ETIOLOGY AND ANTIMICROBIAL RESISTANCE OF PATHOGENS ISOLATED FROM MAXILLARY SINUS ASPIRATE IN ACUTE BACTERIAL SINUSITIS IN CHILDREN

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Abstract

■ Background: Etiological diagnosis of acute bacterial sinusitis (ABS) is difficult since sinus punctures are rarely done in routine practice. The aim of this study was to determine the etiology of ABS in children using maxillary sinus puncture and to determine antimicrobial susceptibility of the most common pathogens.

■ Methods: A total of 65 children (37 boys and 28 girls) with ABS aged from 6 to 14 (9.6 + 3.98) years were enrolled in the study. Maxillary sinus punctures were performed and aspirates were obtained in all children. Clinical specimens were cultured on blood and chocolate agar; bacterial isolation and identification were done according to the laboratory standards. Susceptibility testing was done by broth microdilution with interpretation of the results according NCCLS guidelines.

■ Results: Pathogens were isolated in 33/65 (50.8%) of patients. In 30/33 (90.9%) of patients with positive cultures single bacterial pathogen was found, in 3/33 (9.1%) of patients mixtures of various bacterial species were isolated. The main bacterial pathogens were *Haemophilus influenzae* - 15/33 (45.5%) and *Streptococcus pneumoniae* - 5/33 (15.2%), *Streptococcus pyogenes* - 4/33 (12.1%) and other beta-hemolytic streptococci - 5/33 (15.2%). *Moraxella catarrhalis* was isolated from only one patient (3.0%). Combination of *S.pneumoniae* and *H.influenzae* was found in 3/33 (9.1%) of cases. All isolated bacteria were highly susceptible to amoxicillin, amoxicillin/clavulanate, cephalosporins, azithromycin and clarithromycin.

■ Conclusion: The mail causative agents of ABS in children are *H.influenzae*, *S.pneumoniae* and *S.pyogenes*. The antibiotics of choice for ABS could be aminopenicillins, oral cephalosporins or modern macrolides.

Introduction

Acute rhinosinusitis accompanies almost all cases of upper respiratory tract infections (URTI) in children and therefore is one of the most common conditions patients present with to the pediatricians office. It has been estimated that approximately 5-10% of URTI are complicated by bacterial infection of the sinuses. It is extremely important to distinguish between viral URTI with rhinosinusitis and acute bacterial sinusitis (ABS) since patients with ABS undoubtedly benefit from specific antimicrobial therapy.

Diagnosis of ABS is based on clinical signs and symptoms that persist for >10 days and are more severe then common URTI cases; X-ray data (mucosal thickening of at least 4-5 mm, complete opacification or air-fluid level) and specific findings on physical examination. Etiological diagnosis of ABS is difficult since sinus punctures are rarely done in routine practice and are indicated to manage severe and complicated cases, treatment failures and immunocompromised patients.

The choice of antimicrobials for the treatment of ABS in children is empirical in most of the cases and based on the knowledge of the potential pathogens and epidemiological data on the antimicrobial susceptibility of these bacteria in the specific region. Most of the authors agree that *H.influenzae, S.pneumoniae* and *M.catarrhalis* are the leading pathogens of ABS in children. At the same time resistance (rates of beta-lactamases production in *H.influenzae* and *M.catarrhalis*, penicillin- and macrolides resistance in *S.pneumoniae*) varies significantly and may be of great clinical importance in some regions.

Russian data concerning the etiology and antibiotic resistance of pathogens causing ABS in children are few, sometimes conflicting and inconsistent thus providing a background for implementation of this study.

Objective

The aim of this study was to determine the etiology of ABS in children in Smolensk (a medium-size city located in the central part of Russia) using maxillary sinus punctures and to determine the antimicrobial susceptibility profiles of the most common pathogens.

Methods

Children treated in Smolensk Regional Clinical Hospital with clinical and roentgenological diagnosis of acute bacterial sinusitis (ABS) requiring sinus puncture (opacification or air-fluid level on the sinus X-ray, clinical signs and symptoms of moderate to severe ABS) were enrolled in the study during the period of 1999-2003. Maxillary sinus punctures were performed and aspirates were obtained. Clinical specimens were cultured on blood and chocolate agar; bacterial isolation and identification were done according to the internal laboratory standards. Susceptibility testing was done by broth microdilution in compliance with the NCCLS procedure and the results interpretation was also performed in accordance with the NCCLS (2004) standards. Susceptibility of testing panel included:

for *S.pneumoniae* and *Streptococcus spp.* - Penicillin G (PEN), Ampicillin (AMP), Amoxicillin/Clavulanate (AMC), Cefotaxime (CTX), Ceftriaxone (CRO), Cefepime (FEP), Erythromycin (ERY), Clarithromycin (CLA), Azithromycin (AZI), Clindamycin (CLI), Tetracyclin (TET), Levofloxacin (LEV), Chloramphenicol (CHL), Trimethoprim/Sulfamethoxazole (SXT), Rifampicin (RIF), Vancomycin (VAN), Linezolid (LNZ);

for *H.influenzae* - Ampicillin (AMP), Amoxicillin/Clavulanate (AMC), Cefotaxime (CTX), Ceftriaxone (CRO), Cefepime (FEP), Clarithromycin (CLA), Azithromycin (AZI), Tetracyclin (TET), Ciprofloxacin (CIP), Levofloxacin (LEV), Chloramphenicol (CHL), Trimethoprim/Sulfamethoxazole (SXT), Rifampicin (RIF).

Quality control of antimicrobial susceptibility testing procedure was performed in accordance with the NCCLS requirements using the recommended ATCC strains *S.pneumoniae* ATCC 49619 and *H.influenzae* ATCC 49247 and ATCC 49766.

Results

A total of 65 children (37 boys and 28 girls) with ABS aged from 6 to 14 (9.6 + 3.98) years were enrolled in the study. Maxillary sinus punctures were performed and aspirates were obtained in all children.

Pathogens were isolated in 33/65 (50.8%) of patients. In 30/33 (90.9%) of patients with positive cultures single bacterial pathogen was found, in 3/33 (9.1%) of patients mixtures of various bacterial species (*S.pneumoniae* and *H.influenzae*) were isolated.

The main bacterial pathogens were *Haemophilus influenzae* - 15/33 (45.5%) and *Streptococcus pneumoniae* - 5/33 (15.2%), *Streptococcus pyogenes* - 4/33 (12.1%) and other - hemolytic streptococci - 5/33 (15.2%). *Moraxella catarrhalis* was isolated from only one patient (3.0%).

Antimicrobial susceptibility testing results of *S.pneumoniae* and *H.influenzae* are presented in Tables 1 and 2.

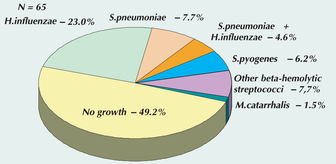
Table 1. Antimicrobial susceptibility testing results of *H.influenzae* isolated from maxillary sinus aspirates in children with ABS

Antibiotic	S, %	I, %	R, %	MIC50 mg/L	MIC90 mg/L	MIC range
Ampicillin (AMP)	94.1	0	5.9	0.25	0.5	0.125-4.0
Amox./Clavulanate (AMC)	100	0	0	0.5	0.5	0.25-2.0
Cefotaxime (CTX)	100	0	0	0.03	1.0	0.03-2.0
Ceftriaxone (CRO)	100	0	0	0.03	1.0	0.03-2.0
Cefepime (FEP)	100	0	0	0.06	1.0	0.03-2.0
Clarithromycin (CLA)	94.1	0	5.9	8.0	8.0	4.0-8.0
Azithromycin (AZI)	100	0	0	1.0	2.0	0.06-2.0
Tetracyclin (TET)	94.1	5.9	0	0.5	1.0	0.25-5.0
Ciprofloxacin (CIP)	100	0	0	0.03	0.03	0.03-0.03
Levofloxacin (LEV)	100	0	0	0.015	0.03	0.008-0.03
Chloramphenicol (CHL)	100	0	0	0.5	0.5	0.25-0.5
Trimeth./Sulfa. (SXT)	52.9	11.8	35.3	0.5	8.0	0.125-8.0
Rifampicin (RIF)	100	0	0	0.25	0.5	0.125-0.5

Table 2. Antimicrobial susceptibility testing results of *S.pneumoniae* isolated from maxillary sinus aspirates in children with ABS

Antibiotic	S, %	I, %	R, %	MIC50 mg/L	MIC90 mg/L	MIC range
Peniicillin G (PEN)	100	0	0	0.03	0.03	0.03–0.03
Ampicillin (AMP)	100	0	0	0.03	0.03	0.03–0.03
Amox./Clavulanate (AMC)	100	0	0	0.03	0.03	0.03–0.03
Cefotaxime (CTX)	100	0	0	0.015	0.015	0.015–0.015
Ceftriaxone (CRO)	100	0	0	0.015	0.015	0.015–0.015
Cefepime (FEP)	100	0	0	0.06	0.06	0.06–0.06
Erythromycin ERY)	100	0	0	0.03	0.03	0.03–0.03
Clarithromycin (CLA)	100	0	0	0.03	0.03	0.03–0.03
Azithromycin (AZI)	100	0	0	0.03	0.06	0.03–0.06
Clindamycin (CLI)	100	0	0	0.015	0.03	0.015–0.03
Tetracyclin (TET)	71.4	0	28.6	0.25	8.0	0.25–8.0
Levofloxacin (LEV)	100	0	0	0.5	1.0	0.5–1.0
Chloramphenicol (CHL)	100	0	0	2.0	4.0	2.0–4.0
Trimeth./Sulfa. (SXT)	71.4	28.6	0	0.25	1.0	0.125–1.0
Rifampicin (RIF)	85.7	0	14.3	0.03	4.0	0.015–4.0
Vancomycin (VAN)	100	0	0	0.25	0.25	0.25–0.25
Linezolid (LNZ)	100	0	0	1.0	2.0	1.0–2.0

Fig.1 The results of sinus aspirates cultures in children with ABS



Discussion

According to the published international data on etiology of ABS in children most of the authors agree that *S.pneumoniae, H.influenzae* and *M.catarrhalis* are the leading pathogens causing this infection. Previously published Russian data concerning this issue are few, sometimes conflicting and inconsistent with the modern standards of microbiology diagnostics. In our study we enrolled 65 children with clinical and roentgenological diagnosis of acute bacterial sinusitis (ABS) requiring sinus puncture (opacification or air-fluid level on the sinus X-ray, clinical signs and symptoms of moderate to severe ABS) treated in Regional Clinical Hospital in Smolensk (medium size city located in central part of Russia) during the period of 1999-2003. Maxillary sinus punctures were performed and aspirates were obtained in all children. Our data show that in 50.8% of cases bacterial pathogens are isolated from maxillary sinus aspirates and 49.2% of aspirates no growth of aerobic bacteria was revealed. The most of the cases of acute bacterial sinusitis in children were caused by *H.influenzae, S.pneumoniae,* and association of the both species, by *S.pyogenes* and other beta-hemolytic streptococci. *M.catarrhalis* was isolated from only one patient and could not be considered the prevalent cause of ABS in children in our region.

Emerging resistance problems among these bacteria according to the international data are beta-lactamases production in *H.influenzae* and *M.catarrhalis*, penicillin- and macrolides resistance in *S.pneumoniae* and macrolides resistance in *S.pyogenes* and other beta-hemolytic streptococci.

The prevalence of the resistance isolates of these bacteria vary significantly depending on the geographical region and may be of great clinical importance in some areas. For example the rates of penicillin-resistant *S.pneumoniae* are as low as 5% in North European countries and up to more than 50% in the South Europe (France, Hungary, Spain), United States and South Africa. Many of the penicillin-resistant pneumococci (PRP) may also be resistant to macrolides (10% at average in the EU and USA, and as high as 50% in Spain). This may cause problems when choosing effective antimicrobial therapy for ABS in children as respiratory fluoroquinoles are not permitted. Beta-lactamases production in *H.influenzae* runs up to 25-30% in some European countries and USA that makes combinations of penicillins with beta-lactamases inhibitors or cephalosporins the first-line drugs for the treatment of ABS.

On the contrary Russian data on the epidemiology of antimicrobial resistance of respiratory pathogens along with the susceptibility data obtained in our study show that penicillin- and macrolides-resistance in *S.pneumoniae* and beta-lactamases production in H.influenzae presently are not urgent for our country. All of the *S.pneumoniae* isolates were fully susceptible to penicillins and macrolides with the low MICs values, and ampicillin-resistance of *H.influenzae* was as low as 5.9%, and all of the cases were completely reversible by addition of clavulanate.

The resistance problems in *S.pneumoniae* and *H.influenzae* detected in our study were: tetracycline-resistance (approximately 1/3 of pneumococci and 6% of intermediate *H.influenzae* isolates) and the resistance to trimethoprim/sulfamethoxazole (approximately 1/3 of pneumococci and about 50% of non-susceptible *H.influenzae* isolates).

Therefore the first-line antimicrobials for ABS in children in our region could be aminopenicillins, oral cephalosporins or modern macrolides, trimethoprim/sulfamethoxazole should not be used due to the resistance and safety problems.

Conclusions

1. Bacterial pathogens could be isolated from 33/65 (50.8%) of maxillary sinus aspirate cultures from children presenting with clinical signs and symptoms, X-ray data and specific physical findings of ABS.

2. The main causative agents of ABS in children are *H.influenzae, S.pneumoniae, S.pyogenes* and other beta-hemolytic streptococci being responsible for 45.5%, 15.2%, 12.1% and 15.2% of all positive culture cases, respectively.

3. Penicillin- and macrolides-resistance in *S.pneumoniae* and beta-lactamases production in *H.influenzae* presently are not urgent for our country. All of the *S.pneumoniae* isolates were fully susceptible to penicillins and macrolides with the low MICs values, ampicillin-resistance of *H.influenzae* was as low as 5.9% and all of the cases were completely reversible by addition of clavulanate.

4. The resistance problems in *S.pneumoniae* and *H.influenzae* were: tetracycline-resistance (approximately 1/3 of pneumococci and 6% of intermediate *H.influenzae* isolates) and the resistance to trimethoprim/sulfamethoxazole (approximately 1/3 of pneumococci and about 50% of non-susceptible *H.influenzae* isolates).

5. The first-line antimicrobials for ABS in children in our region could be aminopenicillins, oral cephalosporins or modern macrolides. Trimethoprim/sulfamethoxazole should not be used due to the resistance and safety problems.