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Bacterial spectrum of orofacial infections and their antibiotic resistance in Belarus

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ABSTRACT

The purpose of the present study was to determine the pathogenic bacterial spectrum and bacterial antibiotic resistance in maxillofacial region of Belarussian patients.

Materials and methods. The study comprised inpatient who were treated by maxillofacial surgeons during 2014 in hospitals of Belarussian region: Brest, Mogilev, Vitebsk, Grodno and Gomel. It was a retrospective study, approval by the institution ethical committee. A microbiological sample was collected before antibiotic treatment. After meticulous disinfection of the skin around the planned extraoral incision site the aspiration of pus was attempted. If aspiration cannot be conducted, the samples were collected by swabbing the area after the incision and discharge of the pus. After sample collection, the material was immediately transported to the laboratory and further processed within 2 hours at the most. All specimens were then tested for the prevalence of the predominant bacteria and their antibiotic susceptibility

Results. At the present stage in Belarussian hospitals the main agents isolating from inflammatory focus of the maxillofacial region are streptococci, staphylococci, enterobacteria, that corresponds with the global data. On the basis of the major pathogen antibiotic resistance data the following antibiotics for initial therapy until the receiving the results of bacteriological tests can be recommended: clindamycin (effective against all studied pathogenic species), ceftriaxone, fluoroquinolones (ciprofloxacin).

Conclusions. It is necessary to conduct further systematic monitoring of microflora in patients with inflammatory diseases of maxillofacial area and studying the bacteria antibiotic resistance in order to improve the patient treatment efficiency.

Keywords: inflammation, maxillofacial area, microorganisms, Belarus

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Introduction

Odontogenic inflammatory disease of maxillofacial area is an infectious and inflammatory process arising from the microflora spread through the tooth root canal affected by caries and its complications, or periodontal pocket in periapical tissue [1]. For a long time it was thought that the microbial landscape with odontogenic infection is represented mainly by monoculture of *Streptococci* or *Staphylococci*. According to the development of microorganism identification methods a lot of other microbial groups were studied and the role of gram-negative opportunistic pathogens was determined. Modern and advanced research technologies depend on the identification of genetic markers of microbial pathogens by polymerase chain reaction (PCR) [2].

Saprophytic microflora colonizing the mouth: *Streptococcus mutans*, *Streptococcus milleri*, *Peptostrepto-*

coccus spp., *Fusobacterium spp.*, *Actinomyces spp.* often appear as odontogenic infection agent. Nowadays more than 600 species of oral microorganisms were isolated and identified [3]. Microorganisms are usually localized on the oral cavity mucous membrane surface, in periodontal pockets, or decayed cavities [4]. According to the WHO classification the microflora of the oral cavity is mainly represented by anaerobic microbes growing in the dental plaque. Resident microflora of the oral cavity is extremely diverse, with low virulence properties [5] and includes bacteria, actinomycetes, fungi, protozoa, spirochetes, rickettsia, and viruses [6].

According to the contemporary professional literature in the field of odontogenic infectious-inflammatory process associations of 2-6 microorganism species had been identified, e.g. facultative anaerobes (*Streptococcaceae* and *Staphylococcaceae*) and obligate anaerobes (*Bacteroides*, *Fusobacteriaceae*, *Peptostreptococcaceae*) [7].

Different microorganisms may cause certain nosology. The development of odontogenic periostitis and osteomyelitis is caused by *Staphylococcus aureus* and *Streptococcus* spp., anaerobic flora (*Peptococcus niger*, *Peptostreptococcus* spp., *Bacteroides* spp.). Methicillin-sensitive *Staphylococcus aureus* (MSSA) is the main causative agent of nonodontogenic osteomyelitis in 52% cases, coagulase-negative staphylococci — 14 %, methicillin-resistant *Staphylococcus aureus* (MRSA) — 2 %, *Pseudomonas aeruginosa* — 4,4 %. Traumatic osteomyelitis is often caused by *Staphylococcus aureus*, *Enterobacteriaceae* spp., *Pseudomonas aeruginosa* [7].

According to European researchers, in patients with odontogenic infection, the most frequently isolated bacteria were as follows: anaerobes (8%), gram-positive cocci (54 %), gram-negative cocci (8 %), *Viridans* group *Streptococci* (49 %), non-haemolytic *Streptococci* (11%), non-haemolytic *Staphylococci* (3 %), haemolytic *Streptococci* (0,5 %), *Enterococcus* spp. (1 %), *Escherichia coli* (1,5 %), *Staphylococcus aureus* (1 %), *Bacteroides* spp. (3 %) [8].

Thus, the causative agents of inflammatory diseases of maxillofacial area are represented by various species of microorganisms, the odontogenic infection is characterized as polyetiological. Due to the development of new microbiological methods, detection of the inflammatory disease etiology is expanding and updating constantly. All these facts indicate a need for further research in this direction.

Microbiological study of the maxillofacial inflammatory disease causative agents allows the identification of the pathogenic bacteria and determine their sensitivity to chemotherapeutic drugs, though ultimately providing optimum medical and surgical treatment tactics.

Therefore, the aim of the present study was to retrospectively analyse the pathogenic bacterial spectrum and bacterial antibiotic resistance in Belarussian patients with maxillofacial inflammatory disease.

Material and methods

Study population

The study comprised patients, who were treated by maxillofacial surgeons in 2014 in hospitals of Belarussian region: Brest, Mogilev, Vitebsk, Grodno and Gomel. Patients with maxillofacial inflammatory disease accounted for 35% (238 people) of all patients hospitalized in the Maxillofacial Department in Brest, 38,5% (628 people) — n Grodno, 28% (727 people) — n Mogilev, 36% (669 people) — n Vitebsk. A total of 2920 people with maxillofacial inflammatory disease were treated in 5 Belarussian regional hospital in 2014.

Inclusion criteria were odontogenic and non-odontogenic maxillofacial inflammatory process and no prior antibiotic treatment. Exclusion criterion was prior antibiotic treatment. All authors participating in the present study read the Declaration of Helsinki and the study was designed according to its guidelines. It was a retrospective study, approved by the local Ethics Committee.

Data collection

The skin and the oral mucosa of the infected site were rinsed with antiseptic in order to disinfect surface before incision. A microbiological sample was collected before antibiotic treatment. After meticulous disinfection of the skin around the planned extraoral incision site the aspiration of pus was attempted. If aspiration could not be conducted, the samples were collected by swabbing the area after the incision and discharge of the pus. After sample collection, the material was immediately transported to the laboratory and further processed within 2 hours at most. All specimens were then tested for the prevalence of the predominant bacteria and their antibiotic susceptibility [10–11]. The data was collected and analyzed in Microsoft Excell [12].

Results

Isolated bacteria

There were 65 isolates identified in the Department of Maxillofacial Surgery in Brest regional hospital. *Staphylococci* were isolated in most cases — 45 species (70.0%), the most common group representative was *Staphylococcus aureus*. *Enterobacteriaceae* were presented by 7 strains (10.0%). Among them *Escherichia coli* — 3 strains (4.0%) and *Klebsiella pneumoniae* — 2 strains (3.0%) were identified. *Streptococcaceae* were represented by *Streptococcus pneumoniae* — 11 strains (17.0%). Nonfermentative gram-negative rods (NFGNR) were represented by *Acinetobacter baumannii* — 2 strains (3.0%).

There were 799 isolates identified in the Department of Maxillofacial Surgery in Mogilev regional hospital. *Streptococci* were isolated in most cases (30.2%) and were represented by *Streptococcus viridans* — 204 strains (26.0%), *Streptococcus pneumoniae* — 13 strains (1.6%), *Streptococcus pyogenes* — 21 strains (2.6%). Among coagulase-negative *Staphylococci* (CNS) (43.0%) there were *Staphylococcus epidermidis* — 270 strains (35.0%) and *Staphylococcus saprophyticus* — 66 strains (8.0%). Additionally, 139 strains (17.0%) of *Staphylococcus aureus* were isolated. *Enterococci* (2.1%) were represented by *Enterococcus faecalis* — 9 strains (1.0%), *Enterococcus*

faecium — 11 strains (1.1%). *Enterobacteriaceae* (2.72%) were represented by *Klebsiella spp.* — 14 strains (1.7%), *Enterobacter spp.* — 9 strains (1%), *Escherichia coli* — 1 strain (0.02%). *Pseudomonas spp.* were represented by *Pseudomonas aeruginosa* — 6 strains (0.6%).

There were 171 isolates identified in the Department of Maxillofacial Surgery in Gomel regional hospital. *Streptococci* were isolated in most cases (32.4%), represented by *Streptococcus viridans* — 25 strains (14.0%), *Streptococcus pneumoniae* — 3 strains (1.08%), *Streptococcus pyogenes* — 10 strains (5.6%). There were 50 strains (29.0%) of *Staphylococcus aureus*. CNS (21.6%) were identified as *Staphylococcus epidermidis* — 9 strains (5.0%), *Staphylococcus saprophyticus* — 8 strains (4.6%), *Staphylococcus haemolyticus* — 20 strains (12.0%). *Enterobacteriaceae* (8.9%) were represented by *Escherichia coli 7* (4.0%), *Escherichia cloacae* — 3 (1.8%), *Citrobacter spp.* — 1 (0.1%), *Klebsiella spp.* — 5 strains (3.0%). *Enterococcus spp.* was revealed in 1.8% cases — 3 strains. Members of the genus *Pseudomonas* were isolated in 3.0% of studies (5 strains). Other NFGNR were identified as *Acinetobacter baumannii* — 1 strain (0.1%).

There were 120 isolates identified in the Department of Maxillofacial Surgery in Vitebsk regional hospital. *Staphylococci* were isolated in most cases, among them *Staphylococcus aureus* — 18 strains (15.0%), CNS — 76 strains (63.5%). CNS were represented by *Staphylococcus epidermidis*. *Streptococci* were revealed in 8.3% of cases (10 strains). *Enterobacteriaceae* (2.4%) were identified as *Escherichia coli* — 1 strain (0.8%) and *Klebsiella pneumoniae* — 2 strains (1.6%). *Pseudomonas Aeruginosa* was isolated in 5.0% of studies (6 strains), *Acinetobacter spp.* — n 08 % (1 strain).

There were 162 isolates identified in the Department of Maxillofacial Surgery in Grodno regional hospital. *Staphylococci* were the most frequent bacteria detected — 139 strains (85.0%), among them *Staphylococcus aureus* — 76 strains (47.0%), CNS — 63 strains (38.0%). CNS were represented by *Staphylococcus epidermidis* — 45 strains (28.0%), *Staphylococcus haemolyticus* — 12 strains (6.5%), *Staphylococcus hominis* — 3 strains (2.0%), *Staphylococcus capitis* — 2 strains (1.0%) and *Staphylococcus warneri* — 1 strain (0.5%). *Enterobacteriaceae* were represented by 4 strains (2.0%), among them *Klebsiella oxytoca* — 1 strain (0.5%), *Klebsiella pneumoniae* — 1 strain (0.5%), *Pseudomonas mirabilis* — 2 strains (1.0%). There were 11 strains (7.0%) of *Streptococcaceae* and they were represented by *Streptococcus pyogenes* — 3 strains (2.0%), *Streptococcus mitis* — 2 strains (1.0%), *Streptococcus sanguinis* — 2 strains (1.0%), *Streptococcus anginosus* — 2 strains (1.0%) and *Streptococcus pneumoniae* — 2 strains (1.0%). NFGNR were represented by *Acinetobacter* — 1 strain (0.5%) and *Pseudomonas*

aeruginosa — 1 strain (0.5%). Additionally, 1 strain of *Enterococcus spp.* (0.5%) was isolated.

Antibiotic resistance

Antibiotic resistance of *Staphylococcus aureus* was studied in Departments of Maxillofacial Surgery in Vitebsk, Brest, Gomel and Mogilev regional hospitals.

The greatest number of MRSA was detected in Brest — 27.8%. In Vitebsk this rate was 14.8%, in Mogilev — 10.0%, and in Gomel — 5.6%.

Staphylococcus aureus, isolated from the patients with maxillofacial inflammatory process in Vitebsk, was the least resistant to vancomycin (0%), clindamycin (0%), amikacin (3.7%), cefazolin (8.3%), ceftriaxone (11.5%), lincomycin (13.0%), gentamicin (14.8%), ciprofloxacin (18.5%), and ofloxacin (18.5%). The highest level of resistance was noted for cefotaxime (25.0%).

Staphylococcus aureus, isolated in Brest Department of Maxillofacial Surgery, was the least resistant to lomefloxacin, vancomycin, gentamicin, ofloxacin, trimethoprim, pefloxacin (for all 0%), clindamycin (4.0%), linezolid (8.3%), tigecycline (16.7%), and levofloxacin (20.0%). The highest antibiotic resistance level of *Staphylococcus aureus* was revealed for erythromycin (71.4%).

In the Department of Maxillofacial Surgery in Mogilev regional hospital *Staphylococcus aureus* showed the least resistance to vancomycin (0%), clindamycin (5.0%), gentamicin (6.0%), levofloxacin (6.0%), the highest resistance level was detected for amoxicillin (85.0%).

In the Department of Maxillofacial Surgery in Grodno regional clinical hospital *Staphylococcus aureus* did not demonstrate the resistance to vancomycin, gentamicin, levofloxacin (for all 0%). Resistance to linezolid was noted in 1.1% cases, clindamycin — 12.2%, erythromycin — 17.8%.

The resistance of *Staphylococcus aureus* to antibiotics differed in the studied Departments. The resistance of this pathogen to gentamicin was the lowest in Brest and Grodno (0%), in Mogilev regional hospital it was 6.0% and in Vitebsk regional clinical hospital was the highest (14.8%). Resistance of *Staphylococcus aureus* to clindamycin in Vitebsk was 0%, Brest — 4.0%, Mogilev — 5.0%, Grodno — 12.2%. Vancomycin resistance of *Staphylococcus aureus* was not revealed in any hospital.

Based on our findings concerning antibiotic sensitivity of *Staphylococcus aureus* in the Department of Maxillofacial Surgery of Brest, Vitebsk, Mogilev and Grodno regional clinical hospitals, clindamycin can be recommended as initial antibiotic therapy.

Gentamicin was effective against *Staphylococcus aureus* in Brest regional hospital and Grodno regional hospital. The sensitivity of *Staphylococcus aureus* to reserve antibiotic vancomycin was 100% in Vitebsk and

Mogilev. The highest number of MRSA was identified in the Department of Maxillofacial Surgery in Brest regional hospital.

The highest number of methicillin-resistant strains of *Staphylococcus epidermidis* (MRSE) was detected in Grodno — 26.2%, in Vitebsk — 22.4%, in Mogilev — 4.0%.

Staphylococcus epidermidis identified in the Department of Maxillofacial Surgery in Vitebsk regional clinical hospital was the least resistant to vancomycin (0%), amikacin (9.4%), ciprofloxacin (11.5%), clindamycin (14.0%), cefotaxime (14.4%), ceftriaxone (16.5%), ceftazidime (16.6%), ofloxacin (18.4%), with the highest noted resistance to gentamicin (21.3%), and lincomycin (28.8%).

The least resistance of *Staphylococcus epidermidis* isolated in Grodno was to vancomycin, gentamicin and moxifloxacin (for all 0%). Resistance to levofloxacin amounted to 4.8%, to linezolid — 7.1%, to clindamycin — 26.2%.

Vancomycin resistance of *Staphylococcus epidermidis* identified in the Department of Maxillofacial Surgery in Mogilev regional hospital was 0%, resistance to clindamycin was 6.0%, to gentamicin 8.0%, to levofloxacin 19.0%.

The resistance of *Staphylococcus epidermidis* to vancomycin was not detected in the studied hospitals, the highest resistance to clindamycin was detected in Grodno, the highest resistance to gentamicin in Vitebsk.

In Gomel regional hospital *Staphylococci* antibiotic resistance accounted for vancomycin — 0%, doxycycline — 3.3%, ciprofloxacin — 6.6%, clindamycin — 13.0%, penicillin — 50.0%. The number of methicillin-resistant staphylococci was 23,1%.

Streptococci antibiotic resistance was identified in the Department of Maxillofacial Surgery in Vitebsk, Gomel, Brest.

Streptococcus spp. isolated in the Department of Maxillofacial Surgery in Vitebsk regional hospital had the least resistance to clindamycin and vancomycin (for all 0%), cefotaxime (4.0%), ceftriaxone (10.0%), ciprofloxacin (13.3%), and doxycycline (20.0%). The higher level of resistance was identified for co-trimoxazole (24.0%), lincomycin (25.0%), and ampicillin (28.6 %).

Streptococci identified in the Department of Maxillofacial Surgery in Gomel regional hospital had no resistance to ceftriaxone, levofloxacin, doxycycline, amoxicillin/clavulanic acid (for all 0%). Resistance of *Streptococci* to clarithromycin amounted 3.4%, to ofloxacin — 4.5%, to clindamycin — 5.2%, to ciprofloxacin — 5.6%, to tetracycline — 11.1%, to oxacillin — 15.4%.

Streptococcus spp. identified in the Department of Maxillofacial Surgery in Brest regional hospital demonstrated no resistance to ceftriaxone, erythromycin, levofloxacin (for all 0% resistant strains). Resistance to

lincomycin, oxacillin, tetracycline was 12.5%, to erythromycin — 50.0%.

Enterobacterial antibiotic resistance was identified in the Department of Maxillofacial Surgery in Vitebsk, Gomel, Grodno.

Enterobacteriaceae had no resistance to ceftazidime, ceftriaxone, cefotaxime, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, cefoperazone/sulbactam in Vitebsk regional hospital. Resistance to amoxicillin/clavulanic acid amounted 50.0%. The least resistance of *Enterobacteriaceae* to imipenem (0%), amikacin (0%), ceftazidime (5.6%), ciprofloxacin (6.2%), ceftriaxone (17.6 %) was revealed in the Department of Maxillofacial Surgery in Gomel regional hospital. The highest resistance was detected for amoxicillin/clavulanic acid (31.2%) and ceftazidime (33.3%). In Grodno regional hospital *Enterobacteriaceae* had the least resistance to amikacin, ceftazidime, cefotaxime, cefepime, imipenem, meropenem, levofloxacin, tazobactam, tobramycin (0%). Resistance to co-trimoxazole, ciprofloxacin and gentamicin was 9.1%, to piperacillin — 11.0%, to tetracycline, norfloxacin and amoxicillin/clavulanic acids — 25.0%, to penicillin — 40.0%.

Discussion

According to the modern researches the identified causative agents of maxillofacial inflammatory diseases are: *Staphylococcus aureus* — 26.7%, *Staphylococcus epidermidis* — 17.8%, *Streptococcus spp.* — 11.1%, *Escherichia coli* and *Proteus spp.* — 11.1% of cases. In another study conducted in the Clinic of Oral and Maxillofacial Surgery in Nuremberg in 2010, *Streptococci* and *Staphylococci* were dominating among 40 identified aerobic bacterial cultures [13]. This data corresponds well with our results.

The study conducted by O. Ibragimov (2008) showed, that there are certain differences in the selected wound microflora in children with infectious maxillofacial inflammatory disease. In the microflora *Staphylococcus aureus* was dominating (54.1%) and the share of *Enterobacteriaceae* accounted for 37.8% of all isolated microorganisms. In addition, *Candida albicans* was recorded — 2.7%; and even non-fermentative gram-negative rods (*Pseudomonas aeruginosa*) were determined — 5.4%.

Therefore the results of microbiological testing of infectious maxillofacial inflammatory disease carried out in 5 Belarussian hospitals in 2014 were different. However, the general trend is that there is the main contribution of *Streptococci* and *Staphylococci* in the development of this disease.

According to the study of *Staphylococci* antibiotic resistance in the Department of Maxillofacial Surgery

in Vitebsk, Gomel, Mogilev, Brest and Grodno regional hospitals, there was no resistance to vancomycin — the antibiotic of choice for treating MRSA. This result corresponds with the data about the absence of vancomycin-resistant *Staphylococcus spp.* in the Republic of Belarus. Clindamycin, doxycycline (Gomel), gentamicin (Brest, Grodno) can be recommended as empiric, first-line antibiotic therapy of inflammatory diseases of maxillofacial area. MRSA was isolated in all 5 hospitals. Identification of MRSA is associated with low effectiveness of beta-lactam antibiotics (penicillins, cephalosporins, carbapenems, combinations of penicillins with beta-lactamase inhibitors).

Effective antibiotics for streptococcal infections of the maxillofacial region are clindamycin, ceftriaxone and fluoroquinolones (levofloxacin, ciprofloxacin). *Streptococcus spp.* showed the greatest resistance to tetracyclines (tetracycline and doxycycline), that does not allow to recommend these antibiotics as an effective starting therapy.

The most effective antibiotics against *Enterobacteriaceae* are amikacin, ceftazidime, imipenem, ciprofloxacin, ceftriaxone, and the least effective — amoxicillin/clavulanic acid.

Conclusions

Maxillofacial inflammatory disease was a common cause of hospitalizations in the Department of Maxillofacial Surgery in Belarus in 2014. Bacteriological testing seems to be a standard of care in this group of patients. According to the results of bacteriological examinations, the highest number of clinical isolates were identified in the inflammatory focus of the maxillofacial area in Mogilev, a few less in Gomel, Vitebsk and Grodno regional clinical hospitals, the lowest number — in Brest regional hospital.

At the present stage in Belarussian hospitals the main agents isolated from the inflammatory focus of the maxillofacial region are *Streptococci*, *Staphylococci*, *Enterobacteria*, which corresponds well with the global

data. According to our analysis of pathogens antibiotic resistance, the following antibiotics for initial therapy, until receiving the results of bacteriological tests, can be recommended: clindamycin (effective against all studied pathogenic species), ceftriaxone, fluoroquinolones (ciprofloxacin). It is necessary to conduct further systematic monitoring of microflora in patients with maxillofacial inflammatory disease and study the bacterial antibiotic resistance in order to improve the treatment efficacy.

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