Prophylactic antibiotics in total joint arthroplasty

EVOLUTION OR DEVOLUTION?

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,3 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 cement10,11 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 Methicillin resistant Staphylococcus aureus or coagulase negative staphylococcus.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 respondents.15

However, last month in Bone & Joint Research, Hickson et al16 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 impairment17-19 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 al16 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 antibiotics25 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%, 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. This change occurred following a large amount of debate and discussion in the microbiology community to determine optimal antimicrobial prophylaxis for TJA.

However, the evidence for cefuroxime prophylaxis associated C. difficile infection in patients undergoing elective TJA is lacking. A case could be made for giving flucloxacillin systematically 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 centers 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.

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%, 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, and about 200,000 in the United Kingdom. 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.

The article by Hickson et al 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, 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.

References

1. Pitt D, Aubin JM. Joseph Lister: father of modern surgery. Can J Surg 2012;55:E8–E9.
2. Richardson MH. On certain unavoidable calamities following surgical operations. Boston Med Surg J 1904;151:583–588.
3. No authors listed. Classics in infectious diseases. A contribution to the chemotherapy of bacterial infections. Gerhard Domagk, 1935. Rev Infect Dis 1988;8:163–166.
4. Mahoney JF, Arnold RC, Harris A. Penicillin treatment of early syphilis—a preliminary report. Am J Public Health Nations Health 1943;33:1387–1391.
5. Jackson J. Father of the modern hip replacement: Professor Sir John Charnley 1911–82. J Med Biogr 2011;19:151–156.
6. No authors listed. A Comparison of Common Elective Orthopaedic Surgical Procedures. Medscape. http://www.medscape.com/viewarticle/587805 (date last accessed 14 October 2015).
7. Lidwell OM. Sir John Charnley, surgeon (1911-82): the control of infection after total joint replacement. J Hosp Infect 1993;23:5–15.
8. AlBuHailan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. J Bone Joint Surg [Br] 2008;90-B:915–919.
9. Johnson R, Jameson SS, Sanders RD, et al. Reducing surgical site infection in arthroplasty of the lower limb: A multi-disciplinary approach. Bone Joint Res 2013;2:56–65.
10. Chang Y, Tai C-L, Hsieh P-H, Ueng SWN. Gentamicin in bone cement: A potentially more effective prophylactic measure of infection in joint arthroplasty. Bone Joint Res 2013;2:220–226.
11. Chang YH, Tai CL, Hsu HY, et al. Liquid antibiotics in bone cement: an effective way to improve the efficiency of antibiotic release in antibiotic loaded bone cement. Bone Joint Res 2014;3:246–251.
12. Karlakki S, Brem M, Giannini S, et al. Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery: a review of evidence and mechanisms for an emerging indication. Bone Joint Res 2013;2:276–284.
13. Gehrke T, Parvizi J. Proceedings of the International Consensus Meeting on Peri-prosthetic Joint Infection. J Arthroplasty 2014;29(2Suppl):4.
14. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health-Syst Pharm AJHP Off J Am Soc Health-Syst Pharm 2013;70:195–203.
15. Beer J de, Petruccelli D, Rotstein C, et al. Antibiotic prophylaxis for total joint replacement surgery: results of a survey of Canadian orthopedic surgeons. Can J Surg J Can Cir 2009;52:E229–E234.
16. Hickson CJ, Metcaife D, Elgohari S, et al. Prophylactic antibiotics in elective hip and knee arthroplasty: an analysis of organisms reported to cause infections and infections and surgical outcome of clinical practice Bone Joint Res 2015;4:181–189.
17. Bailey O, Torkington MS, Anthony I, et al. Antibiotic-related acute kidney injury in patients undergoing elective joint replacement. Bone Joint J 2014;96-B:385–390.
18. Challagundla SR, Knox D, Hawkins A, et al. Renal impairment after high-dose flucloxacillin and single-dose gentamicin prophylaxis in patients undergoing elective hip and knee replacement. Nephrol Dial Transplant 2013;28:612–619.
19. Vooght AK, Carlsson TL, Waist CJ, Baker R, Lankester BJ. Perioperative gentamicin/flucloxacillin and acute kidney injury in orthopaedic patients. Bone Joint J 2013;95-B(suppl 10):13.
20. Bouvet C, Lübcke A, Bandi C, et al. Is there any benefit in pre-operative urinary analysis before elective total joint replacement? Bone Joint J 2014;96-B:390–394.
21. No authors listed. American Academy of Orthopaedic Surgeons. Information statement: recommendations for the use of intravenous antibiotic prophylaxis in primary total joint arthroplasty. www.aaos.org/about/papers/advisstm/1027.asp (date last accessed 16 December 2015).

22. No authors listed. British Orthopaedic Association. Primary total hip replacement: a guide to good practice. http://almacen-gpc.dynalias.org/publico/Total%20Hip%20Replacement%20BOA%202007.pdf. (date last accessed 16 December 2015. The Parity Investigators).

23. No authors listed. New Zealand Orthopaedic Association total hip joint arthroplasty: Good practice guidelines. http://nzoa.org.nz/system/files/total_hip Replacement_good_practice_guidelines.pdf. (date last accessed 16 December 2015).

24. Thornley P, Evaniew N, Riediger M, et al. Postoperative antibiotic prophylaxis in total hip and knee arthroplasty; a systematic review and meta-analysis of randomized controlled trials. CMAJ Open 2015;3:E338–E343.

25. No authors listed. Scottish Intercollegiate Guidelines Network (SIGN). Antibiotic prophylaxis in surgery (no.104). http://www.sign.ac.uk (date last accessed 16 December 2015).

26. Jenkins PJ, Teoh K, Simpson PM, et al. Clostridium difficile in patients undergoing primary hip and knee replacement. J Bone Joint Surg [Br] 2010;92-B:994–998.

27. Al-Maiyah M, Hill D, Bajwa A, et al. Bacterial contaminants and antibiotic prophylaxis in total hip arthroplasty. J Bone Joint Surg [Br] 2005;87-B:1256–1258.

28. Al-Obaydi W, Smith CD, Foguet P. Changing prophylactic antibiotic protocol for reducing Clostridium difficile-associated diarrhoeal infections. J Orthop Surg (Hong Kong) 2010;18:320–323.

29. Challagundla S, Knox D, Hawkins A, et al. Renal impairment after high-dose flucloxacillin and single-dose gentamicin prophylaxis in patients undergoing elective hip and knee replacement. Nephrol Dial Transplant 2012;27:1–7.

30. Aujla RS, Bryson DJ, Guilhar A, Taylor GJ. Trends in orthopaedic antimicrobial prophylaxis in the UK between 2005 and 2011. Ann R Coll Surg Engl 2013;95:495–502.

31. Kurd MF, Pulido L, Joshi A, Purtill JJ, Parvizi J. Clostridium difficile infection after total joint arthroplasty: who is at risk? J Arthroplasty 2008;23:839–842.

32. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg [Am] 2007;89-A:780–785.

33. No authors listed. 10th Annual Report 2013. National Joint Registry for England, Wales and Northern Ireland. http://www.njrcentre.org.uk/njrcentre/Portals/0/Documents/England/Reports/10th_annual_report/NJR%2010th%20Annual%20Report%202013%20B.pdf (date last accessed 16 September 2015).

34. DeFrances CJ, Lucas CA, Buie VC, Golosinskiy A. National Health Statistics Reports, Number 5. http://www.cdc.gov/nchs/data/nhsr/nhsr005.pdf (date last accessed 16 September 2015).

35. The Parity Investigators. Prophylactic antibiotic regimens in tumour surgery (PARITY): a pilot multicentre randomised controlled trial. Bone Joint Res 2015;4:154–162.

36. Austin DJ, Kristinsson KG, Anderson RM. The relationship between the volume of antimicrobial consumption in human communities and the frequency of resistance. Proc Natl Acad Sci 1999;96:1152–1156.