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EDITORIAL

Prophylactic antibiotics in total joint arthroplasty

EVOLUTION OR DEVOLUTION?

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The surgical profession has come a long way since the catastrophic infection rates that plagued our profession prior to Lord Lister's promotion, and the eventual widespread implementation of aseptic antiseptic technique.[1,2] The successive advance in health care that along with anaesthesia, had a significant impact on the surgical field, was the discovery of antibiotics.[3,4] As these discoveries evolved, post-operative infections became an infrequent, yet no less devastating complication.

Following, Sir John Charnley's development of the total hip replacement,[5] hip and knee arthroplasty procedures have become several of the most effective elective surgical procedures in human health care.[6] However, the insertion of a large foreign implant increases the risk of a deep surgical site infection and accentuates the need for effective peri-operative strategies.[7]

A systematic review from 2008 confirmed that peri-operative antibiotics significantly reduce post-operative infection rates in total joint procedures.[8] However, the approach to infection prevention in these procedures is clearly multi-disciplinary, with techniques such as laminar flow and skin preparation playing integral roles.[9] Other approaches include antibiotic laden cement[10,11] and incisional negative pressure wound therapy.[12]

With respect to the choice of a prophylactic antibiotic regimen, guidelines have been steered by the fact that the majority of surgical site infections in total joint arthroplasty (TJA) have been reported to result from Methillicin resistant *Staphyloccous aureus* or coagulase negative *staphyloccocus*.[9] A first generation cephalosporin such as cefazolin is recommended in North America as first line prophylaxis, and clindamycin or vancomycin recommended for patients reporting a penicillin allergy.[13,14] These guidelines are widely accepted within North America, with cefazolin reported to be the antibiotic of choice for 97% of orthopaedic surgeon survey respondants.[15]

However, last month in *Bone & Joint Research*, Hickson et al[16] report widely varying antibiotic choices (88% use 1 of 3 regimens) and dosages among the acute hospital Trusts in England, and a long list of pathogens isolated from infected wounds. The use of gentamicin is particularly concerning, given the reported incidence of renal impairment[17-19] and the finding that asymptomatic bacteriuria in patients undergoing TJA does not lead to post-operative limb infections.[20]

Although the data reported by Hickson et al[16] indicate that disparity exists in the United Kingdom, it may be fair to say that current antibiotic regimens outside the United Kingdom are also not based entirely on clear evidence. A window of post-operative prophylaxis of 24 to 36 hours is recommended by the major orthopaedic society guidelines.[21-23] However, a recent meta-analysis of randomised trials comparing infection rates in TJA in patients with and without any post-operative doses concluded that post-operative prophylaxis did not lower infection rates, although the overall grade of the available evidence is low.[24] Therefore, the majority of peri-operative doses are administered without any supportive evidence for their use.

Which antibiotic should be used for prophylaxis for hip and knee surgery? There are no easy answers. Current wisdom suggests that the choice is dependent upon local antimicrobial susceptibility profiles,[25] *Clostridium difficile* sparing antibiotics[25] and the provision of coverage for coagulase negative staphylococci and MRSA, which cause around 30% of deep infections.[16] However, cephalosporins have widely been used in North America and Canada for prophylaxis and the post-operative infection rate has remained consistent at 1%[9,24] suggesting that perhaps there are other factors implicated in infection. Furthermore, routine use of local antibiotics in cement distorts our

understanding of the role and ecology of bacterial infections. In the United Kingdom, the use of flucloxacillin and gentamicin has become increasingly popular as the combination is active against a broad range of pathogens and avoids the use of cephalosporins, which have a propensity to cause *C. difficile* associated diarrhea.[17,25] This change occurred following a large amount of debate and discussion in the microbiology community to determine optimal antimicrobial prophylaxis for TJA.[17,25]

However, the evidence for cefuroxime prophylaxis associated *C. difficile* infection in patients undergoing elective TJA is lacking.[26-31] A case could be made for giving flucloxacillin systemically and gentamicin in cement and this would prevent aminoglycoside associated toxicity. However to ensure consistency between hospitals, from a safety perspective, cefuroxime or cefazolin is a reasonable choice for prophylaxis, especially as cephalosporins have been successfully used for many years in the United Kingdom and North America.

When we use prophylaxis, inevitably, the organisms become resistant to antimicrobials. Previous joint arthroplasty and antimicrobial exposure increase the risk of antimicrobial resistance, and we really need to understand all of the risks for antimicrobial resistant infections. There is no real information on the frequency of carriage of resistant organisms in the community and amongst the patient groups in the majority of centres undertaking the procedures.

So what information are we using for determining our prophylaxis? Until we have evidence relating to the pre-operative resistance profile, or unless the pre-operative flora have a high degree of resistance to cefuroxime, we suggest standardisation with cefuroxime as a single dose for prophylaxis given to all patients undergoing primary or revision prosthetic joint implant surgery, except for those cases with beta lactam allergy or colonisation with MRSA. Cefuroxime has a half-life of up to two hours and if the surgery is prolonged and there is significant blood loss (> 1500 ml), further doses are required to ensure adequate tissue and serum concentration of the antimicrobial during surgery.[14,25]

Going forward, how can we move towards a truly evidence-based approach to prophylactic antimicrobials in TJA? Given the relatively low event rate of approximately 1%,[9] a randomised clinical trial showing efficacy of one regimen over another would require thousands of patients. However, TJA procedures are high volume, with just under one million hip and knee procedures undertaken per year in the United States alone,[32] and about 200 000 in the United Kingdom.[33,34] Thus, with multi-centre collaboration, recruitment would be rapid. Indeed, in the field of orthopaedic oncology where disease rates are rare, a large group of collaborative surgeons has recently proven the feasibility of running a large international multi-centre RCT in assessing the relative efficacy of one or five days of post-operative prophylactic antimicrobials in complex lower limb reconstruction.[35]

The article by Hickson et al[16] is an important wake-up call for the orthopaedic community. Our fear of infection has led us to a 'data free zone' where we are treating our patients without clear evidence for our choices. Antimicrobial related complications and resistant organisms are on the rise,[36] whereas infections continue to plague a small but confounded group of patients. The evolution of high-impact medical advances of the 20th century has lost some traction with devolving practices. There is a clear role for standardisation of antibiotic prophylaxis, which facilitates good practice and ensures that patient safety is maximised.

Dr J. Dave's opinions, expressed in this article, are the author's own and do not reflect the view of Public Health England.

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