

ETIOLOGY AND DRUG SUSCEPTIBILITY OF BACTERIAL AGENTS INVOLVED IN ACUTE AND CHRONIC SINUSITIS

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ABSTRACT:

RECOGNITION OF THE UNIQUE MICROBIOLOGY OF CHRONIC SINUSITIS AND ANTIMICROBIAL SUSCEPTIBILITY IS VERY IMPORTANT FOR SELECTING ANTIMICROBIAL THERAPY. THE AIM OF THIS STUDY WAS TO DETERMINE THE ETIOLOGY AND ANTIBIOTIC SUSCEPTIBILITY OF THE BACTERIA CAUSING ACUTE AND CHRONIC SINUSITIS. THE STUDY GROUP INCLUDED 111 BACTERIAL STRAINS ISOLATED FROM SINUS PUNCTURE OBTAINED FROM 150 PATIENTS HOSPITALIZED AT COUNTY CLINICAL EMERGENCY HOSPITAL, CRAIOVA, ROMANIA FROM 01.01.2014 TO 01.01.2016. THE ISOLATES WERE IDENTIFIED BY CONVENTIONAL MICROBIOLOGICAL PROCEDURES. ANTIMICROBIAL SUSCEPTIBILITY TESTING WAS DETERMINED BY DISK DIFFUSION METHOD ON MUELLER-HINTON AGAR (BIOMERIEUX, USA) FOLLOWING CRITERIA AS RECOMMENDED BY THE CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI, DENVER, USA). THE PREVALENCE OF BACTERIAL AGENTS WAS: PSEUDOMONAS AERUGINOSA STRAINS 24 (13,11%), STAPHYLOCOCCUS STRAINS FOR S.AUREUS AND S. EPIDERMIDIS 26 (14,20%) RESPECTIVELY 47 (25,68%) AND ACINETOBACTER BAUMANNII STRAINS 14 (7,65%). OF ALL P. AERUGINOSA CULTURED, 83.33% WERE RESISTANT TO CIPROFLOXACIN AND 97.92% SENSITIVITY TO COLISTIN. OF THE 26 STRAINS OF STAPHYLOCOCCUS AUREUS, 10 (38,46%) WERE MRSA

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AND 16 (61,54%) MSSA. IN TERMS OF THE SPECTRUM OF SENSITIVITY - THE MOST SENSITIVE DRUG WAS LINEZOLID (96.15%) AND RESISTANT 84.62%, TETRACYCLINE. STAPHYLOCOCCUS EPIDERMIDIS STRAINS, 47 (25,68%) WERE RESISTANT TO TETRACYCLINE (91.49%) AND AN INCREASED SENSITIVITY TO MOXIFLOXACIN (78.72%), VANCOMYCIN (82.97%). FOR ACINETOBACTER STRAINS MOST EFFECTIVE ANTIBIOTIC COLISTIN WAS (85.71%) AND INCREASED RESISTANCE TO CIPROFLOXACIN (64.29%). ANTIMICROBIAL RESISTANCE IS INCREASING IN CHRONIC AND ACUTE BACTERIAL SINUSITIS. THE EMERGENCE OF MRSA AND GRAM NEGATIV BACTERIA CAUSING CHRONIC SINUSITIS IS INCREASING.

KEY WORDS: CHRONIC SINUSITIS, ACUTE SINUSITIS, BACTERIA, ANTIBIOTIC RESISTANCE

INTRODUCTION

Rhinosinusitis is a significant health problem worldwide. Commonly symptoms are such as headache, facial pain, nasal congestion, or rhinorrhoea to “sinus trouble”, symptoms that may be due to various other reasons. Primary care physicians often tend to think of sinusitis as an acute bacterial infection, hence antibiotics are prescribed in 92% of patients in the UK¹⁰ and 85–98% of sinusitis patients in the US¹¹. The number of medical prescriptions for acute bacterial sinusitis was over 7.6 million in Germany¹². In France, around 7% of all antibiotics are prescribed to treat suspected acute bacterial sinusitis¹³.

In US, rhinosinusitis are one of the 10 most common conditions treated in ambulatory practice, because they accounted 12% of antibiotics prescribed to adults and 12 to 17 million annual visits to physicians¹⁴. The enormous use of antibiotics contribute to the emergence and spread of antibiotic-resistant bacteria and also has a financial impact on the health services

Bacterial microorganisms involved in acute sinusitis are represented by Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis, whereas in chronic sinusitis. Staphylococcus aureus and some anaerobic bacteria (Prevotella and Porphyromonas, Fusobacterium, and Peptostreptococcus spp.) are the most common isolates in chronic rhinosinusitis (CRS). Appropriate antibiotic treatment requires sinusitis bacteriology assessment. The aim of this study was to isolate bacteria in clinical samples from patients with chronic sinusitis. Methicillin-resistant S. aureus (MRSA) accounted for over 60 % of S. aureus isolates

¹⁰ Ashworth MA, Charlton J, Ballard K, et al. Variations in antibiotic prescribing and consultation rates for acute respiratory infection in UK general practices 1995–2000. Br J Gen Pract 2005;55:603–8.

¹¹ Gonzales R, Steiner JF, Lum A, et al. Decreasing antibiotic use in ambulatory practice: impact of a multidimensional intervention on the treatment of uncomplicated acute bronchitis in adults. JAMA 1999;281:1512–19.

¹² Institut für Medizinische Statistik. Verordnungsindex Pharmazeutika 2003.

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¹⁴ Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1996. Vital Health Stat 1998;134:1–37.

and *Pseudomonas aeruginosa* and other aerobic Gram-negative are frequently recovered in nosocomial sinusitis¹⁵.

In the last years, recent data have shown the emergence of antibiotic resistance bacteria in sinusitis and the increasing rate of multidrug resistance (MDR) enterobacteriaceae causing chronic sinusitis¹⁶. As one of the most prevalent chronic illnesses, treatment of chronic sinusitis, is complicated due to increase of antibiotic-resistant bacteria¹⁷.

The aim of this study was to determine the etiology and antibiotic susceptibility of the bacteria causing acute and chronic sinusitis in Emergency Hospital from Craiova.

MAIN TEXT

METHODS

The study group included 111 bacterial strains isolated from sinus puncture obtained from 150 patients hospitalized at County Clinical Emergency Hospital, Craiova, Romania from 01.01.2014 to 01.01.2016. The isolates were identified by conventional microbiological procedures. Antimicrobial susceptibility testing was determined by disk diffusion method on Mueller-Hinton agar (Biomérieux, USA) following criteria as recommended by the Clinical and Laboratory Standards Institute (CLSI, Denver, USA). For some strains the identification and antibiotic susceptibility testing was performed through bacterial identification system for ID / AST VITEK® 2. The interpretation of the results was performed according to CLSI (Clinical and Laboratory Standards Institute)¹⁸. *S. aureus* isolates were screened for oxacillin resistance using Clinical and Laboratory Standards Institute (formerly the National Committee for Clinical Laboratory Standards) disc diffusion method (NCCLS, 2003). Overnight cultures from blood agar plates were suspended in Mueller–Hinton broth to the turbidity of a 0.5 McFarland standard, plated on Mueller–Hinton agar and a 1 mg oxacillin disc was placed onto the inoculum. Zone diameters were measured and recorded after 24 h incubation at 35 °C and susceptibility/ resistance was recorded as follows: susceptible, equal or greater than 13 mm diameter; intermediate, 11–12 mm diameter; resistant, equal to or less than 10 mm diameter. MRSA strains were not typed.

RESULTS

Out of total number of patients (150), 111 strains were evaluated in our study, 70 were males (63,06%) and 41 were females (36,94%)

¹⁵ Farajzadeh Sheikh A, Ahmadi K, Nikakhlagh S. Detection of *Streptococcus pneumoniae* and *Moraxella catarrhalis* in patients with paranasal chronic sinusitis by polymerase chain reaction method. *J Chin Med Assoc.* 2016 Aug;79(8):440-4. doi: 10.1016/j.jcma.2016.03.002. Epub 2016 Jun 6.[pubmed]; Brook I. Microbiology of chronic rhinosinusitis. *Eur J Clin Microbiol Infect Dis.* 2016 Jul;35(7):1059-68. doi: 10.1007/s10096-016-2640-x. Epub 2016 Apr 16.[pubmed].

¹⁶ Boase S, Foreman A, Cleland E, et al. The microbiome of chronic rhinosinusitis: culture, molecular diagnostics and biofilm detection. *BMC Infect Dis* 2013; 13: 210; Hsu J, Lanza DC, Kennedy DW. Antimicrobial resistance in bacterial chronic sinusitis. *Am J Rhinol* 1998; 12: 243-8; Eslami G, Salehifar E, Behbudi M, Rezai MS. Rational Use of Amikacin in Buali-Sina Hospital in Sari, 2011. *J Mazandaran Univ Med Sci* 2013; 23: 2-9.

¹⁷ Solares CA, Batra PS, Hall GS, Citardi MJ. Treatment of chronic rhinosinusitis exacerbations due to methicillin-resistant *Staphylococcus aureus* with mupirocin irrigations. *Am J Otolaryngol* 2006; 27: 161-5; Rahmati M, Mohebi S, Shahmohammadi S, Rezai M. Fluticasone nasal spray as an adjunct to Amoxicillin for acute sinusitis in children: a randomized controlled trial. *Eur Rev Med Pharmacol Sci* 2013; 17: 3068-72.

¹⁸ CLSI. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Third Informational Supplement. M100-S23. Clinical & Laboratory Standards Institute 2013. <https://books.google.com/books?id=ARhelwEACAAJ>

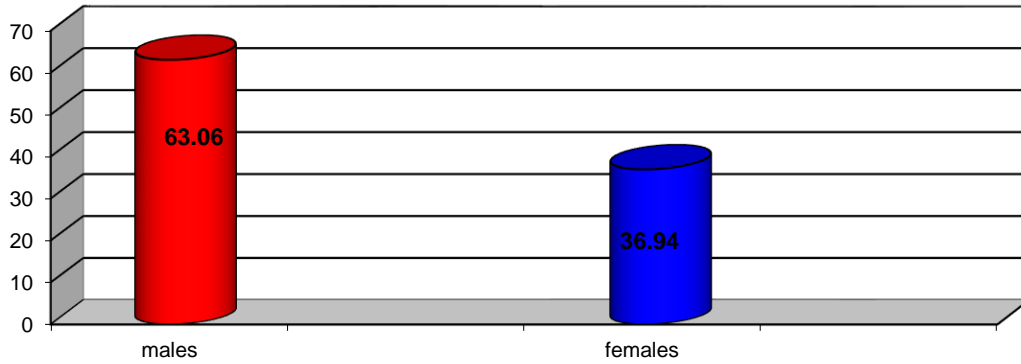


Fig.1. Distribution of cases by sex

The prevalence of bacterial agents was: *Pseudomonas aeruginosa* strains 24 (13,11%), *Staphylococcus* strains for *S.aureus* and *S. epidermidis* 26 (14,20%) respectively 47 (25,68%) and *Acinetobacter baumannii* strains 14 (7,65%)

Distribution of cases according to clinical form highlights the high incidence of acute sinusitis (56,64%) compared to chronic sinusitis (45,35%).

Table.1 . Distribution of cases by clinical form

Clinical form	Nr of cases	% Of the total positive cases
Acute sinusitis	61	56,64
Chronic sinusitis	50	45,35

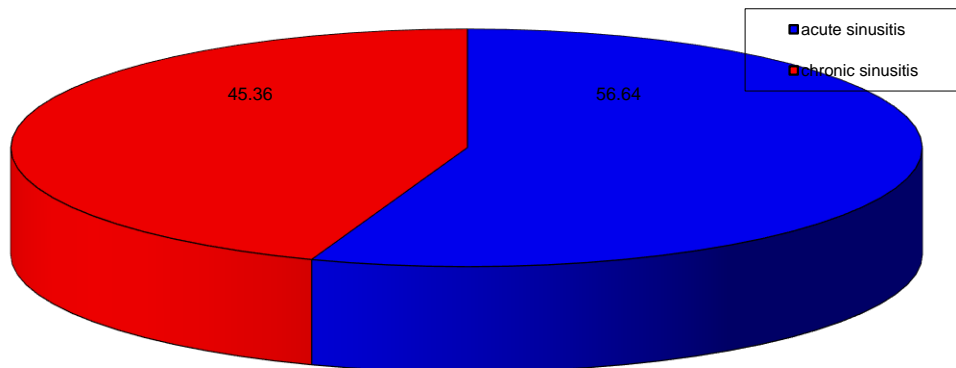


Figure 2. Distribution of cases by clinical form

Regarding the study of antibiotic susceptibility and resistance of germs isolated, are presented in the following results.

PSEUDOMONAS AERUGINOSA

The tested antibiotics for *pseudomonas* strains were: Colistin (CO), Piperacilin/Tazobactam (TZP), Ticarcilin (TIC), Cefoperazone (CFP), Cefotaxime (CTX), Ceftazidime (CAZ), Ceftriaxone (CRO), Cefepime (FEP), Imipenem (IPM), Ertapenem (ETP), Meropenem (MEM), Amikacin (AN), Gentamicină (GM), Netilmicin (NET), Kanamicină (K),

Tobramicin (NN), Ciprofloxacin (CIP), Norfloxacin (NOR), Aztreonam (ATM). Antibiotic susceptibility of *Pseudomonas aeruginosa* is shown in the tabel and figure below:

Table 2. Antibiotic susceptibility of *Pseudomonas aeruginosa* strains

Antibiotic	Susceptible strains		Resistant strains	
	No.	%	No.	%
CO	21	87,50	3	12,50
MEM	20	83,33	4	16,67
TZP	19	79,16	5	20,84
TIC	18	75,00	6	25,00
CFP	10	41,66	14	58,34
CTX	10	41,66	14	58,34
CAZ	9	37,50	15	62,50
CRO	11	45,83	13	54,17
FEP	5	20,84	19	79,16
IPM	19	79,16	5	20,84
ATM	20	83,33	4	16,67
AN	21	87,50	3	12,50
GM	14	58,34	10	41,66
NET	19	79,16	5	20,84
K	6	25,00	18	75,00
NN	21	87,50	3	12,50
CIP	4	16,67	20	83,33
NOR	7	29,17	17	70,83
ETP	18	75,00	6	25,00

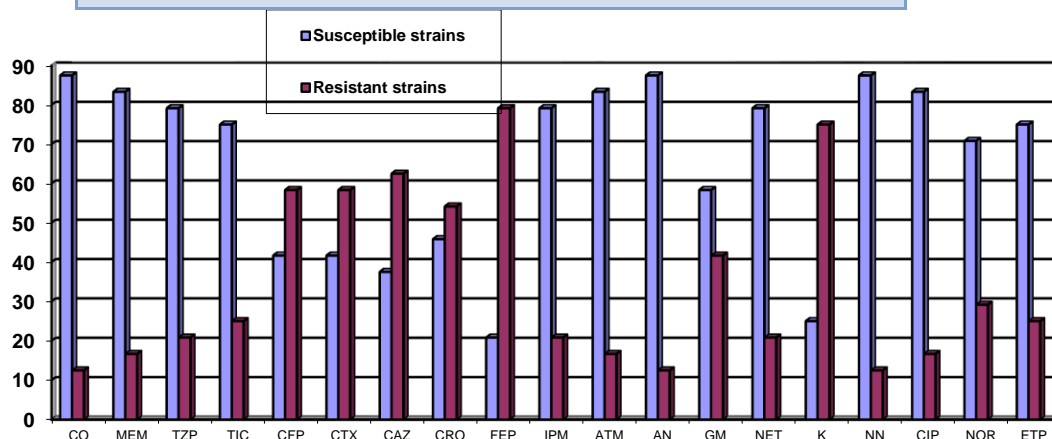


Figure 3. Antibiotic susceptibility of *Pseudomonas aeruginosa* strains

We found an increased sensitivity to colistin (97.92%), aztreonam (97.92%), piperacillin / Tazobactam (96.88%), meropenem (96.88%) while weak activity have cefepime (5, 21%), ticarcillin (18.75%) and kanamycin (6.25%).

STAPHYLOCOCCUS EPIDERMIDIS

Table 3. Antibiotic susceptibility of Staphylococcus epidermidis strains

Antibiotic	Susceptible strains		Resistant strains	
	No.	%	No.	%
Oxaciline (OX)	5	10.63	42	89.37
Tetracycline (TE)	4	8.51	43	91.49
Ampicilin (AM)	7	14.89	40	85.11
Amoxicillin (AML)	26	55.31	21	44.68
Amoxicilin/Acid Clavulanic (AMC)	41	87.23	6	12.77
Rifampicin (RA)	37	78.72	10	21.28
vancomycin (VA)	39	82.97	8	17.03
Cefoxitin (FOX)	12	25.53	35	74.47
Clarithromycin (CLR)	10	21.27	37	78.73
Cefoperazone (CFP)	12	25.53	35	74.47
Moxifloxacin (MXF)	37	78.72	10	21.28
Linezolid (LNZ)	46	98.87	1	1.13

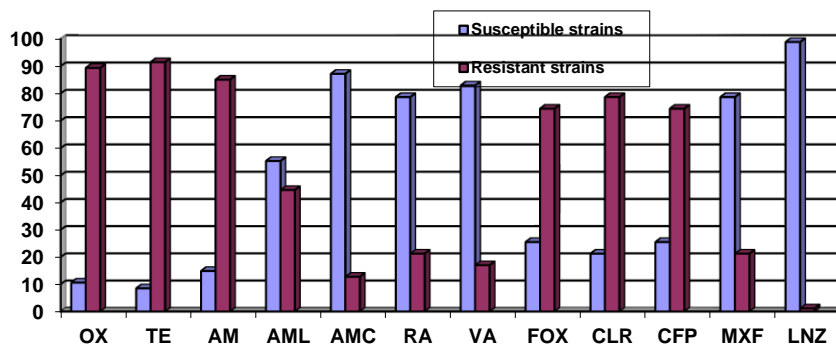


Figure 4. Antibiotic susceptibility of Staphylococcus epidermidis strains

There is an increased sensitivity to moxifloxacin (78.72%), vancomycin (82.97%), rifampicin (78.72%). In the case of linezolid we have found a single resistant strain (1.13%). Observed increased resistance to tetracycline (91.49%), Oxacillin (89.37%) and ampicillin (85.11%).

STAFILOCOCCUS AUREUS

Of the 26 strains of staphylococcus aureus, 10 (38,46%) were MRSA and 16 (61,54%) MSSA. All the strains were sensitive to Vancomycin. In terms of the spectrum of sensitivity - the most sensitive drug was linezolid (96.15%), followed by moxifloxacin (80.79). A high resistance was found for tetracycline (84.62%), ampicilin (65.39%) and clarithromycin (69,24%) (table3,figure4)

Table 4. Antibiotic susceptibility of Staphylococcus aureus strains

Antibiotic	Susceptible strains		Resistant strains	
	No.	%	No.	%
OX	10	38,46	16	61,54
TE	4	15,38	22	84,62
AM	9	34,61	17	65,39
AML	11	42,30	15	57,70
AMC	15	57,69	11	42,31
RA	14	53,84	12	46,16
VA	26	100%	0	0%
FOX	10	38,46	16	61,54
CLR	8	30,76	18	69,24
CFP	9	34,61	17	65,39
MXF	21	80,79	5	19,21
LNZ	25	96,15	1	3,85

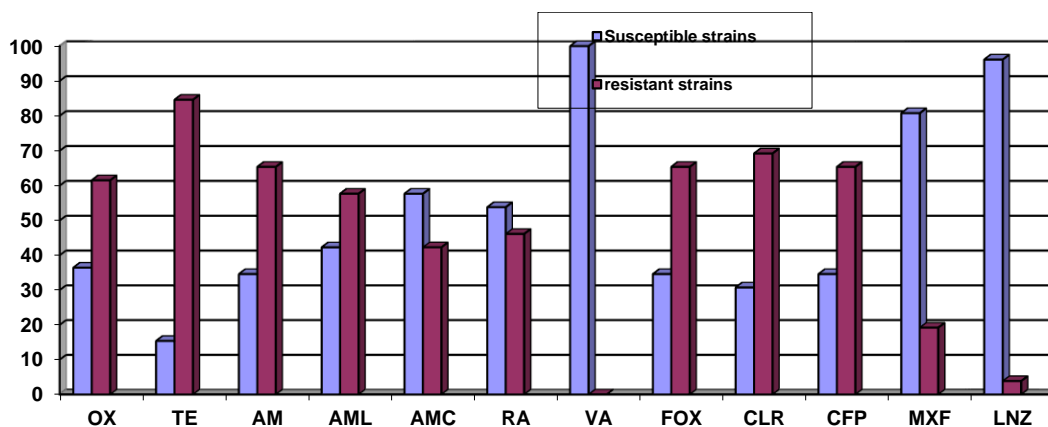


Figure 4. Antibiotic susceptibility of Staphylococcus aureus strains

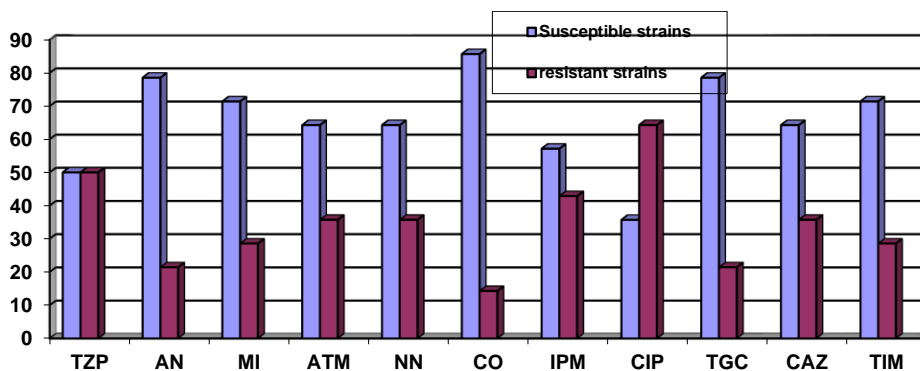
ACINETOBACTER BAUMANNII

For Acinetobacter strains the identification and antibiotic susceptibility testing was performed through bacterial identification system for ID / AST VITEK® 2. Results interpretation was performed according to CLSI (Clinical and Laboratory Standards Institute)

Sensitivity and resistance of 14 strains of Acinetobacter baumannii were tested: Piperacillin-Tazobactam (TZP), Amikacin (AN), minocycline (MI) Aztreonam (ATM), tobramycin (NN) Colistin (CO), imipenem (IPM) and ciprofloxacin (CIP), Tigecycline (TGC), Ceftazidime (CASE), ticarcillin / clavulanic acid (TIM).

Table 4. Antibiotic susceptibility of *Acinetobacter baumannii* strains

Antibiotic	Susceptible strains		Resistant strains	
	No.	%	No.	%
TZP	7	50	7	50
AN	11	78,57	3	21,43
MI	8	71,42	6	28,58
ATM	9	64,28	5	35,72
NN	9	64,28	5	35,72
CO	12	85,71	2	14,29
IPM	8	57,14	6	42,86
CIP	5	35,71	9	64,29
TGC	11	78,57	3	21,43
CAZ	9	64,28	5	35,72
TIM	10	71,42	4	28,58

Figure 5. Antibiotic susceptibility of *Acinetobacter baumannii* strains

Most effective antibiotic colistin was (85.71%), followed by Minocycline (71.42%), Amikacin (71.42%), ticarcillin / acidclavulanic (71.42%); with increased resistance to ciprofloxacin (64.29%), imipenem (42.86%).

DISCUSSION

In United States, sinusitis is a common disorder that affects more than 30 million individuals each year¹⁹. About 90% of patients visit primary care physician for sinusitis treatment and it is important for him to be attentive to this condition because its incidence appears to ascending. Prompt, effective therapy is required to reduce lost work time for adults and to allow children to return to school and parents to return to work. Antimicrobial resistance patterns have changed to create increasingly complicated problems with antimicrobial therapy²⁰.

¹⁹ United States Department of Health and Human Services. National health survey. Prevalence of selected chronic conditions, United States, 1983–85. Hyattsville, Md: US Department of Health and Human Services, 1987.

²⁰ Adelglass J, Jones TM, Ruoff G, Kahn J, Wiesinger B, Reilly-Gauvin K, et al. A multicenter, investigator-blinded, randomized comparison of oral levofloxacin and oral clarithromycin in the treatment of acute bacterial sinusitis.

We found in our study that *S. aureus* has an increased rate of antibiotic resistance. For example we reported 10 (38,46%) of Staphylococcus strains were increasing MRSA strains, a major problem in the hospital and community settings²¹. Brook et al. compared rate of recovery for methicillin-resistant *S. aureus* between 2001-2003 and 2004–2006. In that study *S. aureus* was found in 15% of the patients with chronic sinusitis between 2001 and 2003, 27% were MRSA, and from 20% of the patients with chronic sinusitis during 2004-2006, 61% were MRSA ($P<0.05$)²². Davoudi et al. reported resistance to vancomycin observed in one isolated *S. aureus* and the rate of MRSA *S. aureus* was 54.2%. These findings are in concordance. Clinical trials involving treatment of community-acquired respiratory infections demonstrate high bacterial eradication rates and clinical cure rates. In the treatment of community-acquired respiratory tract infections, the various new fluoroquinolones appear to be comparable to each other, but may be more effective than macrolide or cephalosporin-based regimens. The new fluoroquinolones, such as moxifloxacin have much to offer in terms of bacterial eradication, including activity against resistant respiratory pathogens such as penicillin-resistant, macrolide-resistant, and multidrug-resistant *S. pneumoniae*. However, ciprofloxacin-resistant organisms, including ciprofloxacin-resistant *S. pneumoniae*, are becoming more prevalent, thus prudent use must be exercised when prescribing these valuable agents. In our study we reported 80,79% moxifloxacin sensibility in concordance with literature²³.

PSEUDOMONAS AERUGINOSA

In nearly 1 of 5 patients with chronic rhinosinusitis and a history of sinus surgery is cultured *Pseudomonas aeruginosa*. Fluoroquinolones, administered antibiotics with efficacy against *P. aeruginosa*, their frequent empiric use in the community raises concern for a rise in resistance²⁴. Our results showed a total of 24 (13,11%) of *Pseudomonas* strains

In concordance with literature, in our study we reported 83.33% ciprofloxacin resistance and also 70,83% norfloxacin resistance. Brook I. Et al found that *Pseudomonas aeruginosa* and other aerobic and facultative Gram-negative rods are frequently recovered in nosocomial sinusitis, the immunocompromised host, individuals with human immunodeficiency virus infection, and in cystic fibrosis. The CRS infection evolves the formation of a biofilm that might play a significant role in the pathogenesis and persistence of CRS (chronic rhinosinusitis)²⁵. In our study we found 13,11% of strains was cultured with *pseudomonas aeruginosa*.

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²² Brook I, Foote PA, Hausfeld JN. Increase in the frequency of recovery of methicillin-resistant Staphylococcus aureus in acute and chronic maxillary sinusitis. J Med Microbiol. 2008;57:1015[PubMed]

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²⁵ Brook I, Foote PA, Hausfeld JN. Increase in the frequency of recovery of methicillin-resistant Staphylococcus aureus in acute and chronic maxillary sinusitis. J Med Microbiol. 2008;57:1015[PubMed]

ACINETOBACTER BAUMANNII

One of the most common causes of fever of unknown origin in critically ill patients and is rhinosinusitis and should be systematically searched. Mendes Neto JA evaluate diagnostic and therapeutic effect of maxillary sinus puncture performed in patients with infective rhinosinusitis hospitalized in an Intensive Care Unit of a high complexity care hospital. He found that the most commonly found organisms in sinus aspirates were *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. In our study 7,85% strains were cultured with *Acinetobacter baumannii*. The antibiotic susceptibility was in concordance with literature, imipenem 42,86% resistance, ciprofloxacin 64,29% resistance²⁶.

CONCLUSION

The antibiotic therapy depends on the probable infecting pathogens, bacterial antibiotic resistance. In addition to antibiotics, adjuvant therapies and surgery are used in bacterial sinusitis management. An accurate diagnosis when choosing therapy for rhinosinusitis will optimize chances to achieve early recovery and avoid complications.

ACKNOWLEDGMENTS

All authors equally contributed in the research and drafting of this paper

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