The Journal of Orthopaedics Trauma Surgery and Related Research

© J ORTHOP TRAUMA SURG REL RES
12(2) 2017
Research Article

Efficacy of single dose versus multiple dose injectable antibiotics in hip joint surgery

NISHIT BHATNAGAR, SUMIT SURAL, SUMIT ARORA, PURUSHOTHAM LINGAIAH AND ANIL DHAL

Department of Orthopaedic Surgery, Maulana Azad Medical College & associated Lok Nayak Hospital, New Delhi, India

Address for correspondence:
Nishit Bhatnagar,
Senior Resident, Department of Orthopaedic Surgery, Maulana Azad Medical College & associated Lok Nayak Hospital, New Delhi-110002, India
Tel: +91 9910465639,
E-mail: nishitbhatnagar@yahoo.co.in

Statistics

Figures	00
Tables	02
References	28

Received: 14.07.2017
Accepted: 11.08.2017
Published: 14.08.2017

Abstract

Objective: To compare the efficacy of two prophylactic antibiotic regimens in preventing surgical site infection.

Setting: Tertiary level hospital in India.

Methods: We enrolled 104 consecutive patients undergoing elective implant surgery around the hip and randomized them into two groups. Group A (53) received a single dose of injectable cefazolin prior to skin incision, while group B (51) received additional 5 doses of injection cefazolin 12 hourly after the procedure. They were followed up for a minimum duration of 12 months and observed for the evidence of surgical site infection.

Results: None of the patients from group A had surgical site infection, while 3 patients of group B (5.8%) developed infection. However, difference in infection rate was not significant statistically (p=0.114). Staphylococcus was isolated from 2 of the 3 infected surgical sites and Klebsiella from the third.

Conclusion: Additional postoperative doses of cefazolin offer no advantage over its single pre-operative dose.

Key words: Surgical site infection; Hip fractures; Prophylactic antibiotic therapy

INTRODUCTION

The prophylactic use of antibiotics in surgery was initially started by Miles in 1957 and Burke in 1961 [1]. Schonholtz et al. through their study showed that there was no advantage of an extended antibiotic regimen [2]. Out of nearly 30 million operations in the United States each year more than 2% are complicated with surgical site infections [3].

The World Health Organization (WHO) has included prophylactic antibiotics in its surgical safety check list before any surgical procedure [4]. The use of prophylactic antibiotics has reduced the risk of surgical site infection (SSI) from 15% to less than 1% [5]. A recent systematic review found that antibiotic prophylaxis reduced the absolute risk of wound infection by 81% compared with no prophylaxis [6].

American Association of Orthopaedic Surgeons (AAOS) recommends a single dose of injection cefazolin 60 minutes prior to the skin incision as adequate prophylaxis for clean orthopaedic implant surgeries [7]. Inspite of these recommendations surgeons, even in developed countries tend to extend the duration of antimicrobial prophylaxis [8]. Hence surgeons of the developing world, fearing higher risk of SSI also tend to give prolonged antibiotic prophylaxis. Such indiscriminate use of antibiotics has been shown to contribute to the rise of antimicrobial resistance [9]. The authors declare that there were no conflicts of interest.

METHODS

The study was conducted at a single tertiary level center in India between August 2014 and March 2016. Patients undergoing elective implant surgeries around the hip, in the age group of 18-70 years were included. The exclusion criteria were presence of active distant infective focus, immunocompromised state and patients suffering from psychiatric disorders. Written, informed consent was obtained authorizing treatment, photographic documentation and radiographic examination. Institutional review board and ethical committee clearance was granted.

The patients age, gender, body-mass index (BMI), haemoglobin level, total leucocyte count (TLC) and C-reactive protein (CRP) were recorded. The other recorded parameters included time lag between the trauma and surgery, duration of surgery, blood loss, numbers of scrubbed members, number of personnel in operation theatre (OT), time duration until suction drain was retained, duration of hospital stay, urinary catheterisation, soakage of dressing, and post-operative evidence of infection. Patients were randomized into two groups based on a computer generated random number sequence. All patients received an intravenous (I.V.) injection of cefazolin 1 g 60 minutes prior to skin incision. Post-operatively patients of group A were given 5 doses of 10mL normal saline injections at 12 hourly intervals to ensure patient blinding. Patients of Group B received 5 doses of cefazolin 1 g I.V. at 12 hourly intervals. Group allocation was concealed from the chief operating surgeon, who was responsible for follow up care, to ensure double blinding. Wound inspection was done if there was fever on the 3rd post-operative day or soakage. Patients were discharged on post-operative day 3 unless otherwise indicated and were instructed to follow up for suture removal on the 14th day. However, in case of fever or soakage they were asked to report to the concerned surgeon. All the cases were reassessed periodically for upto one year.

SSI was defined as any patient who had undergone surgery and developed purulent discharge at the operation site with microbiologically positive cultures. Failed implant with a culture negative discharge or patients with post-operative fever, significant rise in TLC with signs of inflammation of incisional site were also included in the case definition [10]. Such patients were treated with wound lavage under appropriate anaesthesia and implant removal if found loose. Swabs from the surgical site were taken for culture and antimicrobial susceptibility testing.

The aim of the study was to compare the efficacy of two prophylactic antibiotic regimens in preventing surgical site infection.

Statistical analysis was performed with Statistical Package for Social Sciences (SPSS, version 16, Chicago, US). Results were tested using Chi square test and Mann Whitney test. A two-tailed p value of <0.05 was considered as statistically significant.

RESULTS

Inclusion criteria was met by 118 patients, however, 4 declined to participate, 7 were immunocompromised (uncontrolled diabetics, Hba1c>7), 2 had sacral pressure sores (active infective focus) and 1 had bipolar disorder. Out of the total 104 patients included in the study, 53 belonged to Group A and 51 belonged to group B. The patients of group A and B were compared to look for selection bias (Table 1). Both the groups were comparable in terms of age (p=0.127), gender (p=0.578), BMI (p=0.163), preoperative haemoglobin levels (p=0.532), TLC (p=0.219), ESR (p=0.444), serum proteins (p=0.856), serum albumin levels (0.086), time lag between the trauma and surgery (p=0.146), time duration untill suction drain was retained (p=0.943), duration of hospital stay (p=0.075), and urinary catheterization (p=0.905). Statistically significant difference was observed between these groups in other parameters like CRP (p=0.011), duration of surgery (p=0.016), blood loss (p=0.029), numbers of scrubbed members of surgical team (p=0.025), number of personnel in operation theatre (p=0.019), soakage of dressing with urine/ blood (p=0.005).

Table 1. Comparative evaluation of the patients between both the groups with p values is presented.

Parameters		Group A	Group B	P-value
Age (years)*		49	53	0.127
Gender	Male	38	34	0.578
	Female	15	17	
Hemoglobin (gm %)*		11	11.3	0.532
TLC*		10108	9500	0.219
CRP**		5	6.4	0.011
BMI*		21	21.6	0.163
Duration from trauma to surgery (days)**		9	10	0.146
Stay in hospital in days*		11.9	12.2	0.075
Duration of surgery (minutes)*		78	114	0.016
Blood loss (mL)*		300	419	0.029
Number of surgeons*		2.7	3	0.025
Number of personnel in theatre*		7.7	8	0.019
Duration of suction drain (hours)*		33.7	32	0.943
Urinary catheterization		13	12	0.905
Postoperative soakage		7	19	0.005
Infection		0	3	0.114

The superscript single star (*) denotes mean values, double star (**) denotes median values and all other values are absolute numbers.

The mean age in the study was 51 years (range; 18 years to 70 years) and 45% of the patients were over 60 years of age. The most common injury was inter-trochanteric fracture of the femur (47.1%) followed by the neck of femur fracture (33.6%).

In our study, we observed three cases of surgical site infections (2.8%), 1 superficial and 2 deep (Table 2). These three patients were above 60 years of age, anaemic and had co-morbidities. The organisms isolated from surgical site was *Staphylococcus aureus* in two cases and *Klebsiella* in one case. All three patients belonged to group B. However, the difference in the incidence of infection between the 2 groups was not statistically significant as per the Fisher's exact test (p = 0.1).

Table 2. Comparative evaluation of all the 3 infected patients in Group B.

Parameters	Patient # 1	Patient # 2	Patient # 3
Age (Years)/Sex	70/Male	60/Male	65/Male
Diagnosis	Inter-trochanteric #	# Neck femur	Sub-trochanteric #
Surgery	Dynamic hip screw	Hemi-arthroplasty	Dynamic hip screw
Co-morbidity	Hypertension	Coronary artery disease	Pulmonary fibrosis
BMI	28.3	19.1	18.3
Time between trauma and surgery (days)	18	12	22
Hospital stay (days)	13	15	22
Soakage	No	Yes	Yes
Urinary catheterization	No	Yes	Yes
Duration of surgery (minutes)	120	70	100
Infection	Deep	Deep	Superficial
Organism isolated	*Staphylococcus* sensitive to linezolid	*Staphylococcus* sensitive to clindamycin	*Klebsiella* sensitive to ciprofloxacin
Management	Debridement, lavage and implant removal	Debridement, lavage and implant removal	Debridement and lavage
Outcome	Wound healed by secondary intention in 2 months	Wound healed by secondary intention in 2 months	Wound healed by primary intention in 2 weeks

DISCUSSION

Majority of SSI after orthopaedic surgeries are due to *Staphylococcus* spp. from the skin of the patient, suggesting intra-operative contamination [11]. Cefazolin, a first-generation cephalosporin is relatively nontoxic, inexpensive, and effective against *Staphylococcus* making it the preferred antibiotic for prophylaxis in implant surgeries worldwide.

With the emergence of Methicillin Resistant *Staphylococcus aureus* (MRSA), there was a debate about using other broad-spectrum antibiotics. Sewick et al. observed no reduction in infection rate inspite of addition of vancomycin along with cefazolin [12]. They suggested that vancomycin prophylaxis should be considered only for known MRSA carriers.

The development of surgical site infection appears to be multifactoral. One of the important factors responsible for the development of early infection is the number of bacteria present in the surgical wound. The host defence mechanism works to decrease the overall number of bacteria during the first 2 hrs. Rate of bacterial multiplication and bacterial killing by the host immune mechanism remains fairly balanced during the next 4 hours. The initial 6 hours are hence called the "golden period". It is after this period that the bacterial multiplication outpaces bacterial killing and bacteria multiply exponentially. Antibiotics play their part by decreasing bacterial growth and delaying bacterial reproduction. The administration of prophylactic antibiotics expands the golden period [13].

Intravenous injection of cefazolin takes 30 min-60 mins to reach peak serum concentration. Therefore, antibiotic must be administered 1 hour prior to skin incision [7]. By ensuring the appropriate timing of administration, serum concentration of cefazolin just before wound closure, is above the target concentration (40 µg/mL-70 µg/mL) required. The serum concentration at 60 min after administration of 1 g and 2 g intravenous cefazolin was 50 µg/mL to 70 µg/mL and 130 µg/mL, respectively [14]. Concentration below 100 µg/mL are not associated with toxicity [15]. Hence, the consensus was to use 1 g intravenous cefazolin 60 minutes prior to skin incision.

It has been suggested in literature that short course antibiotic prophylaxis is as effective in preventing surgical site infection as long course antibiotic regimens. Fonseca et al. studied the incidence of surgical site infections across different specialties including orthopaedics, vascular surgery, urology, gastrointestinal, and oncology [16]. They concluded that shortening the 24 h prophylactic antibiotic regimen to a single dose of cefazolin did not lead to an increase in rates of surgical site infection. Reducing the duration of antibiotics which are not necessary, is likely to prevent antibiotic resistance and also reduces the cost of treatment to the patient and the state [17].

The incidence, risk factors and ideal prophylactic regimen for surgical site infection in arthroplasty is an extensively researched topic. However, there are very few studies comparing short and long antibiotic regimens in orthopaedic traumatology. Morrison et al. could find no definite evidence that multiple dose antibiotic prophylaxis is superior to a single preoperative dose in surgical fixation of low-energy closed fractures [18].

Similarly, Slobogean failed to demonstrate the superiority of multiple-dose antibiotic prophylaxis over a single-dose strategy in patients undergoing surgery for closed long bone fractures [19]. Kumar et al. from India observed no change in the incidence of surgical site infection after changing from a 10 days antibiotic regimen to a 3 days antibiotic strategy [20]. Ali et al. also from the Indian subcontinent reported no significant difference in infection rates in clean orthopaedic surgeries when using a single dose or multiple dose antibiotic regimens [11]. Hence, we designed our study to compare a single preoperative dose versus a 3-day antibiotic regimen.

Most of the literature on antibiotic prophylaxis in orthopaedic surgeries is from the developed world and it reports an incidence of SSI of 0.6% to 2.4% for clean elective orthopaedic implant surgeries [21-23]. Jain and Banerjee reported a SSI rate of 18% in clean orthopaedic surgeries at their centre in central India [24]. They attributed the infection rate to poor surgical set up and a lack of attention towards the basic infection control measures. Mohammed et al. reported an SSI rate of 11.6% among clean elective orthopaedic surgeries from a tertiary level centre in southern India [25]. Their explanation for a higher incidence of surgical site infection was a lack of economic assets, obsolescent instruments and improper ventilation in their operating theater, as well as ineffective infection prevention stratagies. It is for such reasons that recommendations from the developed world cannot be blindly applied in developing nations. Recent studies from India on patients undergoing clean elective orthopaedic implant surgeries reported a relatively high SSI rate of 6.9% [26,27].

Inspite of high rates of SSI reported from India, our study shows that even in developing countries, the recommendations of the developed world can be followed and produce comparable results. Jain et al., also from India reported a SSI rate of 2.1% among orthopaedic patients requiring surgery which was comparable to the SSI rate in our study (2.8%) [28].

Due to the fear of postoperative surgical site infection many orthopaedic surgeons in India continue to give prolonged antibiotics postoperatively. In our study, we found a higher rate of infection in the group receiving a prolonged antibiotic regimen. However, the difference in infection rates between the two groups was not statistically significant.

CONCLUSION AND LIMITATIONS

The limitation of our study was the small number of cases due to time restriction. A regression analysis to delineate the risk factors of infection could not be done and no conclusions could be drawn regarding emergence of antimicrobial resistance. Inspite of randomization of the study population, there was some unintentional skewing in distribution of certain parameters between the two groups. However, it is worth noting that of the 51 patients who received a single antibiotic dose, none developed a SSI. Hence, we suggest that even for developing countries, single preoperative dose of cefazolin is adequate prophylaxis against surgical site infection in orthopaedic surgeries around the hip.

ACKNOWLEDGEMENTS

Financial support: None reported.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

References:

1. *Matti P.R., Querol R.C., Velmonte M.A., et al.: Prescribing practices of surgeons and factors that limit adherence to the Philippine College of Surgeons Clinical Practice Guidelines on anti-microbial prophylaxis for elective surgical procedures at the UP-PGH surgical wards. Phil J Microbiol Infect Dis. 2002;31:107-124.*
2. *Schonholtz G.J., Borgia C.A., Blair J.D.: Wound sepsis in orthopaedic surgery. J Bone Joint Surg Am. 1962;44:1548-1552.*
3. *Musmar S.M., 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.*
4. *WHO: Geneva, Switzerland. The Surgical Safety Checklist. World Health Organisation; 2008.*
5. *Weick J.A., Jackson J.K., O-Brien T.J., et al.: Efficacy of prophylactic antibiotic in arthroscopic surgery. Orthopaedics. 1997;20:133-134.*
6. *AlBuhairan B., Hind D., Hutchinson A.: Antibiotic prophylaxis for wound infections in total joint arthroplasty: A systematic review. J Bone Joint Surg Br. 2008;90:915-919.*
7. *[No authors listed]. Anti-microbial prophylaxis for surgery. Treat Guidel Med Lett. 2009;7:47-52.*
8. *Takahashi Y., Takesue Y., Nakajima K., et al.: Implementation of a hospital-wide project for appropriate antimicrobial prophylaxis. J Infect Chemother. 2010;16:418-423.*
9. *Harbarth S., Samore M.H., Lichtenberg D., et al.: Prolonged antibiotic prophylaxis after cardiovascular surgery and its effect on surgical site infections and antimicrobial resistance. Circulation. 2000;101:2916-2921.*
10. *Horan T.C., Gaynes R.P., Martone W.J., et al.: CDC definitions of nosocomial surgical site infections, 1992; A modification of CDC definitions of surgical wound infections. Infection Control Hosp Epidemiol. 1992;13:606-608.*
11. *Ali M., Raza A.: Role of single dose antibiotic prophylaxis in clean orthopedic surgery. J Coll Physicians Surg Pak. 2006;16:45-48.*
12. *Sewick A., Makani A., Wu C., et al.: Does dual antibiotic prophylaxis better prevent surgical site infections in total joint arthroplasty. Clin Orthop Relat Res. 2012;470:2702-2707.*
13. *Cleveland KB.: General principles of infection. In: Canale ST, Beaty JH, ed. Campbell's Operative Orthopaedics, 12th ed. Philadelphia: Elsevier; 2013: 706-723.*
14. *Yamada K., Matsumoto K., Tokimura F., et al.: Are bone and serum cefazolin concentrations adequate for antimicrobial prophylaxis? Clinical Orthopaedics and Related Research. 2011;469:3486-3494.*
15. *Zeller V., Durand F., Kitzis M.D., et al.: Continuous cefazolin infusion to treat bone and joint infections: clinical efficacy, feasibility, safety, and serum and bone concentrations. Antimicrob Agents Chemother. 2009;53:883-887.*
16. *Fonseca S.N., Kunzle S.R., Junqueira M.J., et al.: Implementing 1-dose antibiotic prophylaxis for prevention of surgical site infection. Arch Surg. 2006;141:1109-1113.*
17. *Huttner A., Harbarth S., Carlet J., et al.: Antimicrobial resistance: A global view from the 2013 World Healthcare-Associated Infections Forum. Anti-microbial resistance and infection control. 2013;2:31.*
18. *Morrison S., White N., Asadollahi S., et al.: Single versus multiple doses of antibiotic prophylaxis in limb fracture surgery. ANZ J Surg. 2012;82:902-907.*
19. *Slobogean G.P., Kennedy S.A., Davidson D., et al.: Single- versus multiple-dose antibiotic prophylaxis in the surgical treatment of closed fractures: a meta-analysis. J Orthop Trauma. 2008;22:264-269.*
20. *Kumar S., Behera B., Farooque K., et al.: Efficacy of a short course antibiotic prophylaxis for open reduction of closed fractures: first report from India. J Physicians Ind. 2010:58.*
21. *Li G.Q., Guo F.F., Ou Y., et al.: Epidemiology and outcomes of surgical site infections following orthopedic surgery. Am J Infect Control. 2013;41:1268-1271.*
22. *Edwards J.R., Peterson K.D., Mu Y., et al.: National Healthcare Safety Network (NHSN) report: Data summary for 2006 through 2008, issued December 2009. Am J Infect Control. 2009;37:783-805.*
23. *Lin S., Mauffrey C., Hammerberg E.M., et al.: Surgical site infection after open reduction and internal fixation of tibial plateau fractures. Eur J Orthop Surg Traumatol. 2014;24:797-803.*
24. *Jain B.K., Banerjee M.: Surgical site infections and its risk factors in orthopaedics: A prospective study in teaching hospital of central india. Int J Res Med. 2013;2:110-113.*
25. *Mohammed P.A., Sharma D., Patro D.K., et al.: A study of incidence and risk factors of Surgical site infection following orthopedic surgical procedure in a tertiary care hospital in south India. Int J Med Res Rev. 2015;3:983-989.*
26. *Amrutha G., Satyanarayana V., Prasad V.G.: Lymph node aspiration cytology finding in HIV infected cases of a rural population in South India. Journal of Evolution of Medical and Dental Sciences. 2015;83:14576-14581.*
27. *Chhabra A., Sachdeva G.D.: Early surgical site infection: incidence and risk factors. Int J Med Res Prof. 2015;1:22-26.*
28. *Jain R.K., Shukla R., Singh P., et al.: Epidemiology and risk factors for surgical site infections in patients requiring orthopedic surgery. Eur J Orthop Surg Traumatol. 2015;25:251-254.*