ORIGINAL ARTICLE

The most common etiological agents of prosthetic joint infections in orthopaedics

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ABSTRACT

Aim To determine the spectrum of causative agent of prosthetic joint infections in orthopaedics.

Methods In the group of 50 patients with periprosthetic infection the results of microbiological analysis of minimally two samples gained intraoperatively were analysed.

Results The only pathogen in the group of acute infection was *Staphylococcus* (*S.*) *aureus*. In case of delayed infection the most frequent pathogen was also *S. aureus* and in case of late infection it was coagulase-negative staphylococcus.

Conclusion A better *understanding* of the most common agents responsible for prosthetic joint infection helps us to properly prepare the patient (by eradicating of potential focus) with adequate antibiotic prophylaxis and early treatment of suspected infections to further reduce the incidence of infectious complications in orthopaedics. It is important to bear in mind that patients who have undergone total joint replacement have a risk of infection for the rest of their lives.

Key words: coagulase-negative staphylococcus, *Staphylococcus aureus*, total joint replacement

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INTRODUCTION

The implantation of total endoprosthesis is becoming more common orthopaedic operation mainly with knee and hip joint injuries. It provides significant improvement of the patients´ quality of life including pain relief and mobility improvement (1,2). Literary data show that infection complication occurs in 1-5% of implanted endoprosthesis (3). The important fact is that as the number of implantations of endoprosthesis is increasing each year, also the number of cases with infection complication is growing (4). Yet infection complication after total joint replacement (TJR) occurs less frequently than mechanical loosening of endoprosthesis (2). Prosthetic infection is considered a more severe complication related to endoprosthesis, which often leads to long term hospitalisation of patients, repeated surgeries and in certain cases even to definite loss of implant, with shortening of affected limb, its deformation and major lasting function limitation (1,2).

The aim of this study was to determine causative microorganisms of prosthetic joint infections, to set the range of main agents of individual types of prosthetic joint infection in orthopaedics, as well as to show the importance of infection prevention.

PATIENTS AND METHODS

Patients and study design

A total of 64 patients with infection of endoprosthesis of hip and knee joint, who were operated from 2013 to 2017 in the Orthopaedic Clinic in Banska Bystrica were included in the analysis. A total of 50 patients met inclusion criteria and were included in the study: they had an operation performed in our workplace maximally 5 years before the first signs of infection appeared, and unequivocally infection with adequate laboratory, bacteriological, local tissue changes and prospectively X-ray finding.

Results of microbiological analysis of minimally two samples gained intraoperatively were analysed. Sampling was performed in patients with symptoms of inflammation of the operational region (from the wound, pus from the wound, tissue, material from drainage, pus in anaerobically closed syringe).

For classification of prosthetic joint infections the Fitzgerald's classification system was applied (5), and patients were divided into 3 groups according to time distance of infection and primary operation: acute post-operation infection, which occurred within 3 months after the operation, deep delayed infection, which occurred from 3 months to 2 years after the operation, and late hematogenous infection, which occurred more than two years after the operation.

Methods

The material was sent to the microbiological laboratory. The processing of the sample was performed according to the local standard operational processes (SOP) for clinical material:

inoculation on blood agar and MacConkey agar for Gram-negative rods and fungi and cultivation in aerobic conditions; inoculation to nutrition broth and cultivation in aerobic conditions and identification by biochemical tests and MALDITOF (identification according to proteins detected – proteomic) (6); inoculation on Sabouraud agar and cultivation and identification for yeasts and moulds; inoculation of material for anaerobic cultivation on VL (viande-levure, meat-bread-yeast) agar.

Colonies growing only in anaerobic conditions were identified by biochemical tests and MALDITOF (identification according to proteins detected – proteomic) (7).

Every colony that was consistent with inoculation was identified by phenotype characteristics done by standard biochemical tests.

Antibiotic (ATB) susceptibility tests according to the identified bacterium were performed by disc diffusion tests, E-test or tests for minimal inhibition concentration (MIC) according to the Clinical Laboratory Standards Institute (CLSI) (8).

Identification of methicillin-resistant *Staphylococcus (S.) aureus* (MRSA) strains was performed with oxacillin (methicillin) (1 μg) and cefoxitin (30 μg) disks. If the test was consistent with the resistance to oxacillin– the sample was tested by minimal inhibitory concentration (MIC) tests (E-test) and consequently confirmed by polymerase chain reaction (PCR) – Cepheid (9).

Statistical analysis

Descriptive statistics were used to describe the basic features of the data. Continuous variables were reported as the mean values and categorical variables are reported as proportions. The test for two proportions (z-test and Mann – Whitney test) was used and statistical significance was set as $p < 0.01$.

RESULTS

Calculated mean value for age in 50 patients with prosthetic joint infections was 63 years and mean value of body mass index (BMI) was 31.18. Proportion of hip and knee arthroplasties was comparable (half of our patients have knee endoprosthesis and half have hip endoprosthesis). The overall mean time from implantation to revision of endoprosthesis was 25 months.

The occurrence of types of infection was as follows: acute post-operation infections in five (10%), deep delayed infections in 22 (44%) and late hematogenous infections in 23 (46%) patients.

Sixty-two pathogens from 50 patient samples were isolated: Gram-negative microorganisms were represented in nine (14.52%) cases and the rest of 53 (85.48%) were Gram-positive microorganisms; 40 (80%) patients had monomicrobial and 10 (20%) polymicrobial infection (8 patients with 2 pathogens and 2 patients with 3 pathogens).

Staphylococcus aureus was detected in 14 (22.58%), coagulase negative *Staphylococcus* (CoNS) in 21 (33.87%), MRSA in five (8.06%) cases. *Enteroccocus faecium* was the most frequent Gram-negative bacteria, in seven (11.29%) cases, followed by *Escherichia coli*, in three (4.84%) cases (Table 1).

Table 1. The distribution of microorganisms isolated in 50 patients with prosthetic joint infections

Microorganism	No (%) of patients
Gram-negative	
Staphylococcus aureus	14 (22.58)
Coagulase-negative Staphylococcus	21 (33.87)
MRSA	5 (8.06)
Streptococcus agalactiae	2 (3.23)
Streptococcus viridans	2 (3.23)
Streptococcus mitis	1 (1.61)
Gram-positive	
Enteroccocus faecium	7 (11.29)
Escherichia coli	3 (4.84)
Klebsiella pneumoniae	2 (3.23)
Enterobacter cloacae	2 (3.23)
Prevotella disiens	1 (1.61)
Acinetobacter calcoaceticus	1 (1.61)
Micrococcus luteus	1 (1.61)
Total	62 (100.0)

MRSA, methicillin-resistant *Staphylococcus aureus*

The only pathogen in the group of seven patients with acute post-operation infection was *S. aureus*.

In the group of 28 patients with delayed infection the most frequent pathogen was also *Staphylococcus* spp. in (71.43%) cases. *S. aureus* dominated, 11 (39.29%). Other pathogens were isolated in eight (28.57%) cases (p=0.00164) (Table 2).

Table 2. The distribution of microorganisms in 28 patients with deep delayed infection

Deep delayed infection	No (%) of patients
***Staphylococcus* spp.**	
S. aureus	11 (39.29)
Coagulase-negative *Staphylococcus*	9 (32.14)
Total	20 (71.43)
Other pathogens	
Escherichia coli	3 (10.71)
Enteroccocus faecium	3 (10.71)
Klebsiella pneumoniae	1 (3.57)
Prevotella disiens	1 (3.57)
Total	8 (28.57)
Total	**28 (100.00)**

Staphylococcus infections occurred in 29 patients with late haematogenous infection in greatest extent, 15 (51.72%); CoNS was the most frequent pathogen, 12 (41.38%). *Streptococcus* spp. caused infection in five (17.24%) cases, and nine (31.03%) infections were caused by other pathogens (p=0.0913) (Table 3).

Table 3. The distribution of microorganisms in 29 patients with late hematogenous infection

Late hematogenous infection	No (%) of patients
***Staphylococcus* spp.**	
S. aureus	3 (10.34)
Coagulase-negative *Staphylococcus*	12 (41.38)
Total	15 (51.72)
***Streptococcus* spp.**	
S. agalactiae	2 (6.90)
S. mitis	1 (3.45)
S. viridans	2 (6.90)
Total	5 (17.24)
Other pathogens	
Acinetobacter calcoaceticus	1 (3.45)
Enterobacter cloacae	2 (6.90)
Enteroccocus faecium	4 (13.79)
Klebsiella pneumoniae	1 (3.45)
Micrococcus luteus	1 (3.45)
Total	9 (31.03)
Total	**29 (100.00)**

DISCUSSION

In general, the cause of prosthetic infection could be practically every microbe and endoprosthesis implantation, which means the risk of infection for its owner during all their life (10). The most important source of infection is the patient´s own skin, followed by a doctor performing the operation and his/her teams'skin, and the last, but not least, pathogens from the air (11).

The most frequent pathogen was coagulase-negative staphylococci followed by *S. aureus* and staphylococcus infections are responsible for

nearly 64% infections in our patients. *S. aureus* was most frequently isolated pathogen in case of acute as well as delayed infection and coagulase-negative staphylococci in case of late hematogenous infection. Individual representation of pathogens in our group of patients is similar to the one in other studies (10, 12).

Polymicrobial infections were noticed in 20% patients (8 patients with 2 pathogens and 2 with 3), which is equal to the work of Benito et al. (17%) (13). According to our study polymicrobial infections occurred only in case of delayed and late infections and the most frequent pathogen present was coagulase-negative staphylococcus, and per one patient it was on average 1.24 of pathogen.

Patients with acute prosthetic joint infection represented 10%, with delayed infection 44% and with late infection 46% of our group. Pulido et al. achieved similar results in their study of 63 prosthetic joint infections (14). Average time since the operation to subsequent revision due to infection was 25 months in our group of patients.

Li et al. (15) found in the group of 59 patients with prosthetic joint infection 69 different bacterial strains and Gram-positive bacteria was the most frequent one causing as many as 86.96% infections, which is equal to our work (85.94%).

Tande et al. (10) found predominance of *S. aureus* and coagulase-negative staphylococcus responsible for as many as 60 –70% of prosthetic joint infections, whereas streptococcus and enterococcus together represented in only approximately 18%. The ratio of infections caused by *Staphylococcus aureus* and CoNS was nearly the same; aerobic gram-negative bacilli were presented in 12% cases of knee and hip joint infections (10). In our work we have achieved similar results: staphylococcus infections occurred in 80% of patients with prosthetic infection, other pathogens occurred together in 44%, some patients were affected by a combination of pathogens; streptococcus and enterococcus were responsible for 24% of infections. Gram-negative bacteria represented 15% from all isolated pathogens and they contributed to the beginning of prosthetic joint infection by 18% in our group of patients, which is a similar result to other studies (10,14,15).

The most frequently isolated microorganisms were staphylococci, especially *S. aureus*. Equally, Parvizi et al. (16) in their work proved, that the most frequent agent in their group of patients with acute infection was *Staphylococcus aureus*, which they attributed to its high virulence. Increased virulence of this pathogen probably leads to start of the symptoms during the first few months after the operation (17).

Identification of a probable cause of prosthetic joint infection with an early start is particularly important because these infections are most frequently solved by debridement of joint with keeping the implant (10). On the other hand, delayed beginning of the infection (from 3 months to 2 years after implantation) is often due to the occurrence of less virulent microorganisms infecting the joint during surgery. Contamination happens during the operation and, in general, it is often due to normal microflora of the skin, mostly coagulase-negative staphylococci, such as staphylococcus epidermidis (18).

In our work CoNS contributed to the beginning of delayed infection by 32%. Phillips et al. (19) achieved similar results in his work. CoNS include a group of microorganisms, while many of them are present on skin and mucosa of humans and animals as a part of their physiological flora (20). CoNS causes infections firstly by its ability to adhere to prosthetic materials and produce biofilm (21).

Late prosthetic joint infections starting after 2 years after implantation are often a consequence of hematogenic transfer of pathogen from an infection in another place. Most frequently isolated microbe in this group of infections in our group was coagulase-negative staphylococci, followed by streptococci and enterococci, and also Tande et al. achieved similar results (10).

Knowledge of the most frequent pathogens of prosthetic infections is very important not only when determining prevention precautions leading to decrease of their occurrence, but also when setting the right empirical treatment to patients without waiting cultivation results (22). It is, for example, related to patients with sepsis or patients with suspected prosthetic joint infection in spite of negative cultivation.

The aim of our work was to contribute to decreased occurrence of prosthetic joint infection. Knowledge of the most frequent pathogens responsible for the beginning of prosthetic infecti-

on should be an important fact when selecting both the right ATB prophylaxis and suitable ATB when empirically administered. Last but not least, knowledge of the most frequent infection agents plays a significant role in prevention from the beginning of infection whether in pre-operation phase when searching for potential focuses or in post-operation phase when administering ATB in cases of surgeries and gynaecological or bigger tooth operations.

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