SMJ Saratov Medical Journal
ISSN 2712-8253, Saratov Medical Journal
2023. Volume 4. Issue 2 . Article CID e0203
DOI: 10.15275/sarmj.2023.0203

Original article

Reprint

Microbiological aspects of acute odontogenic osteomyelitis in children

Elena E. Khalyuta[1] ✉, Svetlana B. Mokhnacheva[1], Irina G. Dugina[2], Anastasia D. Kutarenko[1], Alina A. Fomina[1]
✉elenahaluta@gmail.com

[1] Izhevsk State Medical Academy, Izhevsk, Russia
[2]Udmurt Republican Children's Clinical Hospital, Izhevsk, Russia

Received 19 January 2023, Accepted 25 May 2023

Abstract:
Objective: to identify the species composition of pathogens causing acute odontogenic inflammatory process in the children's jaws; to examine the sensitivity and resistance of the isolated microflora to antibiotics of various groups; and to determine the dependence of the disease clinical course on the type of dominant pathogen.
Materials and Methods.The results of a microbiological study of exudate from purulent odontogenic foci of 900 children regarding periostitis and osteomyelitis of the jaws were analyzed.
Results. In 65.6% of cases, the causative agent was Streptococcus pyogenes known as group A beta-hemolytic streptococcus (GABHS) possessing a high sensitivity to vancomycin (99%), fluoroquinolones (98%), beta-lactam antibiotics (91%), and the highest resistance to macrolides (41%). We have also isolated Streptococcus viridans (6.1%), Streptococcus pneumoniae (4.3%) andmixed microflora (14.3%). The syndrome of endogenous intoxication of the body was manifested by high fever in 56% of cases, by leukocytosis in 38% of patents, and by acceleration of the erythrocyte sedimentation rate in 57.4% of study subjects. There was no statistically significant difference in the degree of endogenous intoxication between groups with different types of streptococci.
Conclusion. The cause of the inflammatory process in the jaws was GABHS (65.6% of cases) with a high sensitivity to vancomycin (99%), fluoroquinolones (98%), and beta-lactam antibiotics (91%).

Keywords: acute odontogenic periostitis, osteomyelitis, sensitivity and resistance to antibiotics, childhood

Cite as: Khalyuta EE, Mokhnacheva SB, Dugina IG, Kutarenko AD, Fomina AA. Microbiological aspects of acute odontogenic osteomyelitis in children. *Saratov Medical Journal* 2023; 2 (3): e0203. https://doi.org/10.15275/sarmj.2023.0203

Introduction

Odontogenic osteomyelitis of the jaw is an infectious purulent and necrotic process in the bone tissue of the jaw. Acute purulent osteomyelitis develops as a consequence of the odontogenic mixed infection [1].

The clinical course of the jaw osteomyelitis can vary, which depends on the characteristics of the microflora, nonspecific and specific protective factors, other individual characteristics of the body, as well as the location, extent and stage of the disease [2].

Currently, main causative agents of purulent infections in the maxillofacial area are associations of obligate anaerobes with aerobes. The main role in the development of abscesses and phlegmons in this area is played by the fungal microbiota and bacterial microflora. In particular, the causative agent for an acute purulent periostitis is often a combination of streptococci and Candida fungi. Abscesses are caused by streptococci and Penicilliumfungi, whereasphlegmon is triggered by streptococci, staphylococci, actinomycetes, and fungi of the genera Candida, Penicillium andRhodotorula [3, 4].

One of the important regarding the measures ofosteomyelitis effective treatment is the timely identification of the infection causative agent and sanitation of the lesion followed by antibiotic therapy [5]. When choosing an antibiotic, the following characteristics are taken into account: its bactericidal action, creation of its high concentrations in bones and soft tissues, the possibility of its long-term use, and its safety [6]. Resistance to antibacterial medicines occurs for various reasons, including inadequate prescription of medications and an overall decrease in the body immune response [7]. In this regard, an important issue in the early prescription of antibiotic therapy is continuous bacteriological monitoring of the pathogen composition of purulent inflammatory diseases, aiming to bring the spectrum of action of empirically prescribed drugs closer to the spectrum of the most frequently prescribed etiologically justified antibiotics [8].

Objective–to identify the species composition of pathogens causing acute odontogenic inflammatory process in the children's jaws; to examine the sensitivity and resistance of the isolated microflora to antibiotics of various groups; and to determine the dependence of the disease clinical course on the type of dominant pathogen.

Materials and Methods

We retrospectively studied a sample of 900 medical records of 0–15-year-old inpatients hospitalized in the Department of Maxillofacial Surgery of the Udmurt Republican Children's Clinical Hospital from 2019 to 2021with diagnoses of acute odontogenic periostitis and acute odontogenic osteomyelitis of the jaws.

Microbiological research methods were employed, including microscopy, culturing method, and determination of the sensitivity of the pathogen isolated from a purulent wound:

1) Microscopic examination of clinical samples with Gram staining;

2) Growing the test material on the following nutrient media: 5% sheep blood agar and salt egg yolk agar for staphylococci, 5% sheep blood agar, chocolate agar and sugar broth for streptococci, Endo's medium for Enterobacteriaceae, chromogenic agar for Candida spp., and anaerobic blood agar for anaerobes. Subsequent generic and species identification of microorganisms using the following test systems: Strepto 16, Biochemical Plate Differentiating Staphylococci and Biochemical Plate Differentiating Enterobacteria;

3) Examination of the isolated pathogen sensitivity to antimicrobial medicines via the disk diffusion method on Mueller–Hinton agar.

To assess the general condition of the body, we used objective data, such as body temperature, the number of leukocytes in the blood and the erythrocyte sedimentation rate (ESR).

Statistical data processing was carried out using Microsoft Excel and IBM SPSS STATISTICA. All variables were tested for normalityby a one-tailed Kolmogorov–Smirnov test. Most of the studied indicators complied with the law of normal distribution. The digital material was processed to determine the arithmetic mean (M), root mean square error (m). Statistical comparisons were performed via the Student'st-test for parametric variables and the nonparametric Wilcoxon–Mann–Whitney U test. Statistical significance was assumed at $p<0.05$.

Results

In the vast majority of cases (65.6%), the causative agent of the inflammatory process in jaws was Streptococcus pyogenes known as group A beta-hemolytic streptococcus (GABHS). Much less often we isolated other pathogens: Streptococcus viridians (6.1%), Streptococcus pneumoniae (4.3%), Candida spp. (3%), Staphylococcus aureus (2.8%) and Moraxella catarrhalis (1.2%). Staphylococcus epidermidis, Escherichia coli, Enterobacter, Klebsiella pneumoniae andPseudomonas aeruginosawere detected very rarely (*Table 1*). Mixed microflora was identified in 14.3% of cases (of those, the associations of bacteria with Candida were detected in 10.7% of cases, while associations with both Candida and GABHS were observed in 7.6% of cases). In 1.9% of cases, we revealed an association of GABHS with Staphylococcus aureus. The lack of microflora growth, detected in 0.8% of cases, was probably due to improper collection, storage or transportation of the material.

Susceptibility testing of GABHS yieldedits high sensitivity to vancomycin (99%), fluoroquinolones (98%), and beta-lactam antibiotics (91%). Values of sensitivity to clindamycin, macrolides and linezolid were 65%, 59% and 57%, respectively. The highest values of resistance were noted in respect to macrolides (41%) and clindamycin (33%), slightly smaller resistance was exhibited to linezolid (15%) (*Table 2*).

Spectra of antibiotic resistance of other relatively common microorganisms (Str. viridans, Str. pneumoniae, S. aureus) showed that the percentages of strains sensitive to inhibitor-resistant beta-lactam antibiotics were 80%, 26% and 92%, respectively; to clindamycin, 78%, 69% and 76%, correspondingly; to vancomycin, 100%, 95% and 4%, respectively; and to fluoroquinolones, 20%, 97% and 96%, correspondingly.

Strains of Str. viridans, Str. pneumoniae, and S. aureuswere resistant to inhibitor-resistant beta-lactam antibiotics in 20%, 74% and 4% of cases; to macrolides, in 16%, 36% and 20% of cases; to clindamycin, in 20%, 18% and 24% of cases; and to linezolid, in 4%, 18% and 12% of cases, respectively. Strains of Str. viridansand Str. pneumoniaewere resistant to fluoroquinolones in 2% and 3% of cases, correspondingly.

Table 1. Frequencies of pathogen isolation in acute odontogenic inflammatory process in the jaws of children

Causative agent of jaw inflammation	Quantity	
	Abs.	%
Streptococcus pyogenes (GABHS)	590	65.6
Streptococcus viridans	55	6.1
Staphylococcus aureus	25	2.8
Streptococcus pneumoniae	39	4.3
Moraxella catarrhalis	11	1.2
Staphylococcus epidermidis	7	0.8
Escherichia coli	6	0.7
Enterobacteriaceae	1	0.1
Klebsiella pneumoniae		
Pseudomonas aeruginosa		
Staphylococcus saprophyticus		
Candidaspp. + GABHS	68	7.6
Candidaspp. + Staphylococcus aureus	9	1
Candidaspp. + Klebsiella pneumoniae	3	0.3
Candidaspp. + Escherichia coli		
Candidaspp. +Streptococcus viridans	5	0.6
Candidaspp. + Moraxella catarrhalis	2	0.2
Candidaspp. + Staphylococcus saprophyticus	1	0.1
Candidaspp. + Staphylococcus epidermidis	2	0.2
Candidaspp. +Streptococcuspneumoniae + Escherichia coli		
Candidaspp. +Streptococcuspneumoniae + S. aureus	1	0.1
GABHS + Staphylococcus aureus	17	1.9
GABHS + Staphylococcus epidermidis	8	0.9
GABHS + Moraxella catarrhalis	3	0.3
Escherichia coli + Staphylococcus aureus	1	0.1
Escherichia coli + GABHS	2	0.2
Staphylococcus epidermidis +Streptococcuspneumoniae		
Candidaspp.	27	3
No growth detected	7	0.8

Table 2. Sensitivity and resistance of microorganisms isolated from purulent lesions to antibiotics, %

Antibiotics	*Streptococcuspyogenes*		*Streptococcusviridans*		*Staphylococcusaureus*		*Streptococcuspneumoniae*		*Moraxellacatarrhalis*	
	S	*R*	*S*	*R*	*S*	*R*	*S*	*R*	*S*	*R*
Beta-lactams	91	9	80	20	92	4	26	74	91	9
Macrolides	59	41	9	16	80	20	62	36	55	45
Clindamycin	65	33	78	20	76	24	69	18	0	
Vancomycin	99	1	100	0	4	0	95	0		
Fluoroquinolones	98	2	20	2	96		97	3	36	64
Linezolid	57	15	20	4	88	12	59	18	0	
Aminoglycosides	0				96	0	3	0		

S, sensitivity; *R*, resistance

The syndrome of endogenous intoxication of the body was manifested in 56% of cases by high fever; in 38% of patients, by significant leukocytosis; and in 57.4% of study subjects, by an acceleration of ESR.

We analyzed the dependence of the manifestations of endogenous intoxication syndrome on the type of pathogen that most often caused the inflammatory process. In the largest group of patients, where the causative agent of the inflammatory process was Str. pyogenes, there was a significant increase in the number of leukocytes in the blood to 16.1±0.29×109/L, which was 78% higher than the upper limit of the normal range. ESR increased to 183% and was 22.5±0.36 mm/hr. Body temperature increased to 38±0.03°C. These valuesimplied the hyperergic responseof the body to the purulent inflammatory process.

In the indicators of the second group, where the causative agent was Str. viridans, the mean number of leukocytes increased by 94% and was equal to 17.48×109/L ± 2.45×109/L, which was 16% higher than in the first group. ESR increased to 21.2±1.08 mm/hr, which reflected a 177% increase. Body temperature raised to 38.2±0.61°C. The body's response to inflammation in patients of the second group was hyperergic.

In the group of Str. pneumoniae, the body responded by increasing the number of leukocytes to a mean of 16.2±0.78×109/L (180% of the norm). ESR increased to 24.7±1.42 mm/hr, which was 106% higher than normal. Body temperature was recorded at 37.9±0.09°C. The body's response to inflammation in patients of the third groupwas hyperergic as well.

In the fourth group of patients, where the microflora was mixed, and an association of microorganisms and fungi was detected in the pus (Candida spp. and Str. pyogenes), the meannumber of leukocytes was 15.1±0.63×109/L, which corresponded to the normergic body response. Similarly, the increase in ESR corresponded to the normergic response (only by 30% of the upper limit of the norm: 15.6 ± 0.63 mm/hr). Body temperature increased to 37.9±0.05°C.

We compared these indicators between the Str. haemoliticusgroup (this pathogen was the leading one) and other groups (Str. viridans, Str. pneumoniae, Candida + Str. pyogenes) The differences in all indicators (the number of leukocytes, ESR, body temperature values) were not statistically significant (p>0.05).

Analyzing the changes in the leukocyte quantity and ESR, we noted the predominance of a hyperergic body response in children to streptococcal infection, which did not depend on the streptococcus species (pyogenes, pneumoniae orviridans). The addition of fungi to streptococci implied a change in the child's immunity towards a decrease in the immune response. The degree of endogenous intoxication in the course of odontogenic inflammatory process in children did not depend on the type of pathogenin most cases, but rather on other factors (e.g., the condition of the body, as well as the patient's age and immunity status).

Discussion

According to our study, the leading causative agent of the inflammatory process in the jaws in childhood years is GABHS (65.6%), as well as mixed microflora (14.3%, of which the association of microorganisms with Candidaconstitutes 10.7%). Thesefindings are consistent with the 2010 data of I.Yu. Stolbov and 2017 data of T.K. Supieva, who believed that in acute purulent periostitis, the causative agent was often a combination of streptococci and Candidafungi [3, 4].

2016 study by I.M. Makeeva demonstrated that in patients with exacerbations of odontogenic inflammatory processes, microbial associations were found, including actinomycetes, periodontopathogens, and enterococci [9], which differed from our data.

Long-term microbiological monitoring is required to formulate an antibacterial therapy strategy.

In the treatment of acute and aggravated odontogenic inflammatory processes and periodontal diseases, beta-lactam antibiotics (amoxicillin/clavulanic acid, cephalosporins), imidazole derivatives, and, more recently, fluoroquinolones are most often used [10]. The feasibility of using these medicineswas confirmed by the results of our studies, such as high sensitivity of hemolytic streptococcus to fluoroquinolones (98%) and beta-lactam antibiotics (91%).

High sensitivity and low resistance of Str. pneumoniae, Str. pyogenes (GABHS) andS. aureus to fluoroquinolones to this group of antibacterial drugs is explained by the fact that their administration is possible from the age of 18 years.

We should emphasize low sensitivity (26%) and high resistance (74%) of Str. pneumoniae to the group of beta-lactam antibiotics, while among other pathogens beta-lactams give good treatment results. Considering that Str. pneumoniae was the causative agent of odontogenic

inflammation in children in 4.3% of cases, it can be predicted that in 3.2% of cases, in the treatment of odontogenic inflammation, the prescription of beta-lactam antibiotics may be ineffective.

Research by I.M. Makeeva demonstrated that for generalized chronic periodontitis and odontogenic inflammatory processes, representatives of the lactamase-resistant penicillin group are recommended as the drugs of choice: Amoxiclav® (79-100% of sensitive strains), macrolides (e.g., azithromycin with 62-90% of sensitive patients), fluoroquinolone (ciprofloxacin with 73-85% of sensitive strains) [9]. Our data are consistent with these results with respect to beta-lactam antibiotics (the sensitivity of hemolytic streptococcus to beta-lactams was 91%), but differ with respect to macrolides, to which the highest antibiotic resistance (41%) was established in our study in strains of Streptococcus pyogenes thatwas the chief pathogen.

Conclusion

The leading causative agent of the inflammatory process in the jaws was Str. pyogenes (in 65.6% of cases). Other pathogens were Str. viridans (6.1%), Str. pneumoniae (4.3%), Candida spp. (3%), S. aureus (2.8%), and Moraxella catarrhalis (1.2%). Mixed microflora was detected in 14.3% of cases. Susceptibility testing of GABHS exhibitedits high sensitivity to vancomycin (99%), fluoroquinolones (98%), and beta-lactam antibiotics (91%). The highest antibiotic resistance in GABHS was detected to macrolides (41%) and clindamycin (33%). The absence of a statistically significant difference in the degree of endogenous intoxication between groups of patients with different species of streptococciimplied that in most cases it did not depend on the streptococcus species, but rather on some other factors.

Author contributions: All authorsequally contributedtothepreparationofthemanuscript.

Conflict of interest: None declared.

References

1. DrobyshevAYu, Yanushevich OO. Maxillofacial Surgery. *Moscow: GEOTAR-Media* 2018; 880 p. (In Russ.).
2. Bazikyan EA, Chunikhin AA. Odontogenic inflammatory diseases – Simply about the complex. *Moscow: GEOTAR-Media* 2017; 160 p. (In Russ.).
3. StolbovIYu, Kuznetsova NL. Complex treatment of patients with chronic osteomyelitis of the lower jaw. *Problems of Dentistry* 2010; (4): 54-5. (In Russ.).
4. Supiev TK, Negametzyanov NG, Nurmaganov SB.Prevention and treatment of odontogenic inflammatory diseases in children in the Republic of Kazakhstan. *Pediatric Dentistry and Prevention* 2017; 16 (4): 53-6. (In Russ.).
5. Fantoni M, Taccari F, Giovannenze F. Systemic antibiotic treatment of chronic osteomyelitis in adults. *Eur Rev Med Pharmacol Sci.* 2019; 23 (2 Suppl): 258-70. https://doi.org/10.26355/eurrev_201904_17500.
6. Badikov VD. Microbiological Basis of Antimicrobial Therapy of Infectious Diseases: A guide for physicians. *Saint Petersburg* 2005; 184 p. (In Russ.).
7. Privolnev VV, Rodin AV, Karakulina EV. Local use of antibiotics in the treatment of bone infections. *Clinical Microbiology and Antimicrobial Chemotherapy* 2012; 14 (2): 118-31. (In Russ.).
8. Minaev SV, Filipyeva NV, Leskin VV, et al. Microbiological spectrum of pathogens of purulentinflammatory diseases in children at a multidisciplinary hospital. *Medical Bulletin of the North Caucasus* 2018; 13 (1): 112-4. (In Russ.).
9. Makeeva IM, Daurova FYu, Byakova SF, et al. Sensitivity of microbial associations of periodontal pocket exudate and odontogenic lesion to antibacterial medicines. *Dentistry* 2016; 95 (3): 2630. (In Russ.).
10. Ippolitov EV, Didenko LV, Tsarev VN. Features of the morphology of periodontal biofilm in inflammatory gum diseases (chronic catarrhal gingivitis, chronic periodontitis, Candida-associated periodontitis) according to electron microscopy. *ClinicalLaboratoryDiagnostics* 2015; 60 (12): 59-64. (In Russ.)

Authors:
Elena E. Khalyuta – PhD, Assistant Professor, Department of Surgical Dentistry and Maxillofacial Surgery, Izhevsk State Medical Academy, Izhevsk, Russia, https://orcid.org/0009-0003-6341-1042;
Svetlana B. Mokhnacheva – PhD, Associate Professor, Chair of the Department of Surgical Dentistry and Maxillofacial Surgery,Izhevsk State Medical Academy, Izhevsk, Russia, https://orcid.org/0000-0002-3133-0227 ;
Irina G. Dugina – Head of the Division Clinical Diagnostic Laboratory #2, Udmurt Republican Children's Clinical Hospital, Izhevsk, Russia;
Anastasia D. Kutarenko – Student, Izhevsk State Medical Academy, Izhevsk, Russia, https://orcid.org/0009-0005-0846-0209;
Alina A. Fomina – Student, Izhevsk State Medical Academy, Izhevsk, Russia, https://orcid.org/0009-0002-1165-503X.