacter on the culture medium at all. The latter showed sensitivity to gentamicin to a percentage of about 67.

Cephalothin, amikacin, nitrofurantoin and chloramphenicol were the only antimicrobial agents with the potency to inhibit the growth of citrobacter species isolated on the culture medium. These organisms were all resistant to ampicillin and amoxicillin.

Although chloramphenicol was the most effective antibiotic in 100% of the cases of proteus origin, it is usually not used in eradicating the condition. Ampicillin, cephalothin and amoxicillin were all able to eradicate proteus infections in 75% of the cases, In contrast, this gram-negative organism showed resistance to tetracycline in 75% of the cases.

Pseudomonas aeruginosa was sensitive to gentamicin and amikacin in 80%, to cephazolin in 50% and showed resistance to cephalothin in 70% and to cephazolidine in 50% of the patients.

DISCUSSION

Since the pathogenic agents which may cause inflammatory processes in the sinus mucosa are in turn affected by various biologic factors (the variety of which are geographical, socioeconomical and cultural), a wide variety of invasive organisms are now implied in the etiology of sinusitis. The results of studies in this field show significant distinctions in

Table III. Continued.

Organism	Proteus						Pseudomonas					
Effective / Antibiotic	S		I		R		S		I		R	
	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER	NO	PER
AM	3	75	1	25	--	---	2	30	3	30	4	40
GM	2	50	1	25	1	25	8	80	1	10	1	10
TE	1	25	--	--	3	750	--	--	--	--	--	--
C	4	100	--	--	--	--	--	--	--	--	--	--
CF	3	75	1	25	--	--	1	10	2	20	7	70
SXT	1	25	1	25	2	50	--	--	--	--	--	--
AMX	3	75	1	25	--	--	--	--	--	--	--	--
AMK	2	50	1	25	1	25	8	80	--	--	2	20
CFS	--	--	--	--	--	--	5	50	--	--	5	50
PB	--	--	--	--	--	--	4	40	2	20	4	40

different parts of the world with respect to the etiologies. Therefore, as to the abundance of patients of this kind in Iran, it seems rational to have some knowledge of the epidemiologic aspects of the etiologies to manage the condition successfully.

The results obtained in this study are as follows:

1) The most common organism isolated from the patients stuided was staphylococcus which was resistant to several antibiotics (even to penicillinase-resistant ones such as cloxacillin). Staphylococci are capable of developing sinusitis primarily. However, they may localize within the sinuses secondarily after an initial inflammation of viral, fungal, bacterial or allergic origin and may interfere with the resolution of signs and symptoms.

Other studies[15] show that the people in the community may be healthy carriers of this organism. Thus it is not unusual for the agent to be found frequently in chronic and nosocomial infections.

2) In this study haemophilus accounts for a low percentage of the cases (6%) although it is considered important in the etiology of sinusitis. It is revealed that the organism would rather involve children and young sters and the sinusitis it causes progresses in a more or less acute course. Haemophilus may appear in the sinus mucosa in a latent state; isolation by swab sampling is, therefore, troublesome.[5] This may explain the low percentage of its occurrence in the study.

3) *Pseudomonas aeruginosa* is isolated more often from patients who were repeatedly treated with various antibiotics and their sinuses were irrigated several times. It is presumed that the low degree of immunity in involved elderly patients might be a predisposing factor, since pseudomonas would rather involve people of older age groups.

4) In a considerable percentage of patients with positive cultures (32.3%) the infections were found to be of multiple etiologies (more than one genus of bacteria could be isolated). These settings are characterized[12] by the fact that:

a) The causative agents are only of minimal virulenence under most conditions.

b) Predisposing factors such as underlying debilitating diseases, immunodeficiencies, etc. play important roles in establishing the infection.

c) Koch's law cannot be studied nor proved in these circumstances.

d) The organisms in these infections may not only be isolated from the exact site of inflammatory reactions but also spread over neighbouring sites and hence result in their isolation even when the principal infectious process has subsided.

Therefore it is obvious that the eradication of these sort of sinus infections with antimicrobials with respect to the high degree of resistance of the causative organisms, which are in the majority of cases normal flora of the nose, mouth and pharynx, may be difficult. Thus, these characteristics and the complex antagonism between the organisms and between the host result in the high potential risk for the infectious process to pursue a chronic course. It is in these circumstances that irreversible lesions formed within the sinus mucosa ultimately result in severe complications. Therefore, due to the wide spectrum of bacteria (with distinct biologic characteristics and various sensitivities to common antibiotics used in the treatment of sinusitis), infectious processes may develop within the sinus mucosa and cavity because:

1) In view of the contribution of normal flora in limitiating infectious processes and providing the circumstances for the infection to persist within these anatomic sites repeat cultures are necessary for precise identification of etiologic organisms in these patients.

2) Low vascularity of sinuses in mammals including

human beings (even relative to the posterior part of the nasal cavity, which in turn possesses much less vascularity relative to the anterior regions) results in retardation of tissue absorption of drugs such as antibiotics, decongestants, etc.

3) Effectiveness of certain drugs *in vivo* in contrast to their ineffectivity *in vitro* demonstrate that antibiotics should be chosen on the basis of cultures and antibiograms.

In addition to initial therapy, antibiotics of two congeners should be used and the drug administration should cease following the completion of the natural course of the disease, which is confirmed by resolution of clinical signs and symptoms, clearing of radiologic features, and on the grounds of negative cultures.

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