The microbiology of the infected knee arthroplasty

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Received: 21 April 2009 / Accepted: 23 April 2009 / Published online: 21 May 2009
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Abstract We describe the results of a retrospective analysis of patients with microbiologically proven infection, who underwent revision TKA between 1994 and 2008. Of the 121 patients included in the study, 61 (50%) were male and 60 (50%) were female. The mean age was 71 (range 42–88) years. The most common organisms identified were Coagulase negative Staphylococcus (CNS) (49%) and *Staphylococcus aureus* (SA) (13%). The prevalence of CNS appears to be increasing, while that of SA and other organisms is decreasing. Vancomycin and teicoplanin were the most effective antibiotics with overall sensitivity rates of 100% and 96%, respectively. The results of our theoretical model suggest that gentamicin combined with vancomycin is the most effective empirical regimen. Staphylococcal species are the most common organisms encountered in deep infection of the knee. Gentamicin combined with vancomycin offers the most comprehensive protection and potentially allows for infected knee arthroplasties to be treated with a one-stage procedure.

Introduction

When performed successfully, total knee arthroplasty (TKA) can be a life-changing procedure, restoring function,

relieving pain, and offering high patient satisfaction. However, it is not a procedure without risk of complications. One of the most serious complications of knee arthroplasty is deep infection. Strategies including the use of intravenous antibiotics, antibiotic loaded cement, body exhaust suits and laminar flow positive pressure operating theatres, have all been successfully employed to minimise the infection risk. Despite this, published data suggest that the prevalence of deep infection following TKA is between 0.86–2.5% [1–7].

When infection does occur, early recognition and appropriate management are required in order to minimise the damage caused. Antibiotic suppression [8], joint lavage [9], debridement with exchange of polyethylene liner [10], and complete revision [11–13], are all strategies which have been employed to manage deep infection. In severe cases arthrodesis [14] or even amputation [15] are sometimes required when all other options fail. Even with early diagnosis, infection is associated with patient morbidity as well as increased treatment costs [16, 17].

The use of appropriate antibiotics at the time of recognition can limit the degree of joint destruction. However, as the use of antibiotics increases, organisms are becoming more resistant to conventional agents [18]. This combined with the development of iatrogenic problems related to antibiotic therapy, such as *Clostridium difficile* infections, has meant that it is increasingly important to use an effective antibiotic in the first-instance.

The aims of this paper are to describe the microbiology of infected knee arthroplasty, identify emerging patterns of resistance over the last decade, and suggest appropriate empirical regimens which can be used as a prophylactic measure in primary knee arthroplasty and as a method of infection eradication in revision knee arthroplasty.

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Table 1 Microbiology of infected knee replacements, 1994–2008

Organism	(%)
Coagulase negative Staphylococcus	49
<i>Staphylococcus aureus</i>	13
<i>Escherichia coli</i>	7
<i>Enterococcus faecalis</i>	6
Other	25

Materials and methods

A retrospective analysis was performed of all patients who were treated for deep infection following TKR between August 1994 and April 2008. All the patients were treated at a tertiary referral centre for peri-prosthetic infection.

Prior to operation all patients were reviewed by a consultant orthopaedic surgeon specialising in revision knee arthroplasty and clinically diagnosed as suffering from deep infection. At operation, multiple samples and tissue samples were taken for microbiological and histological examination. All patients were then given empirical antimicrobial therapy until accurate sensitivities were obtained.

Contamination of the operative field is a common problem, with contamination rates of 63% having been reported in the primary arthroplasty setting [19]. Despite this, few patients actually develop deep infection as a result of intra-operative contamination. Revision arthroplasty is not without the risk of contamination. To minimise the risk that positive microbiological specimens were the result of contaminants, in order to be included in the study, the following criteria had to be met. First, there must have been clinical suspicion of deep infection. Secondly at operation, pathogenic organisms had to be identified by at least two separate microbiological cultures from different areas of the joint.

Once the suitable patients were identified, their notes were obtained to verify the clinical history, ascertain the

causative organism and assess corresponding sensitivity profiles. Due to the changing use of antibiotics, not all samples over the investigative period were tested against the same antibiotics. The data was then collated to determine the most common causative organisms, changing patterns of antibiotic resistance, and the antibiotics which are currently most effective at treating deep infection.

A theoretical model has been postulated—individual micro-organism sensitivities against a specific antibiotic were combined with the sensitivity of micro-organisms to Gentamicin, which is commonly used in bone cement. This allows the overall sensitivities of the antibiotics used in revision surgery to be identified, enabling this to be used as a guide for empirical treatment.

Results

One hundred and twenty-one patients met the study criteria and were included in the study. Of these, 61 (50%) were male and 60 (50%) were female. All the patients were diagnosed both clinically and microbiologically as suffering from deep infection of the knee joint. All patients underwent either a one- or two-stage revision. In all cases, microbiological samples were obtained intra-operatively during the first revision procedure. Per-operatively all patient were given empirical IV antibiotics after microbiological samples were obtained. These were continued post-operatively and altered accordingly when the causative organism and corresponding sensitivities were identified. The mean age at the first stage of the revision operations was 71 (range 42–88) years.

Table 1 shows the causative organisms identified. Coagulase negative Staphylococcus (CNS) was by far the most common causative organism, occurring in 59 (49%) cases. *Staphylococcus aureus* (SA) was the second most common organism, occurring in 16 (13%) cases. Figure 1

Fig. 1 Changing pattern of microbiology, 1994–2008

Fig. 2 Sensitivities of all organisms to antibiotics

shows how the microbiology has changed over the study period. The graph shows that while the prevalence of *S. aureus* and other organisms are falling, CNS appears to be increasing in prevalence.

The overall sensitivities of the most commonly tested antimicrobials are shown in Fig. 2. Vancomycin, teicoplanin, and rifampicin appear to be the most effective antibiotics, with the lowest levels of resistance. Unsurprisingly, the antibiotics more commonly used in the general medical setting (penicillin, erythromycin and flucloxacillin) have higher levels of resistance.

The relative sensitivities of the most commonly tested antibiotics to CNS and SA are shown in Fig. 3. Again, both CNS and SA were sensitive in all cases to vancomycin and teicoplanin. *Staphylococcus aureus* was sensitive to rifampicin in all cases, and CNS was sensitive in 96%. Again, higher levels of resistance were seen in the more commonly

prescribed antimicrobials. *Staphylococcus aureus* appears to offer less resistance than CNS, with higher levels of sensitivity observed from all but one antibiotic (penicillin).

Figure 4 shows the changing patterns of sensitivity to CNS over time. Between 1994 and 2008, fusidic acid, gentamicin, erythromycin, ciprofloxacin and flucloxacillin have become increasingly less effective, while vancomycin and teicoplanin have maintained their 100% effectiveness. Between 1994 and 2003, CNS became more sensitive to penicillin. However, since 2004, the sensitivity has decreased.

The devised theoretical model was used to assess the overall sensitivities of the staphylococcal species. The results are shown in Fig. 5. The combination of gentamicin, with either vancomycin or teicoplanin appears to be the most effective, offering 100% effectiveness in both cases. Gentamicin combined with rifampicin is effective in 97% of cases.

Fig. 3 Sensitivity of Coagulase negative Staphylococcus (CNS) and *Staphylococcus aureus* (SA) to antibiotics

Fig. 4 Changing sensitivity of Coagulase negative Staphylococcus (CNS) to antibiotics, 1994–2008

Discussion

Infection plays a small but devastating role in prostheses failure. The treatment of infection associated with knee arthroplasty often requires a period of empirical antimicrobial treatment before the results of microbiological sampling can be obtained. In order to use an effective empirical therapy, it is vital to understand the microbiology of the infected knee arthroplasty. The data presented in this paper suggest that coagulase negative Staphylococcus remains the most common causative organism in infected knee arthroplasty, occurring in 49% of cases. This result is similar to that found in other studies [3, 20, 21]. CNS is commonly found as part of the skin's microflora. This would suggest that the source of infection is likely to be contamination at the time of primary arthroplasty, rather than blood-borne transmission of infection. As previously mentioned, it has been suggested that contamination occurs in up to 63% of operations [19]; however, the vast majority of these cases do not lead to infection.

The microbiological makeup of infection is changing. Since the beginning of the study period CNS has become more prevalent, with *Staphylococcus aureus* and other organisms declining in prevalence. This is the converse of infected hip prosthesis, in which the prevalence of *S. aureus* is increasing, while that of CNS is decreasing [22].

The sensitivity profiles of organisms to commonly used antibiotics are also changing. Unsurprisingly, resistance is growing towards the more traditionally used antibiotics, especially those which are commonly used in the community. We are unable to suggest the reason for the increased sensitivity towards penicillin between 1994 and 2003; however, resistance towards penicillin appears to be developing in recent years, and overall effectiveness is only 28%. Vancomycin remains the most effective antibiotic, offering 100% effectiveness to all bacteria it was tested against. Teicoplanin is increasingly being used in orthopaedic surgery, thanks to its effectiveness against MRSA. Teicoplanin offered 100% effectiveness against both CNS and *S. aureus*, with the only organisms offering resistance being

Fig. 5 Combination of gentamicin and other antibiotics to staphylococcal species

Pseudomonas aeruginosa and Coliform species. Rifampicin, ciprofloxacin and gentamicin were all 100% effective against *S. aureus*, but less so against CNS. This suggests that methicillin-resistant *S. aureus* (MRSA) is not currently a problem in infected knee arthroplasty; however, methicillin-resistant CNS (MRSE) does appear to be developing.

The hypothetical model suggests that a combination of gentamicin with either vancomycin or teicoplanin is the most effective antimicrobial therapy at revision surgery. While the parenteral administration of these drugs has potentially serious nephrotoxic side-effects, they can be added to bone cement relatively safely. Given that some species have exhibited resistance to teicoplanin, and that unlike teicoplanin, vancomycin is heat-stable and known to elute from polymethylmethacrylate (PMMA) cement [23–25], a combination of gentamicin and vancomycin in bone cement, would be recommended for use as a first-line empirical therapy. As this gave 100% protection in our series, the use of these antibiotics in bone cement, combined with intravenous teicoplanin, could be used for infection prophylaxis in the first few days following primary knee arthroplasty. This empirical regimen also potentially allows for a one-stage revision procedure to be conducted when deep infection arises.

A strength of this study is that it was conducted over a relatively long period (14 years), which should increase the generalisability of results, offering a picture of the changing pattern of microbiology, instead of a snapshot of a particular period. The fact that the operations were conducted at a specialist orthopaedic hospital, which accepts tertiary referrals is also of benefit to this study, as it gives a more generalisable picture of what is happening in the region, rather than in one particular hospital.

One limitation of the study was that only patients with microbiologically-proven infection were included. In some cases, infection may be missed at the time of revision, for example, as a result of pre-operative antimicrobial therapy inducing changes in the bacteria rendering them viable, but not culturable. Alternatively, a swab may be taken from a site that macroscopically appears infected but is actually aseptic. Although multiple samples were taken at the time of revision, there is a theoretical risk that an infective case may have been missed and not included in the study. The retrospective design of the study means that we were unable to determine which antibiotics were previously received by patients who were referred to us.

Conclusion

Infection in the presence of joint prosthesis is rare, but it still remains one of the orthopaedic surgeon's greatest challenges. Understanding the microbiology of this com-

plication allows surgeons to treat the infection as effectively as possible. Vancomycin and teicoplanin appear to be the most effective antimicrobials, with relative invulnerability to the development of resistance. The data presented in this paper give an analysis of our experience of the problem and can be used as a foundation for those dealing with this problem, and it is hoped that it will help those facing this presentation to rationalise antibiotic strategies when treating infected arthroplasty. The rationale use of antibiotics may also help limit the amount of antibiotic resistance that develops in the future.

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