Editorial

Prophylactic antibiotics in orthopedic surgery
Controversial issues in its use

Infection in orthopedic surgery is one of the most dreaded complications. It is associated with prolonged morbidity, disability and increased mortality. Surgical site infection in clean wounds (closed uninfected wounds) includes incisional and organ space infections.[1] Out of nearly 30 million operations in the United States each year more than 2% are complicated with surgical site infections.[1] The mortality rate increases 2–3 times after infection. In another research article incidences reported of surgical site infection varies from 14% to 16%.[2] This complication occurs in 2–5% of patients after clean extraabdominal operations and in up to 20% of patients undergoing intraabdominal procedures.[2] Approximately, 1–5% of wounds develop a superficial or deep infections, in clean orthopedic operations such as total hip replacement (THR) and total knee replacement (TKR).[2] The World Health Organization (WHO) has recommended 19 items surgical safety check list before any surgical procedure [Table 1] to reduce complications.[3-4] It also includes prophylactic antibiotics.

Systemic antibiotic prophylaxis in orthopedic implant surgeries is the standard practice of care being used for last three decades.[5] Many studies have shown that even with ultra-clean theaters, prophylactic antibiotics reduce the risk of infection, where an implant is being used, although the evidence is not entirely undisputed.[6] There is enough evidence to say that prophylactic antibiotics should be used in orthopedics to reduce surgical site infection.[1,7,8] A recent systematic review by AlBuhairan *et al*.[7] on effectiveness of antibiotic prophylaxis in patients undergoing total hip and knee replacement found that antibiotic prophylaxis reduced the absolute risk of wound infection by 81% compared with no prophylaxis ($P < 0.001$) (pooled analysis of 7 studies; $n = 3065$).[7] However, three controversial issues persist in the use of prophylactic antibiotics namely; (1) Timing of administration (2) which antibiotics to be used (3) duration of prophylactic antibiotics.

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Timing of administration

The preoperative antibiotic prophylaxis is crucial to ensure adequate antibiotic concentration.[9] The timing of administration remains controversial. It varies in different studies from 15 min to 120 min before the skin incision.[6,8,10,11] Yeap *et al*.[6] advocated administration of antibiotics 30–60 min before the surgery or at the time of induction of anesthesia or at least 10 min before inflation of tourniquet.[6] The authors reported that initiating prophylaxis after the skin is incised, is ineffective. Niimi *et al*. in a case control study of 223 patients administered intravenous infusion of antibiotics 30 min before surgery.[10] None of these arthroplasty patients developed wound infection immediately or at minimum of 12 months followup after surgery. Stefánsdóttir *et al*. considers that most of the antibiotics used should be administered 30 min before skin incision. Administration >60 min before surgery/incision is associated with higher risk of surgical infections.[12] This is because of short half-life of the most commonly used antibiotics such as cloxacillin and cephalosporin. The half-life of cloxacillin is 30 min. Most of the studies agree that prophylactic antibiotics should ideally be administered 30–60 min before skin incision.[8,11] Antibiotic concentration in blood and bone typically appear within 20 and 60 min, respectively and need to be maintained above the minimum inhibitory concentration of the infecting organisms until skin closure.[8] The prophylaxis has least effect when antibiotic is given after the application of a tourniquet. Thus the extremity remains unprotected for a large duration from antibiotic prophylaxis.

Which antibiotics

The antibiotic selected should in general, be inexpensive, nontoxic and of limited spectrum.[1] The most prevalent organisms in prosthetic related infections are Gram-positive *Staphylococcus aureus* and epidermidis. They are normally present as skin flora and can adhere to implant and multiply.[7] The type of antibiotics administered at any time preoperatively are β-lactams such as cephalosporins, penicillin and its derivatives such as cloxacillin, glycopeptides as teicoplanin and aminoglycosides such as gentamicin.[7] According to American Society of Health System Pharmacists (ASHP) cefazolin was the most used antibiotic in preoperative prophylaxis, combination of cefazolin with gentamicin was the second common regimen while 3rd generation cephalosporin were 3rd widely used antibiotics.[2] National clinical practice guidelines on rationale use of

Table 1: Surgical safety checklist (reproduced with permission of the WHO)

Surgical safety checklist (first edition)		
Before induction of anaesthesia	**Before skin incision**	**Before patient leaves operating room**
Sign in	**Time out**	**Sign out**
☐ Patient has confirmed • Identity • Site • Procedure • Consent	☐ Confirm all team members have introduced themselves by name and role	Nurse verbally confirms with the team ☐ The name of the procedure recorded ☐ That instrument, sponge and needle counts are correct (or not applicable) ☐ How the specimen is labelled (including patient name)
☐ Site marked/not applicable	☐ Surgeon, anaesthesia professional and nurse verbally confirm • Patient • Site • Procedure	☐ Whether there are any equipment problems to be addressed
☐ Anaesthesia safety check completed	Anticipated critical events ☐ Surgeon reviews: what are the critical or unexpected steps, operative duration, anticipated blood loss? ☐ Anaesthesia team reviews: are there any patient-specific concerns? ☐ Nursing team reviews: has sterility (including indicator results) been confirmed? Are there equipment issues or any concerns?	☐ Surgeon, anaesthesia professional and nurse review the key concerns for recovery and management of this patient
☐ Pulse oximeter on patient and functioning Does patient have a: Known allergy? ☐ No ☐ Yes Difficult airway/aspiration risk? ☐ No ☐ Yes, and equipment/assistance available Risk of >500 ml blood loss (7 Ml/kg in children)? ☐ No ☐ Yes, and adequate Intravenous access and fluids planned	Has antibiotic prophylaxis been given within the last 60 minutes? ☐ Yes ☐ Not applicable Is essential imaging displayed? ☐ Yes ☐ Not applicable	

antibiotics in orthopedic surgery in Malaysia recommends cloxacillin in combination with gentamicin as first choice, 2nd generation cephalosporin as second choice antibiotics in arthroplasty and open reduction and internal fixation of fractures. Yeap *et al*. in their study compared 2nd generation cephalosporin and 3rd generation cephalosporin antibiotics prophylaxis. Cefuroxime (2nd generation cephalosporin) was used in 52.7% cases and 3rd generation (cefoperazone or ceftriaxone) was used in 47.3% cases of internal fixation in this series. In patients undergoing arthroplasty 2nd generation (cefuroxime) was used in 11.8% cases, in rest of cases 3rd generation cephlosprin (cephotriaxone and cefoperazone) was used in same series. They concluded that cephalosporins are by far the most popular choice of antibiotics for prophylaxis. In this study, 3rd generation cephalosporins were used for arthroplasty and 2nd generation cepholospirins were used for fracture fixation.[6] Although the spectrum of infecting organisms in surgery for closed fractures is similar to that following prosthetic joint surgery.[13] The most common organisms causing infections are probably *S. aureus*. Theoretically 3rd generation cephalosporins are less active against Gram-positive bacteria than 2nd generations, but they are more active against Gram-negative bacteria, which is superior statistically yet to be proved. This study[13] further concludes first line antibiotic recommended as prophylaxis is 2nd generation cephalosporin followed by 3rd generation cephalosporin, with the trend to use 3rd generation cephalosporins in patients undergoing arthroplasty. Swedish orthopedic teaching hospital recommended cloxacillin as first line treatment/prophylaxis.[11,12] Second generation cephalosporins (cefuroxime) have been widely recommended as choice by many studies.[1,5,7,8] However, there is insufficient evidence to suggest that particular generation of cephalosporin is more effective and it is superior to cloxacillin.

In a systematic analysis "cephalosporin versus teicoplanin; cephalosporin versus penicillin derivatives (cloxacillin) and comparisons between 2nd generation and 1st generation

cephalosporins, there was no significant difference in clinical effect.

Duration of antibiotics

The controversy persists in administration of antibiotics varying from a single dose to 3 doses to 5 days or 14 days.[6] Musmar *et al*. suggests that antibiotics should be discontinued within 24 h after end of surgery to prevent emergence of resistance.[1] Thonse *et al*.[8] recommended prophylactic antibiotic regimen at time of induction of anesthesia and two subsequent doses at 8 and 16 h postoperatively. Another study by Andersson *et al*.[11] suggest same recommendations of 3 doses within 24 h. Stefánsdóttir *et al*. recommended two doses, one at the time of induction and another 6 h after surgery.[12] Niimi *et al*.[10] in a retrospective study compared the outcome of 1-day intravenous administration with that of long term intravenous administration in arthroplasty cases. They used antibiotics for 1-day (n = 233) and for at least 3 days (n = 104). India being a tropical country, with a hot and humid climate is a conducive environment for both Gram-positive and Gram-negative bacterial colonization of skin, linen, and wards in general. Therefore we need studies tailored to our environment. Antibiotics should not stop at skin closure but should continue till epithelization of wound occurs. The surgery was performed in vertical laminar flow operation theatre with body exhaust system. None of these patients developed wound infection during followup (minimum 12 months). They concluded that 1-day antibiotic infusion was as effective as long term antibiotic infusion preventing infection after arthroplasty. Long term use was associated with drug resistant bacteria, drug induced hepato/nephropathy and high medical cost. The ideal duration of postoperative antibiotics is not yet clearly defined although most reports say that there is no additional benefit when prophylactic antibiotics are given more than 24 h postsurgery. According to ASHP guidelines[2] minimal duration of antimicrobial coverage includes time from incision to closure of incision, which is usually covered by single antibiotic dose.

The duration of postoperative antibiotics is highly variable, and single dose prophylaxis was rarely practiced. Thus, there is still considerable discussion in the current literature as to the duration of prophylactic antibiotics and no consensus has yet arrived.

Conclusion

It is clear that surgical prophylactic antibiotics are to be used. There is a controversy in the literature with no evidence regarding timing, choice of antibiotics and duration of prophylactic antibiotics in orthopedic surgery. The trend in western literature is to use 2nd generation cephalosporins (cefuroxime) prophylactic antibiotics 30 min to 1 h before skin incision and preferable for 24 h to 3 days in intravenous infusion postoperatively.

Cefuroxime has high bioavailability in tissue and serum after a single dose and is efficacious for preventing perioperative infection. However, in our scenario and milieu, theater conditions and prevalent pathogens are different.[14] Our patient population has different socioeconomic backgrounds cannot be compared with the developed western world. Hence, if we need an answer to these 3 queries we require large multicentric indigenous studies in our country. We need to have level 1 studies to formulate guidelines for our country.

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References

1. Musmar SM, Ba'ba H, Owais A. Adherence to guidelines of antibiotic prophylactic use in surgery: A prospective cohort study in North West Bank, Palestine. BMC Surg 2014;14:69.
2. Rafati M, Shiva A, Ahmadi A, Habibi O. Adherence to American society of health-system pharmacists surgical antibiotic prophylaxis guidelines in a teaching hospital. J Res Pharm Pract 2014;3:62-6.
3. Sewell M, Adebibe M, Jayakumar P, Jowett C, Kong K, Vemulapalli K, *et al.* Use of the WHO surgical safety checklist in trauma and orthopaedic patients. Int Orthop 2011;35:897-901.
4. WHO. The Surgical Safety Checklist. Geneva: World Health Organisation; 2008. Available from: http://www.who.int/patientsafety/safesurgery/tools_resources/SSSL_Manual_finalJun08.pdf. [Last accessed on 2015 Jun 01].
5. Mathur P, Trikha V, Farooque K, Sharma V, Jain N, Bhardwaj N, *et al.* Implementation of a short course of prophylactic antibiotic treatment for prevention of postoperative infections in clean orthopaedic surgeries. Indian J Med Res 2013;137:111-6.
6. Yeap JS, Lim JW, Vergis M, Au Yeung PS, Chiu CK, Singh H. Prophylactic antibiotics in orthopaedic surgery: Guidelines and practice. Med J Malaysia 2006;61:181-8.
7. AlBuhairan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: A systematic review. J Bone Joint Surg Br 2008;90:915-9.
8. Thonse R, Sreenivas M, Sherman KP. Timing of antibiotic prophylaxis in surgery for adult hip fracture. Ann R Coll Surg Engl 2004;86:263-6.
9. W-Dahl A, Robertsson O, Stefánsdóttir A, Gustafson P, Lidgren L. Timing of preoperative antibiotics for knee arthroplasties: Improving the routines in Sweden. Patient Saf Surg 2011;5:22.
10. Niimi R, Hasegawa M, Kawamura G, Sudo A. One-day antibiotic infusion for the prevention of postoperative infection

following arthroplasty: A case control study. ISRN Orthop 2011;2011:839641.
11. Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. The application of evidence-based measures to reduce surgical site infections during orthopedic surgery – Report of a single-center experience in Sweden. Patient Saf Surg 2012;6:11.
12. Stefánsdóttir A, Robertsson O, W-Dahl A, Kiernan S, Gustafson P, Lidgren L. Inadequate timing of prophylactic antibiotics in orthopedic surgery. We can do better. Acta Orthop 2009;80:633-8.
13. Antimicrobial prophylaxis for orthopaedic surgery. Drug Ther Bull 2001;39:43-6.
14. Behera B, Mathur P. High levels of antimicrobial resistance at a tertiary trauma care centre of India. Indian J Med Res 2011;133:343-5.

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