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Antimicrobial Resistance Patterns of Aerobic Organisms in Patients With Chronic Rhinosinusitis in Hamadan, Iran

Farhad Farahani [1,*]; Rasoul Yousefi Mashouf [2]; Farnaz Hashemian [1]; Rasoul Esmaeili [3]

[1]Department of Otolaryngology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, IR Iran
[2]Department of Microbiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, IR Iran
[3]Student's Research Committee, School of Medicine, Hamadan University of Medical Sciences, Hamadan, IR Iran

*Corresponding author: Farhad Farahani, Department of Otolaryngology, School of Medicine, Hamadan University of Medical Sciences, Shahid Fahmideh St. Hamadan, IR Iran. Tel: +98-9181115972, E-mail: Farahani@umsha.ac.ir

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Background: Although effective strategies have been presented for preventing the spread of antibiotic resistance in Iran, recent reports have revealed increasing antibiotic resistance among children and adults.

Objectives: In the present study, we tried to provide a clear view of the antibiotic resistance status of aerobic organism as the most prevalent organism in patients with rhinosinusitis in Hamadan, Iran.

Patients and Methods: A cross-sectional study was conducted on 216 consecutive patients referred to otolaryngology clinics of Imam Khomeini and Besat University hospitals in Hamadan with clinical and radiological manifestations of chronic rhinosinusitis. Two specimens were taken from each patient; one from the affected maxillary sinus by aspiration and another from the middle meatus and nasopharynx by swabbing. Antibiotic susceptibility was tested by Kirby Bauer's method; distributions of the isolates from middle meatus, nasopharynx and sinus were determined and the results of susceptibility test were analyzed.

Results: Among the aerobic organism from meatus and oropharynx, the most frequent isolated strains were *alpha-hemolytic Streptococcus* (15.4%), followed by *coagulase-negative Staphylococcus* (14.6%), and *Branhamella catarrhalis* (13.2%), and the most prevalent isolated strains from sinus were *S. aureus* (19.1%), *Klebsiella pneumonia* (16.4%), and *B. catarrhalis* (15.6%), respectively. The highest antibiotic susceptibility was detected to ciprofloxacin and ceftriaxone in most of the strains; susceptibility to ciprofloxacin ranged from 76.7% (for *Pseudomonas aeruginosa*) to 100% (for *Escherichia coli* and *Haemophilus influenza*); susceptibility to ceftriaxone ranged from 71.4% (for *Acinetobacter baumannii*) to 100% (for *S. pneumonia*, *Corynebacterium diphtheria*, and *H. influenza*). Besides, regardless of strain, the highest resistance was mostly detected to penicillin (ranging from 33.3% to 91.7%), and to ampicillin (ranging from 38.4% to 83.7%).

Conclusions: Our study showed that resistance to some antimicrobial agents including penicillin subgroups was considerably high for managing sinusitis. Therefore, public health policies should be more focused on minimizing the misuse of these subgroups as well as limiting the inappropriate use of other agents with high susceptibility.

Keywords: Rhinosinusitis; Antibiotic Susceptibility; Antibiotic Resistance; Aerobic Organism

1. Background

Increase of resistance to antimicrobial agents is now an important problem in our community and has been identified as a serious and critical issue for public health (1-3). Although effective strategies have been proposed to prevent the spread of antibiotic resistance in Iran including education of physicians and patients to use antimicrobial agents appropriately, published reports from medical centers reveal the increasing trend of antibiotic resistance in both adults and children (4-7). Irrational use of antibiotics develops resistant bacterial strains (8). Overusing antibiotics in different medical fields has resulted in increasing rates of community-acquired infections caused by antibiotic-resistant bacteria (9). In addition, most antibiotics are rather inexpensive in most developing countries in addition to being available without prescription (10). These and many other reasons can result in higher spread of antimicrobial resistant strains in the community.

Antibiotics constitute the main medical treatments for different infectious diseases such as bacterial sinusitis (11). Due to some difficulties for obtaining sinus culture as well as differentiating bacterial sinusitis from other nonbacterial types of sinus involvements, a large spectrum of antibiotics may be empirically used (12-14). Therefore, inappropriate usage of large-spectrum antibiotics may lead to increased bacterial resistance and virulence. Meanwhile, not only there are limited reliable data on common pathogens associated with sinusitis in Iranian patients, but also no comprehensive information is available on bacterial resistance to common antibiotics used for treating sinusitis.

2. Objectives

The aim of this study was to determine a clear view of the antibiotic resistance status of aerobic organisms as a

common etiology in patients with chronic rhinosinusitis in Hamadan, since control and treatment of this disease are considered as medical problems in most communities worldwide.

3. Patients and Methods

This cross-sectional study was performed in 2012 on 216 consecutive patients with chronic rhinosinusitis according to the American Academy of Otolaryngology criteria. In this study, we enrolled patients with chronic rhinosinusitis who had the disease symptoms for more than 12 weeks according to the American Academy of Otolaryngology criteria for rhinosinusitis. These criteria are for acute rhinosinusitis. Therefore, we diagnosed the patients who had the criteria, but only enrolled the ones who had the symptoms for more than 12 weeks. These criteria include: up to four weeks of purulent nasal drainage accompanied by nasal obstruction, facial pain/pressure/fullness, or both. The patients referred to the otolaryngology clinic of Imam Khomeini and Besat university hospitals in Hamadan, Iran and were candidate for endoscopic sinus surgery. This study was approved by the Ethical Committee of Hamadan University of Medical Sciences and informed consents were obtained from the all the patients. Two specimens were taken from each patient; one from the affected maxillary sinus by aspiration in the operating room and another from the middle meatus and nasopharynx (associated with nasal or pharyngeal bacterial flora) by swabbing. The specimens swabbed from meatus and nasopharynx as well as the specimens from sinus secretion were inoculated into thioglycollate liquid medium with agar and sent to the microbiology laboratory of Hamadan University of Medical Sciences. Simultaneously, the patients' demographic characteristics including gender, age, residence and admission date were recorded on the study self-administered questionnaires. Preliminary diagnostic tests were performed and the specimens were cultured on eosin methylene blue (EMB) agar, blood agar, and chocolate agar. Next, specific differential biochemical tests including catalase, oxidase, mannitol, coagulase, urease, nitrate, H_2S production, indole, triple sugar iron (TSI), phenylalanine, pigment, methyl red, and Voges-Proskauer were performed to characterize different species of bacteria, using different enzymes. Each colony was considered as representative of a microorganism.

Antibiotic susceptibility of the isolates was tested by Kirby Bauer's method (15), using antibiotic disks; the isolates were screened using ampicillin (20 μg), tetracycline (10 μg), chloramphenicol (30 μg), gentamicin (10 μg), kanamycin (10 μg), ciprofloxacin (5 μg), penicillin (20 μg), and ceftriaxone (30 μg). These antibiotic disks were purchased from Padtan Teb Co. (Tehran, Iran). At first, four to five pieces of separate colonies were cultured in 4-5 mL of tryptic soy broth (TSB) medium. The surfaces of five-millimeter-thick Mueller-Hinton agar plates were inoculated with a bacterial suspension, visually adjusted to 0.5 McFarland (108 CFU/mL) and diluted 100 folds. Then, eight-millimeter holes were made in agar plates with sterile die cutter and the wells were loaded with topical agents. The inhibition diameters were measured after six to eight hours of incubation at 35°C. Distribution of the isolates obtained from meatus, nasopharynx and sinus samples were determined and results of the susceptibility test were analyzed.

4. Results

Among 216 patients enrolled in the study, 134 (62.1%) were male and others were female. In our study, 122 (56.4%) subjects lived in urban and 94 (43.6%) in rural areas. More than half of the participants aged 30-49 years old (Figure 1). Among all the strains obtained from meatus and nasopharynx, the most frequent isolated strain was *alpha-hemolytic Streptococcus* (15.4%), followed by *coagulase-negative Staphylococcus* (14.6%), and *Branhamella catarrhalis* (13.8%). In addition, the most prevalent isolated strains from sinus in those with sinusitis were *S. aureus* (19.1%), *Klebsiella pneumonia* (16.4%), and *B. catarrhalis* (15.6%), respectively (Table 1). Assessment of antibiotic resistance and susceptibly patterns of 384 isolates showed that the highest antibiotic susceptibility was detected to ciprofloxacin and ceftriaxone in most of the strains that susceptibility to ciprofloxacin ranged from 76.7% (for *Pseudomonas aeruginosa*) to 100% (for *Escherichia coli* and *Haemophilus influenzae*); susceptibility to ceftriaxone ranged from 71.4% (for *Acinetobacter baumannii*) to 100% (for *Streptococcus pneumonia*, *Corynebacterium diphtheriae* and *H. influenzae*) (Table 2). Besides, regardless of strain, the highest resistance was mostly detected to penicillin (ranging from 33.3% to 91.7%), ampicillin (ranging from 38.4% to 83.7%), tetracycline (ranging from 50.0% to 57.6%), and chloramphenicol (ranging from 33.3% to 62.3%).

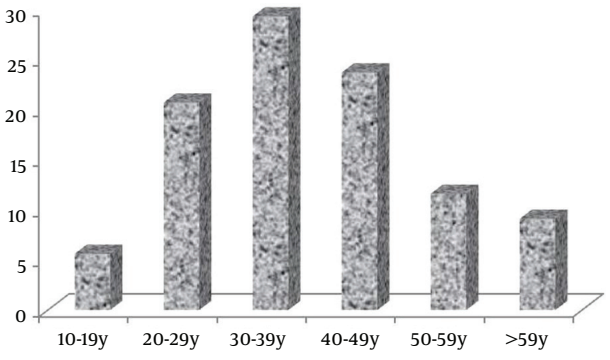

Figure 1. Age Distribution in Patients With Sinusitis

Table 1. Frequency of Isolates from Meatus, Pharynx and Sinus [a]

Organism Type	Total, No. (%)	Meatus and Pharynx, No. (%)	Sinus, No. (%)
Alpha-hemolytic *streptococcus*	59 (15.4)	48 (17.5)	11 (10.0)
Coagulase-negative *Staphylococcus*	56 (14.6)	42 (15.3)	14 (12.6)
Branhamella catarrhalis	53 (13.8)	36 (13.2)	17 (15.6)
S. aureus	49 (12.8)	28 (10.2)	21 (19.1)
Klebsiella pneumonia	43 (11.2)	25 (9.1)	18 (16.4)
S. pneumonia	29 (7.5)	23 (8.4)	6 (5.6)
Acinetobacter baumannii	28 (7.3)	18 (6.6)	10 (9.1)
Escherichia coli	24 (6.2)	19 (6.9)	5 (4.5)
Proteus mirabilis	13 (3.4)	13 (4.7)	0 (0.0)
Pseudomonas aeruginosa	12 (3.1)	7 (2.6)	5 (4.5)
Corynebactrium diphtheriae	12 (3.1)	12 (4.4)	0 (0.0)
Haemophilus influenzae	6 (1.6)	3 (1.1)	3 (2.6)

[a] Data are presented as No.(%).

Table 2. Maximum Antibiotic Sensitivity and Resistance Patterns of Isolates [a]

Organism Type	Maximum Sensitivity, No. (%)	Maximum Resistance, No. (%)
Alpha-hemolytic *Streptococcus* (n = 59)	Ceftriaxone, 55 (93.2)	Tetracycline, 34 (57.6)
	Ciprofloxacin, 51 (86.4)	Chloramphenicol, 30 (50.9)
Coagulase-negative *staphylococcus* (n = 56)	Ceftriaxone, 46 (82.2)	Penicillin, 49 (87.5)
	Ciprofloxacin, 45 (80.4)	Ampicillin, 43 (76.8)
***Branhamella catarrhalis* (n = 53)**	Ceftriaxone, 49 (92.4)	Chloramphenicol, 33 (62.3)
	Ciprofloxacin, 48 (90.6)	Ampicillin, 27 (60.0)
***S. aureus* (n = 49)**	Ceftriaxone, 45 (91.8)	Ampicillin, 41 (83.7)
	Ciprofloxacin, 41 (83.7)	Cephalexin, 42 (81.7)
***Klebsiella pneumonia* (n = 43)**	Ceftriaxone, 36 (83.7)	Ampicillin, 31 (72.1)
	Gentamicin, 35 (81.4)	Penicillin, 29 (67.4)
***S. pneumonia* (n = 29)**	Ceftriaxone, 29 (100)	Chloramphenicol, 12 (41.4)
	Cephalexin, 26 (89.6)	Kanamycin, 10 (34.5)
***Acinetobacter baumannii* (n = 28)**	Ciprofloxacin, 24 (85.7)	Penicillin, 24 (85.7)
	Ceftriaxone, 20 (71.4)	Ampicillin, 22 (78.6)
***Escherichia coli* (n = 24)**	Ciprofloxacin, 24 (100)	Penicillin, 22 (91.6)
	Gentamicin, 21 (87.5)	Ampicillin, 12 (50.0)
***Proteus mirabilis* (n = 13)**	Ceftriaxone, 12 (92.3)	Penicillin, 6 (46.2)
	Ciprofloxacin, 12 (92.3)	Ampicillin, 5 (38.4)
***Pseudomonas aeruginosa* (n = 12)**	Ciprofloxacin, 8 (76.7)	Penicillin, 11 (91.7)
	Chloramphenicol, 5 (41.7)	Ampicillin, 10 (83.4)
***Corynebacterium diphtheriae*(n = 12)**	Ceftriaxone, 12 (100)	Tetracycline, 6 (50.0)
	Kanamycin, 11 (91.7)	Penicillin, 4 (33.3)
***Haemophilus influenzae* (n = 6)**	Ciprofloxacin, 6 (100)	Tetracycline, 3 (50.0)
	Ceftriaxone, 6 (100)	Chloramphenicol, 2 (33.3)

[a] Data are presented as No.(%).

5. Discussion

Broad-spectrum empirical antibiotics are commonly used in clinical settings; however, the use of these antibiotics, especially regardless of the type of specific pathogenic agents, can lead to increased bacterial resistance and virulence. In many geographic areas, penicillin group is a reasonable first-line antibiotic for treatment of sinusitis (16). When first-line agents fail or there is a high prevalence of β–lactamase resistance, second or third-generation cephalosporins as well as quinolones provide broader coverages (16). Nevertheless, due to the wide distribution of bacterial resistance to these agents, restriction of inappropriate use of these antibiotics has been considered strongly. In our community, some subtypes of antibiotics including penicillin subgroups have been extensively prescribed, leading to considerable resistance to this antibiotic in different ages (17, 18). These observations have been confirmed by our findings in the current study among patients with sinusitis. Meanwhile, surveillance studies have indicated a significant resistance development due to alteration of penicillin binding proteins (19, 20).

In our study, the commonest aerobic pathogens found in middle meatus were *alpha-hemolytic Streptococcus*, followed by coagulase-negative *Staphylococcus*. Similar observations were reported by Klossek (21) and Gordts (22), stating that coagulase-negative *Staphylococcus* was the most common bacterial isolate in both studies. Despite similarity in types of common isolates, frequency of these pathogens in chronic sinusitis was widely different; so that the prevalence rate of coagulase-negative *Staphylococcus* among our population was 14.6%, while it was reported 50% by Klossek et al. (21) and 35% by Gordts et al. (22). This discrepancy can be related to patients' age, disease duration, differences in the sampling techniques, site of specimen collection, specimen transportation method, inoculation media, and previous antibiotic therapies (23).

Although aerobic pathogens accounted for most common isolated specimens in our study, previous studies that evaluated the sinus aspirates obtained from patients with chronic sinusitis yielded complex findings, varying from absence of anaerobes to anaerobes constituting 56% of all isolated pathogens (24-29). In a study by Finegold et al. (30), *Streptococcus* species (21.4%), *H. influenzae* (15.7%) and *M. catarrhalis* (10.0%) were among the most frequently isolated aerobic and/or facultative pathogens, which were partially consistent with our findings.

Antibiotic resistance is a global health problem. In spite of therapeutic technological advances, development of new antimicrobial agents is now in a slow trend. Almost all the developing countries are adopting a policy to limit and prevent antibiotic resistance by a multi-faceted approach to improve the public health. Since the most important cause of bacterial resistance is misuse of these agents, the strategy should address the rational prescription of antibiotics; thus, scheduling nationwide antibiotic restriction programs can effectively reduce the antibiotic-resistance rate.

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