

## Prosthetic joint infections-a clinico-microbiological perspective: Review article

Pravin K Nair, Vivek G Bhat, Michelle S Vaz

Pravin K Nair, Michelle S Vaz, Department of Microbiology, Holy Spirit Hospital, Andheri (E), Mumbai 400093, India

Vivek G Bhat, Department of Microbiology, ACTREC-Tata Memorial Center, Navi Mumbai 410210, India

**Author contributions:** All the authors contributed equally to the work in literature survey and writing of the paper.

**Correspondence to:** Vivek G Bhat, MD, Associate Professor-Microbiology, Advanced Centre for Treatment, Research and Education in Cancer, Department of Microbiology, ACTREC-Tata Memorial Centre, Navi Mumbai 410210, India. [vivekbhat2005@yahoo.com](mailto:vivekbhat2005@yahoo.com)

Telephone: +91-22-27405093 Fax: +91-22-27405061

Received: June 24, 2014 Revised: July 21, 2014

Accepted: August 20, 2014

Published online: August 25, 2014

### Abstract

Prosthetic joint infections (PJIs), although not very common, currently pose a very significant threat since they are associated with severe complications, high morbidity rates and substantial costs. PJIs are most commonly caused by *Staphylococcus aureus* and coagulase-negative staphylococci. The diagnosis of implant-associated infections is very challenging since no single routinely used laboratory or clinical test has been shown to demonstrate adequate results with respect to sensitivity, specificity and accuracy. In most cases, a sum of clinical signs and symptoms, histopathology, blood tests, radiography, bone scans and microbiological testing is considered to arrive at an accurate diagnosis. Treatment of PJIs is also very difficult since most of the infections are caused by biofilm-producing microorganisms which are significantly more resistant to the hosts natural defense mechanisms and antibiotic treatment. For successful management, a combination of both antibiotic and surgical treatment is most often required, and early diagnosis is of the utmost importance. Thus, a multidisciplinary approach is potentially the best option in dealing with PJI, and should include the involvement of microbiologists,

orthopedic specialists, clinicians, pathologists and radiologists in order to improve decision-making processes and ensure overall success. The following review aims at briefly outlining the microbiology, diagnostic and treatment options, and preventive measures associated with such infections.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

**Key words:** Prosthetic joint infections; Biofilms; Diagnosis; Antimicrobial therapy; Surgical treatment

**Core tip:** Prosthetic joint infections (PJIs), although uncommon, may be associated with significant complications and morbidity. Staphylococci are among the most commonly involved organisms. Diagnosis may be challenging in spite of the availability of various laboratory and radiological tests. Treatment too, is often difficult because most infections are caused by biofilm producing organisms. A combination of prudent surgical intervention and specific antibiotic treatment is the key to a successful management. Thus, a multidisciplinary approach is the best option in dealing with PJI, and should involve a team of orthopedic specialists, clinicians, pathologists, radiologists and microbiologists to ensure best outcomes.

Nair PK, Bhat VG, Vaz MS. Prosthetic joint infections-a clinico-microbiological perspective: Review article. *World J Clin Infect Dis* 2014; 4(3): 9-15 Available from: URL: <http://www.wjgnet.com/2220-3176/full/v4/i3/9.htm> DOI: <http://dx.doi.org/10.5495/wjid.v4.i3.9>

### INTRODUCTION

The use of prosthetic material in orthopedic surgery has become common in recent times, due to its high success rate with total joint replacement and the management of

fractures. Whilst not very common, prosthetic joint infections (PJIs) pose a very significant threat, considering the number of total joint replacements undertaken each year and the millions of people who currently have indwelling prostheses<sup>[1]</sup>. These infections are associated with severe complications, high morbidity rates and substantial costs<sup>[2]</sup>. PJIs linked with total hip and knee arthroplasty occur at an incidence rate of 1.5%-2.5% in the case of primary interventions. However after revision procedures, rates as high as 2%-20% have also been reported<sup>[3]</sup>.

PJIs are generally classified as per their time of onset after surgery. In the case of early PJI, the first signs and symptoms appear in the initial 3 mo post-surgery. However, there are some authors who are in disagreement with the prior mentioned timeframe, and limit the same to the first 2 to 4 wk. Similarly, in delayed manifestations initial infection signs and symptoms occur anywhere between 3 mo and 2 years post-surgery; and late manifestations, > 2 years post-surgery<sup>[4]</sup>.

## RISK FACTORS

Certain groups of individuals can be considered to be at a higher risk of prostheses infections when compared to others. These include patients those who suffer from rheumatoid arthritis, diabetes mellitus, psoriasis, *etc.*; and those who are immunocompromised, aged, infected with human immunodeficiency virus, have had long-term urinary catheterization, and/or have poor nutritional status<sup>[1,5]</sup>. Other risk factors include smoking, obesity, corticosteroids, burns, liver disease, neoplasia, chemotherapy and radiotherapy<sup>[2]</sup>. In cases where PJI patients possess more than one implant, there is a significant risk of a subsequent infection developing in the other prostheses present at the time of infection<sup>[5]</sup>.

Mortality associated with PJIs in the case of elderly patients is as high as 8%<sup>[6]</sup>. In a study conducted by Grammatico-Guillon *et al*<sup>[7]</sup> in 2012, bone and joint infections were found to be not only age related, but were also found to be higher in males. This parallels the general trend of Rheumatoid Arthritis in the same group of individuals. The study also showed that the most frequent comorbidities associated with such infections are diabetes, ulcer sores and peripheral vascular disorders<sup>[7]</sup>.

## PATHOGENESIS

The development of a PJI is the result of an interaction between the patient, pathogen, environment, intervention and wound factors<sup>[2]</sup>. Implanted devices are known to possess a substantial risk of bacterial and fungal colonization. Studies have shown that having a foreign body present significantly decreases the minimal infecting dose of *Staphylococcus aureus* (*S. aureus*) causing a permanent abscess. In an experiment involving animal models, it has also been shown that as low as 100 colony-forming units of *S. aureus* can be sufficient to infect 95% of subcutaneous implants present<sup>[8]</sup>.

Host defense in the vicinity of implant region also plays a significant role in the emergence of PJIs. The most significant microorganisms responsible for causing these infections are *S. aureus* and coagulase-negative staphylococci (CoNS). It has been found that even few of these skin-derived microorganisms are capable of colonizing implants during surgery, since granulocytes surrounding the implant are rendered incapable of clearing bacteria. This is because granulocytes that accumulate around the implant become partially degranulated due to the introduction of a non-phagocytosable foreign object, and superoxide production is also decreased. After a biofilm has been established, even fully functional granulocytes cannot clear adherent staphylococci<sup>[8]</sup>.

PJIs occur usually by one of two routes, the first being introduced at or about the time of operation. This may be caused by wound sepsis post-operatively, by infected haematomas, or by operative contamination. Early infections may be either due to a single organism (*e.g.*, *S. aureus*) or may be polymicrobial in nature. PJIs caused by CoNS tend to present themselves relatively late (even after a year in some cases). However, even these infections are caused at the time of operation itself. The delayed presentation of such organisms is due to their low pathogenicity and tendency to produce biofilms, which allows them to stay sub clinical for considerable periods of time<sup>[8,9]</sup>. The second route is by that of haematogenous spread. Any existing bacteraemia can lead to prosthetic material infection, although *S. aureus* is considered to be the most common cause. In cases where sinuses are present, PJIs may even involve a range of skin organisms, including Gram-negative, Gram-positive and anaerobic bacteria<sup>[9]</sup>.

## MICROBIOLOGY

Prosthetic material provides an ideal environment in which many microorganisms can flourish<sup>[10]</sup>. The most common bacterial agents responsible for close to 65% of all PJIs are *S. aureus* and *Staphylococcus epidermidis*. This is because these bacteria possess surface proteins that have adhesive properties, facilitating their initial colonization. These microorganisms have been reported in early as well as in late infections associated with total knee and total hip arthroplasty, and are commonly found to be methicillin resistant. Recently, Lee *et al*<sup>[11]</sup> reported that not only is *S. aureus* responsible for causing PJIs, it may also be an independent risk factor that may be responsible for treatment failure. Other microorganisms such as streptococci, diphtheroids and enterococci have been found to be responsible for approximately 10% of PJIs each<sup>[2,3]</sup>.

Gram negative microorganisms are less common than Gram positives in PJIs. However, infections caused by them are far more complicated and require longer treatment<sup>[12]</sup>. Polymicrobial infections have been found to occur usually in early PJIs<sup>[13]</sup>. These, along with infections caused by unusual pathogens such as *Brucella* spp. and various mycobacteria; although not as common, have

also been reported. Anaerobic microbes are found usually only as a part of polymicrobial infections<sup>[2]</sup>. In cases of tubercular PJIs, misdiagnosis proves to be a substantial risk owing to the low index of suspicion attributed to such infections. This could lead to a delay in correct diagnosis, with the risk of permanent damage due to a late treatment<sup>[14]</sup>. PJIs are also caused by fungal agents like *Candida* and *Asperillus*<sup>[15]</sup>.

There are several PJI cases where the growth of microorganisms is absent from aerobic and anaerobic cultures of periprosthetic tissue samples<sup>[3]</sup>. Such culture negativity is an important issue in the treatment of PJIs since negative cultures raise uncertainty in the diagnosis of infection and makes choosing the appropriate antibiotics very challenging<sup>[16]</sup>. A study by Choi *et al*<sup>[16]</sup> showed that the success rate of infection control in the case of culture negative infections is higher, suggesting that the culture negativity may not necessarily be a negative prognostic factor for treating prosthetic joint infections.

Microorganisms found in PJIs that are caused by haematogenous dissemination include Gram negative bacilli, enterococci and anaerobes from genitourinary and gastrointestinal tract procedures or infections; *Streptococci viridans*, *Peptococcus* spp. and *Peptostreptococcus* spp. from dentogingival processes and manipulations; and *Streptococcus* spp. from pyogenic skin infections<sup>[3]</sup>. Few cases of PJIs caused by *Haemophilus parainfluenzae* have also been reported, most caused due to bacteraemia from dental origin<sup>[17]</sup>. Recently, Bjerke-Kroll *et al*<sup>[18]</sup> also reported *Streptococcus viridans* as a significant risk factor for transient bacteremia following dental extractions.

## ROLE OF BIOFILMS

PJIs are characteristically caused by biofilm-forming bacteria. Biofilms can be defined as microorganisms possessing altered phenotypes that live together in a self-organized aggregate. This aggregate is embedded in an exopolymer saccharide matrix which is self-produced and allows the attachment of the biofilm to an external surface. Prosthesis colonization by biofilm-producing bacteria can occur during implantation or by haematogenous seeding. A variety of microorganisms are known to grow in biofilms, including *S. aureus* and CoNS, which are of particular importance in PJIs<sup>[3]</sup>. The ability of microorganisms to form biofilms is a virulence factor<sup>[8]</sup>. Biofilm microbes are considered to be around 10 to 1000 times less susceptible to antibiotics, especially cell wall targeting agents. It is also difficult to predict the pharmacodynamic parameters of antimicrobial agents against these microorganisms. Thus, drugs are often used in concentrations higher than would be otherwise required<sup>[3]</sup>.

There have been several postulations and investigations to explain the increased antimicrobial resistance associated with biofilm-producing bacteria. Although the extracellular matrix in biofilms does physically restrict antimicrobial agents to some extent, it does not seem to be the predominant mechanism conferring resistance. Some

bacteria enter a non-growing stationary state due to decreased nutrient and oxygen levels inside the biofilm. As a result, their susceptibility to antimicrobials is reduced given that their action is growth-dependent. Some bacteria also differentiate into phenotypically resistant states; while others have shown to exhibit gene expression that confers antimicrobial resistance which is biofilm-specific, but has no role in biofilm formation<sup>[3]</sup>.

## DIAGNOSIS

PJIs currently have no universal definition. Most generally, a PJI is considered to be present when at least one of the forementioned criteria is fulfilled-evident purulence in the synovial fluid or around the prosthesis; presence of acute inflammation when periprosthetic tissue sections are histopathologically examined; sinus tract communication with the prosthesis; or when the same organism is found to be growing in repeated cultures of either synovial fluid, periprosthetic tissue or the implant itself<sup>[19]</sup>.

With the evaluation of patients suspected to have PJI, clinicians initially have to verify whether the dysfunction has been septic or aseptically caused. In some cases clinical diagnosis of PJIs is possible; however, laboratory testing is often required. On arriving at a satisfactory diagnosis, clinicians look to microbiological results for the identification of the underlying microbial cause, as well as to attain antimicrobial susceptibility levels so as to execute appropriate treatment. When a PJI is due to a virulent organism such as *S. aureus*, clinical symptoms like fever, effusion, warmth, erythema, and pain localized to the joint may occur. However, if the infection is caused due to low-virulence organisms like *P. acnes* or CoNS, pain and/or loosening of the prosthesis can take place without manifesting any further clinical signs. This leads to a challenging situation where the clinician cannot positively distinguish such an infection from aseptic arthroplasty failure<sup>[19]</sup>. When a PJI is suspected, it is recommended to wait a minimum of 15 d post any antibiotic treatment before performing tests in order to decrease the rate of false negative results, following which pre-operative sampling is to be performed. If the results are positive, surgical and antibiotic management can be planned. In the case of fever and other nonspecific clinical symptoms, it is recommended to perform blood cultures for aerobic and anaerobic bacteria so that rapid probabilistic antibiotherapy can be initiated before considering surgery. Negative results do not rule out the possibility of an existing infection<sup>[15]</sup>.

In the diagnosis of PJIs, no single routine clinical or laboratory test is known to demonstrate ideal sensitivity, specificity and accuracy. Therefore, a sum of clinical signs and symptoms, blood tests, histopathology, radiography, bone scans and microbiological testing is collectively used to attain an accurate diagnosis<sup>[3]</sup>. Blood tests are usually the first laboratory tests to be carried out. In the immediate postoperative period, C-reactive protein levels are found to be elevated and leucocytosis is ob-

served, which returns to normal within a few weeks<sup>[2]</sup>. Thus repetitive measurements can be indicative of PJI, but these results are neither sensitive nor specific<sup>[8]</sup>. In histopathological studies, tissue neutrophil levels are known to suggest infection. However, a generally accepted definition does not exist for acute inflammation. Several imaging techniques are employed to detect PJI. These include General Radiography, computed tomography, Ultrasonography, magnetic resonance imaging, Bone Scintigraphy with Technetium-99m-labelled Methylene Diphosphonate and Fluorodeoxyglucose positron emission tomography<sup>[3,8]</sup>.

## MICROBIOLOGIC ANALYSIS

### **Preoperative specimens**

This involves the testing of sinus tracts, superficial wounds, synovial fluid and preoperative tissue samples prior to any surgical revision procedure<sup>[19]</sup>. However, cultures of superficial wounds, sinus tracts often represent microbial colonization which can be misleading, and therefore lack predictive value<sup>[3,19]</sup>. Isolation of *S. aureus* from sinus tracts is considered to be predictive of the causative pathogen<sup>[3]</sup>.

Pre-operative culture of Aspirated Synovial fluid can be useful in the diagnosis of PJIs; especially in patients who have underlying inflammatory diseases, where routine Inflammatory markers may not very reliable<sup>[3,19]</sup>. Synovial fluid cultures allow microorganism identification with a sensitivity of as high as 82%-94%, and a specificity of 94%-97%<sup>[3]</sup>. Use of paediatric blood-culture bottles has been shown to improve sensitivity<sup>[8]</sup>. However, reports of discordance between synovial fluid and intraoperative cultures, with rates of false-positives between 3% to 16% and false-negative results from 8% to 50%. It has been shown that the false-negative results can be attributed to the bactericidal effect of anesthetics, low bacterial loads in synovial fluid and presence of fastidious organisms. The instillation of normal saline into joints to aid aspiration may result in the dilution of the specimen bacterial load. Gomez *et al*<sup>[19]</sup> in 2011 stated that preoperative tissue cultures do not suggest any advantage over synovial fluid cultures.

### **Intraoperative specimens**

Periprosthetic tissue samples are commonly examined to detect infecting microorganisms in PJIs. Prior to sampling, it is imperative to discontinue any antimicrobial therapy for a period of at least 2 wk<sup>[8]</sup>. Gram stains of periprosthetic tissues are rarely given any clinical importance due to their extremely low sensitivity that ranges from 0% to 30%. The sensitivity of bacterial detection from periprosthetic tissue cultures using conventional techniques is between 37% and 61%. This relatively low sensitivity may be attributed to the fact that the growth of the causative microorganisms is more so on the implant surface rather than in the surrounding tissue. To increase sensitivity, it is recommended that the evaluation of a minimum of five

specimens should be carried out<sup>[20]</sup>. Some studies even suggest extending the incubation period for the cultures, and sonication of the tissue samples to disperse adherent bacteria<sup>[3]</sup>. False-positive results are obtained from periprosthetic tissue cultures due to contamination during surgery, specimen transport, or specimen processing, these effect the specificity of results. Moreover, problems with specificity occur due to difficulties in establishing the clinical significance of common skin flora growth in intraoperative cultures<sup>[20]</sup>.

It's a well known fact that Swab cultures are less efficient as compared to tissue and synovial fluid culture samples, and should thus be avoided. They are more prone to contamination and have a high tendency to convey false-positive results. Anaerobes are most commonly isolated using blood culture bottles when compared to isolation from swab and tissue cultures<sup>[20]</sup> thereby indicating loss of bacterial viability during transport that may be responsible for some false-negative culture results.

### **Removed implant or fragments**

The growth of biofilm-forming bacteria may evade detection using periprosthetic tissue cultures<sup>[20]</sup>. Since biofilms play a very important role in infections, implant cultures has been found to be superior as compared to tissue culture. Explanted foreign material is usually vortexed or sonicated before culturing. This detaches the biofilm-associated bacteria, leaving it liberated in the surrounding broth<sup>[8]</sup>. Sonication has been used to diagnose infections of multiple medical device types, including orthopedic devices, breast implants, vascular grafts, cardiac devices, vascular catheters, and ureteral stents. Sonicate fluid has the advantage over periprosthetic tissue culture in having a shorter time to positivity<sup>[20]</sup>.

### **Other non-culture PJI diagnostic techniques**

The serological detection of PJI-causing microorganisms involves the detection of antibodies against such organisms. This technique, although fairly simple to perform, lacks substantial specificity which may be attributed to low basal antibody titers that are often recorded against organisms like CoNS, since they are apart of normal human flora. Direct visualization of PJI-associated bacteria from sonication fluid, using immunofluorescence microscopy by means of pathogen-targeted antibodies, can also be used in the diagnosis of PJI. However this method lacks clarity and provides no evident advantage over conventional culture techniques. Molecular techniques, theoretically, have shown to exhibit very good potential in overcoming drawbacks associated with culture methods when it comes to biofilm-associated infections. Unfortunately, studies evaluating these methods are very limited and are often contradictory. The major disadvantages associated with the molecular diagnosis of PJIs are the inability of the technique to provide essential antimicrobial susceptibility results, and the incidence of false-positive results that occur. False-positive results may be caused by DNA from non-viable bacteria that may have

contaminated patient specimens and reagents; or caused by amplicon contamination<sup>[20]</sup>.

## TREATMENT

Surgical intervention and antimicrobial therapy are the two main modes of treatment for the management of PJIs, which may even be initiated while awaiting microbiological results to avoid permanent joint cartilage damage<sup>[10]</sup>. To achieve complete therapy success, a combination of both these methods is usually required, and early diagnosis is of the utmost importance<sup>[8]</sup>.

### Antimicrobial therapy

There are no general standards for an ideal regimen and duration for the administration of antimicrobial agents in the treatment of PJIs<sup>[3]</sup>. In the presence of a prosthetic device, growth recurrence is frequent. Therefore, as in treating tuberculosis cases, killing of all microorganisms is essential<sup>[8]</sup>.

A well-defined example of optimal antimicrobial therapy is the use of Rifampicin in staphylococcal implant infections<sup>[8]</sup>. It has excellent efficacy against staphylococci in its stationary phase, exceeds minimum inhibitory concentrations (MICs) by a factor of about 10-100 at trough levels and can also be well absorbed orally<sup>[3]</sup>. It also has proven *in vitro* activity in several clinical studies. Rifampin must always be used in combination with another antibiotic so as to prevent the emergence of resistance. When used synergistically, it has shown excellent activity against susceptible slow-growing and adherent staphylococci. Quinolones have been found to be excellent combination drugs owing to their good bioavailability, safety and activity<sup>[8]</sup>. Ciprofloxacin is another drug that is commonly used in combination with Rifampicin. Several studies have demonstrated improved efficacy in favour of the rifampicin/ciprofloxacin combination as opposed to ciprofloxacin monotherapy, to be used in the treatment of staphylococcal infections associated with orthopaedic implant devices<sup>[3]</sup>. Rifampicin can also be used with other antimicrobial agents like fusidic acid, cotrimoxazole, trimethoprim/sulfamethoxazole, linezolid and minocycline<sup>[3,8]</sup>. However negative results have been reported when Rifampicin has been used with Levofloxacin orally<sup>[3]</sup>.

Staphylococci, both *S. aureus* and CoNS, have increasingly shown resistance to methicillin over the past few years; and Methicillin-resistant *S. aureus* (MRSA) infections have had a severe impact on PJIs. Patients with MRSA infections in periprosthetic tissue cultures have a higher probability of treatment failure as compared to those with methicillin-susceptible *S. aureus* infections. Also, patients with MRSA PJIs are prone to hospitalization for longer periods of time (median 15 d *vs* 10 d). Intravenous glycopeptides are primarily used to treat PJIs caused by methicillin-resistant Gram-positive bacteria. For MRSA infections postsurgery, continuous outpatient vancomycin perfusion has been used successfully. Prolonged administration of teicoplanin once daily has also appeared to be

relatively efficacious. Newer antibiotics like quinupristin/dalfopristin, linezolid, daptomycin and tigecycline are active against MRSA strains. Drugs like oritavancin, dalbavancin, faropenem and telavancin have shown promising results<sup>[3]</sup>. Quinopristin/dalfopristin shows activity against *Enterococcus faecium* (including vancomycin-resistant strains) as well as *S. aureus* (including MRSA). In a study of 40 patients suffering from MRSA orthopaedic infections and who were put on Quinopristin/dalfopristin, clinical success was found in 78% and microbial eradication in 69% of the cases<sup>[8]</sup>. However, side-effects and drug interactions has halted its use widely<sup>[3]</sup>.

Linezolid shows potential in the treatment of PJIs because of its bioavailability and antimicrobial spectrum. It possesses a very wide anti-Gram-positive bacterial spectrum, which includes all CoNS species. It also shows good diffusion in bone tissue. In an comparative study by Cobo *et al*<sup>[21]</sup>, 86% of patients treated with linezolid demonstrated clinical and microbiological cure. Unfortunately, toxicity associated with the drug is a matter of concern. Adverse effects like reversible myelo suppression, optic neuropathy and peripheral neuropathy are quite common with linezolid treatment. In most cases, optic neuropathies were resolved after linezolid stoppage, but peripheral neuropathies were found to be irreversible<sup>[8]</sup>.

Drugs like Daptomycin and Tigecycline make for attractive options in the treatment of PJIs<sup>[3,8]</sup>. Daptomycin has rapid bactericidal activity against most Gram-positive microbes, including MRSA, Vancomycin-resistant *S. aureus*, and Vancomycin-resistant enterococci<sup>[8]</sup>. Tigecycline is a novel glycylicycline antibiotic possessing a broad spectrum of activity. It has *in vitro* bacteriostatic activity against several Gram-positive, Gram-negative, anaerobic, atypical and antimicrobial-resistant bacteria. However, there is not enough available data for the application of these drugs in PJI management<sup>[3]</sup>.

### Surgical treatment

The management of suspected PJIs mainly rests in the hands of orthopaedic surgeons since surgical procedures are most often required<sup>[22]</sup>. Debridement is usually the first step in surgical treatment and involves the removal of any scar tissue, haematomas, devitalized tissue, and sinus tracts<sup>[2]</sup>. This method has been found to have limited success (varying from 20%-60%); and prosthesis removal and replacement is frequently required<sup>[2,23]</sup>. This however, may be attributed to the fact that debridement and implant retention has often been carried out on patients who have not entirely been suited to the procedure. Recently several algorithms have been published to aid in the selection process, and have been found to significantly increase the success rate of debridement procedures<sup>[23]</sup>. One-stage or Direct Revision is sought to in patients for whom two staged operations would represent a substantial operative risk<sup>[1]</sup>. It involves the replacement of an old prosthesis with a new one during the same surgical procedure<sup>[8]</sup>.

Two-stage (staged) Revision is the commonest surgi-

cal intervention in PJI management<sup>[9]</sup>. Success rates of > 90% have been reported in several studies for the procedure, when 6 wk of antimicrobial treatment have been administered between the stages<sup>[24]</sup>. Recently, Tsai *et al*<sup>[25]</sup> reported that patients who have undergone two-stage revision are less prone to recurrent infections. The surgery is especially preferred in cases where resistant or difficult-to-eradicate microorganisms are involved like MRSA, enterococci, staphylococci, Multi drug-resistant *Pseudomonas aeruginosa* or fungi<sup>[8]</sup>. In the first stage of the procedure, the prosthesis is removed along with carrying out a thorough debridement of all existing dead and infected tissue. The prosthesis is usually replaced by an antibiotic-loaded cement spacer in order to prevent joint space contracture that may occur between stage<sup>[26]</sup>. Other antibiotics may also be administered systemically. In very few cases that involve an acute infection, the implant may be preserved. The second-stage of the procedure involves the insertion of a new prosthesis into the site previously made sterile, and is usually carried out about 8-12 wk after the first stage once all inflammatory markers have attained normal levels and wound healing is complete<sup>[9]</sup>.

Permanent removal of the prosthetic device is usually reserved for patients with a high risk of reinfection, like those with severe immunosuppression or those who are active intravenous drug users; or when no functional improvement is expected after reimplantation<sup>[8]</sup>. Occasionally, in cases where the patient is not suitable for surgical procedures or for those who refuse operations, a long-term suppressive antibiotic regimen may be employed to suppress bacterial growth and to control symptoms<sup>[1]</sup>. However, since this approach only controls clinical symptoms rather than actually curing PJI, the infection tends to relapse in most patients (> 80%) on discontinuing the antibiotics<sup>[8]</sup>.

## PREVENTION

Adequate antibiotic prophylaxis is essential in reducing the risk of prosthesis-associated infections<sup>[10]</sup>. The objective of antimicrobial prophylaxis is to obtain serum and tissue drug levels that exceed the MICs for organisms that are likely to be a threat, for the entire duration of the operation. Systemic antibiotics should be administered just prior to the surgery. While administering prophylactic treatment, it is important to consider antibiotic resistance patterns associated with individual hospitals, as well as toxic and allergic reactions that may occur in patients undergoing surgery. In Orthopedic surgery, first- or second-generation cephalosporins such as cefazolin or cefuroxime are rational choices. However if the patient suffers from a  $\beta$ -lactam allergy, drugs like vancomycin, teicoplanin or clindamycin should be used<sup>[3,8]</sup>. Recently, Qadir *et al*<sup>[27]</sup> suggested Vancomycin to be used as a topical powder in the prevention of PJI. In settings where there is a high prevalence of MRSA, the use of glycopeptides is considered to be appropriate<sup>[8]</sup>.

From the moment of implantation, there is a constant risk of infection due to transient bacteraemia. Haematog-

enous seeding may occur at any point in the lifespan of a patient; however, the risk is significantly higher in the early stages following implantation. It is recommended to maintain good oral hygiene along with the regular removal of dental plaque to reduce the risk of bacteraemia. Also, if any dental, genitourinary tract or gastrointestinal tract procedure is to be undergone post implantation, a single dose of antibiotic prophylaxis should be utilized<sup>[3,8]</sup>.

## CONCLUSION

Prosthetic Joint Infections are still considered to be a significant risk worldwide due to the high mortality risks and exponential costs associated with them. And although several strides have been made to improve their diagnosis and management, numerous obstacles are yet to be tackled. A multidisciplinary approach is potentially the best option in dealing with PJI, and should include the involvement of microbiologists, orthopedic specialists, clinicians, pathologists and radiologists in order to improve decision-making processes and ensure overall success.

## REFERENCES

- 1 **Darton T**, Townsend R. Bone and Joint Infections. *Surgery* 2009; **28**: 95-100 [DOI: 10.1016/j.mpsur.2009.10.023]
- 2 **Bames R**, Chetter I. Infection in Prosthetic Material. *Surgery* 2012; **30**: 667-672. Available from: URL: <http://yadda.icm.edu.pl/yadda/element/bwmeta1.element.elsevier-49efc1ec-9863-355b-9204-b7c017197511>
- 3 **Esposito S**, Leone S. Prosthetic joint infections: microbiology, diagnosis, management and prevention. *Int J Antimicrob Agents* 2008; **32**: 287-293 [PMID: 18617373 DOI: 10.1016/j.ijantimicag.2008.03.010]
- 4 **Leone S**, Borrè S, Monforte Ad, Mordente G, Petrosillo N, Signore A, Venditti M, Viale P, Nicastrì E, Lauria FN, Carosi G, Moroni M, Ippolito G. Consensus document on controversial issues in the diagnosis and treatment of prosthetic joint infections. *Int J Infect Dis* 2010; **14** Suppl 4: S67-S77 [PMID: 20843721 DOI: 10.1016/j.ijid.2010.05.005]
- 5 **Jafari SM**, Casper DS, Restrepo C, Zmistowski B, Parvizi J, Sharkey PF. Periprosthetic joint infection: are patients with multiple prosthetic joints at risk? *J Arthroplasty* 2012; **27**: 877-880 [PMID: 22386611 DOI: 10.1016/j.arth.2012.01.002]
- 6 **Rao N**, Soxman GL. Prosthetic Joint Infections in the Elderly. *Oper Tech Orthop* 2002; **12**: 131-138. Available from: URL: <https://getinfo.de/app/PROSTHETIC-JOINT-INFECTIIONS-IN-THE-ELDERLY/id/BLSE:RN142747351>
- 7 **Grammatico-Guillon L**, Baron S, Gettner S, Lecuyer AI, Gaborit C, Rosset P, Rusch E, Bernard L. Bone and joint infections in hospitalized patients in France, 2008: clinical and economic outcomes. *J Hosp Infect* 2012; **82**: 40-48 [PMID: 22738613 DOI: 10.1016/j.jhin.2012.04.025]
- 8 **Zimmerli W**. Infection and musculoskeletal conditions: Prosthetic-joint-associated infections. *Best Pract Res Clin Rheumatol* 2006; **20**: 1045-1063 [PMID: 17127196 DOI: 10.3109/17453674.2013.823589]
- 9 **Islam G**, Tomlinson J, Darton T, Townsend R. Bone and Joint Infections. *Surgery* 2013; **31**: 187-192 [DOI: 10.1016/j.mpsur.2013.01.016]
- 10 **Philip B**, Robinson E. Bone and Joint Infection. *Medicine* 2013; **41**: 719-722. Available from: URL: <http://yadda.icm.edu.pl/yadda/element/bwmeta1.element.elsevier-629f37ed-5554-36e8-a658-986abd02194f>
- 11 **Lee J**, Kang CI, Lee JH, Joung M, Moon S, Wi YM, Chung DR, Ha CW, Song JH, Peck KR. Risk factors for treatment

- failure in patients with prosthetic joint infections. *J Hosp Infect* 2010; **75**: 273-276 [PMID: 20635512]
- 12 **Tseng SW**, Chi CY, Chou CH, Wang YJ, Liao CH, Ho CM, Lin PC, Ho MW, Wang JH. Eight years experience in treatment of prosthetic joint infections at a teaching hospital in Central Taiwan. *J Microbiol Immunol Infect* 2012; **45**: 363-369 [PMID: 22578641 DOI: 10.1016/j.jmii.2011.12.014]
  - 13 **Moran E**, Masters S, Berendt AR, McLardy-Smith P, Byren I, Atkins BL. Guiding empirical antibiotic therapy in orthopaedics: The microbiology of prosthetic joint infection managed by debridement, irrigation and prosthesis retention. *J Infect* 2007; **55**: 1-7 [PMID: 17343916]
  - 14 **Carrega G**, Bartolacci V, Burastero G, Finocchio GC, Ronca A, Riccio G. Prosthetic joint infections due to *Mycobacterium tuberculosis*: A report of 5 cases. *Int J Surg Case Rep* 2013; **4**: 178-181 [PMID: 23276761]
  - 15 **Société de Pathologie Infectieuse de Langue Française (SPILF)**; Collège des Universitaires de Maladies Infectieuses et Tropicales (CMIT); Groupe de Pathologie Infectieuse Pédiatrique (GPIP); Société Française d'Anesthésie et de Réanimation (SFAR); Société Française de Chirurgie Orthopédique et Traumatologique (SOFcot); Société Française d'Hygiène Hospitalière (SFHH); Société Française de Médecine Nucléaire (SFMN); Société Française de Médecine Physique et de Réadaptation (SOFMER); Société Française de Microbiologie (SFM); Société Française de Radiologie (SFR-Rad); Société Française de Rhumatologie (SFR-Rhu). Recommendations for bone and joint prosthetic device infections in clinical practice (prosthesis, implants, osteosynthesis). Société de Pathologie Infectieuse de Langue Française. *Med Mal Infect* 2010; **40**: 185-211 [PMID: 20303685 DOI: 10.1016/j.medmal.2009.12.009]
  - 16 **Choi HR**, Kwon YM, Freiberg AA, Nelson SB, Malchau H. Periprosthetic joint infection with negative culture results: clinical characteristics and treatment outcome. *J Arthroplasty* 2013; **28**: 899-903 [PMID: 23523496 DOI: 10.1016/j.arth.2012.10.022]
  - 17 **Bailey C**, Duckett S, Davies S, Townsend R, Stockley I. *Haemophilus parainfluenzae* prosthetic joint infection. The importance of accurate microbiological diagnosis and options for management. *J Infect* 2011; **63**: 474-476 [PMID: 21871487 DOI: 10.1016/j.jinf.2011.08.009]
  - 18 **Bjerke-Kroll BT**, Christ AB, McLawhorn AS, Sculco PK, Jules-Elysée KM, Sculco TP. Periprosthetic joint infections treated with two-stage revision over 14 years: an evolving microbiology profile. *J Arthroplasty* 2014; **29**: 877-882 [PMID: 24199997 DOI: 10.1016/j.arth.2013.09.053]
  - 19 **Gomez E**. Laboratory Diagnosis of Prosthetic Joint Infection, Part I. *Clin Microbiol Newsl* 2011; **33**: 55-60 [DOI: 10.1016/j.clinmicnews.2011.03.004]
  - 20 **Gomez E**, Patel R. Laboratory Diagnosis of Prosthetic Joint Infection, Part II. *Clin Microbiol Newsl* 2011; **33**: 63-70 [DOI: 10.1016/j.clinmicnews.2011.04.001]
  - 21 **Cobo J**, Lora-Tamayo J, Euba G, Jover-Sáenz A, Palomino J, del Toro MD, Rodríguez-Pardo D, Riera M, Ariza J. Linezolid in late-chronic prosthetic joint infection caused by gram-positive bacteria. *Diagn Microbiol Infect Dis* 2013; **76**: 93-98 [PMID: 23541692 DOI: 10.1016/j.diagmicrobio.2013.02.019]
  - 22 **Matthews CJ**. Bone and Joint Infections. *Medicine* 2014; **42**: 266-270 [DOI: 10.1016/j.mpmed.2014.02.007]
  - 23 **Martel-Laferrrière V**, Laflamme P, Ghannoum M, Fernandes J, Di Iorio D, Lavergne V. Treatment of prosthetic joint infections: validation of a surgical algorithm and proposal of a simplified alternative. *J Arthroplasty* 2013; **28**: 395-400 [PMID: 23151368 DOI: 10.1016/j.arth.2012.06.034]
  - 24 **Puhto AP**, Puhto TM, Niinimäki TT, Leppilahti JI, Syrjälä HP. Two-stage revision for prosthetic joint infection: outcome and role of reimplantation microbiology in 107 cases. *J Arthroplasty* 2014; **29**: 1101-1104 [PMID: 24461248 DOI: 10.1016/j.arth.2013.12.027]
  - 25 **Tsai JC**, Sheng WH, Lo WY, Jiang CC, Chang SC. Clinical characteristics, microbiology, and outcomes of prosthetic joint infection in Taiwan. *J Microbiol Immunol Infect* 2013; Epub ahead of print [PMID: 24064293 DOI: 10.1016/j.jmii.2013.08.007]
  - 26 **Cabo J**, Euba G, Saborido A, González-Panisello M, Domínguez MA, Agulló JL, Murillo O, Verdaguer R, Ariza J. Clinical outcome and microbiological findings using antibiotic-loaded spacers in two-stage revision of prosthetic joint infections. *J Infect* 2011; **63**: 23-31 [PMID: 21596440 DOI: 10.1016/j.jinf.2011.04.014]
  - 27 **Qadir R**, Ochsner JL, Chimento GF, Meyer MS, Waddell B, Zavatsky JM. Establishing a role for vancomycin powder application for prosthetic joint infection prevention-results of a wear simulation study. *J Arthroplasty* 2014; **29**: 1449-1456 [PMID: 24636904 DOI: 10.1016/j.arth.2014.02.012]

**P- Reviewer:** Korovessis P, Schoenhagen P **S- Editor:** Ji FF  
**L- Editor:** A **E- Editor:** Liu SQ





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

