Original Article

Randomized controlled trial comparing cefazolin with ceftriaxone in perioperative prophylaxis in orthopaedic surgeries

RPS Kalawar, BP Shrestha, GP Khanal, P Chaudhary, R Rijal, R Maharjan, SR Paneru
Department of Orthopaedics
BP Koirala Institute of Health Sciences, Dharan

Abstract

Background: Surgical site infection is one of the most dreaded complications faced by an orthopaedic surgeon. In spite of cefazolin being recommended as perioperative antibiotic, many orthopaedic surgeons continue to use ceftriaxone as perioperative antibiotic.
Objective: To compare the effectiveness of cefazolin and ceftriaxone as perioperative prophylactic antibiotics in the prevention of surgical site infection in clean elective orthopaedic surgeries.
Methods: We conducted a randomized controlled trial in 197 patients undergoing clean elective orthopaedic surgeries. The patients were divided into two groups. One group received intravenous prophylactic antibiotics cefazolin and gentamicin and the other group received ceftriaxone and gentamicin in standard doses for 48 hours. Both groups were followed by oral Cephadroxyl for 7 days. The patients were followed up for three months.
Results: There was no significant difference in the rate of surgical site infection among the two groups.
Conclusion: We conclude that there is no difference in the effectiveness of prevention of surgical site infection between cefazolin and ceftriaxone.

Keywords: Cefazolin, ceftrinxone, prophylactic antibiotics, surgical site infection.

Introduction

Surgical site infection is one of the most dreaded complications faced by an orthopaedic surgeon. In an era of evidence-based medicine, it is in the interest of the patient and the surgeon to follow practices backed by basic and clinical sciences.[1] There are multiple studies which recommend cefazolin as prophylactic antibiotic in clean elective orthopaedic surgery.[2-4] Using inappropriate antibiotics may contribute to the surgical site infection and development of antimicrobial resistance.[5-7] Many of the orthopaedic surgeons continue to use ceftriaxone in practice as prophylactic

Address for correspondence
Dr. Rosan Prasad Shah Kalawar
Department of Orthopaedics
BP Koirala Institute of Health Sciences, Dharan
Email: docrosan@yahoo.com

antibiotic in clean elective orthopaedic surgery. So, it has become necessary to validate in our conditions what the literatures in the developed countries have been advocating. This study was performed to see if there was any difference in the rate of infection among patients who received cefazolin and those who received ceftriaxone in our setting.

Methods

Randomized controlled trial was conducted in the Department of Orthopaedics, B. P. Koirala Institute of Health Sciences, Dharan, Nepal. The study population included a total of 197 clean elective cases operated by the authors with or without using implants in the Orthopaedic Routine Operation Theater from November 2014 to April 2015. Those patients who had earlier wounds whether healed or otherwise and those patients who had undergone earlier surgeries were excluded from the study. All types of orthopaedic surgeries performed in an orthopaedic operation theater like closed fracture fixation of extremities and spine, soft tissue surgeries like tendon reconstruction or transfers, excision of benign tumours and arthroplasties were included. The records of 2013 showed that the number of cases operated in routine OT from 1st November 2013 to 30th April 2014 was 250. Arbitrarily, it was decided to take 220 of the cases. The 220 patients were randomized into 2 groups using computer generated random number sequence. Patients belonging to Group A were administered 2 gm of injection cefazolin and 80 mg injection gentamicin within 60 minutes before incision. Postoperatively, injection cefazolin one gram and injection gentamicin 80 mg was repeated eight hourly for 48 hours. Patients belonging to Group B were administered injection ceftriaxone, all other remaining the same. It was followed with oral cefadroxil 500 mg twice daily for 7 days. When the duration of surgery exceeded two hours or when there was excessive bleeding, one dose of each antibiotic was repeated intra-operatively. The study was approved by the Ethical Review Board of B. P. Koirala Institute of Health Sciences. Informed consent was taken from all patients included in the study. The authors did not receive any outside funding. The proforma for each patient included information about age, gender, duration of surgery (incision to closure), associated medical illness, preoperative hemoglobin level, preoperative albumin level, blood loss during surgery and preoperative admission days. The patients were discharged after 48 hours of surgery after wound inspection and change of dressing. The patients were followed up after 14 days, six weeks and three months to look

for signs of surgical site infection. The study was considered completed at three months for each patient if there was no infection or whenever an evidence of infection was observed before completion of three months. Our criteria for judging whether or not a wound infection occurred were as follows which has been modified from that of Pavel et al.[8]

1. If a wound drained purulent material irrespective of whether an organism was cultured or not, it was considered infected.
2. When a wound became red, painful or tender, swollen and hot for more than 48 hours, the wound was considered infected.
3. When the patient had fever for more than 48 hours and no other cause could be traced, the wound was considered infected.
4. If the patient had a stitch abscess with a small amount of purulence directly around a suture, but without any signs of inflammation or fever, the wound was not considered infected.

Although some may argue with our criteria, we considered them to be stringent enough not to miss any wound infection.

Data were entered into Microsoft Office Excel program and analyzed using SPSS (Statistical package for social sciences) version 17.0 software. Preliminary analysis was performed by calculating percentage, mean and standard deviation to get an idea about the proportion, central tendency and dispersion respectively. Chi-square and Mann-Whitney tests were applied to find the association of surgical site infection with the antibiotic administration after adjusting the rest of explanatory variables. A p-value < 0.05 was considered significant.

Results

Of the 220 patients we included in the study, 23 were lost to follow up. So, the proforma of 197 patients were analyzed. There were 100 patients in Group A and 97 in group B. Out of the 197 patients, 137 were males and 60 were females. The variables such as: age, sex, duration of surgery, preoperative haemoglobin, preoperative albumin level, blood loss during surgery and preoperative admission days were compared between the two groups and was found to be statistically comparable showing that randomization was appropriate (Table1 and 2).

Table 1: Sex distribution

		Group		Total	λ 2 (chi square value)	P-value
		A	B			
Sex	Male	69 (69%)	68 (70.1%)	137 (69.5%)	0.028	0.866
	Female	31 (31%)	29 (29.9%)	60 (30.5%)		
Total		100 (100%)	97 (100%)	197 (100%)		

Table 2: Comparison of age, preoperative hemoglobin and albumin, perioperative variables

Group		Age (years)	Duration of Surgery (min)	Preop Hb (gm/dL)	Preop Albumin (gm/dL)	Blood Loss (mL)	Preop admission day
A	Mean	33.02	80.02	12.071	4.001	223.50	4.59
	N	100	100	100	96	100	100
	Std. Deviation	20.978	53.314	1.9634	.7011	225.395	5.601
	Std. Error of Mean	2.098	5.331	.1963	.0716	22.539	0.560
B	Mean	35.30	75.89	12.095	3.874	208.40	4.18
	N	97	96	97	91	97	97
	Std. Deviation	22.692	48.303	1.7784	.7012	170.934	5.254
	Std. Error of Mean	2.304	4.930	.1806	.0735	17.356	.533
Total	Mean	34.14	77.99	12.083	3.939	216.07	4.39
	N	197	196	197	187	197	197
	Std. Deviation	21.813	50.833	1.8698	.7022	200.072	5.423
	Std. Error of Mean	1.554	3.631	0.1332	.0513	14.255	.386
P value		0.533	0.692	0.910	0.400	0.872	0.250

The most common medical illness that we encountered was hypertension, followed by diabetes mellitus (Table 3). The associations of presence of associated illness in the two groups were not significant.

Table 3: Associated illness

Associated Illness	Group		Total
	A	B	
Anemia	0	1	1
Asthma	0	2	2
Diabetes Mellitus	1	2	3
Epilepsy	1	0	1
Hypertension	8	6	14
Rheumatoid Arthritis	0	1	1
Rickets	0	1	1
SLE	1	0	1
Cushing's Syndrome	1	0	1
COPD	1	1	2
Total	10	11	21

The percentages of infection in both groups were uniformly high. Nine (9%) out of 100 were infected in Group A. Similarly there were three out of 97 (3.1%) infection in Group B. The mean percentage of infection was 6.1% (Table 4).

Table 4: Comparison of infection rate in two groups

		Group		Total	λ 2 (chi square value)	P-value
		A	B			
Infection	Present	9 (9%)	3 (3.1%)	12 (6.1%)	3.004	0.083
	Absent	91 (91%)	94 (96.9%)	185 (93.9%)		
Total		100 (100%)	97 (100%)	197 (100%)		

Discussion

Postoperative infections have been shown to significantly increase morbidity, extend the patients hospital stay, drastically increase the cost of the medical system and cause severe physical limitations that diminish the quality of life.[9] Decreasing the incidence of surgical site infection is a matter of utmost interest to both the patients and surgeons. Literature is flooded with articles that relate surgical site infection to a variety of factors of which some are modifiable; some are not. The use of prophylactic antibiotics is one of the most important factors in decreasing infection and one that all surgeons are concerned about. The clinical use of prophylactic antibiotics in orthopaedic surgery was not always supported. Early poorly designed studies found that perioperative use of antibiotics in clean orthopaedic cases was associated with increased infection rates.[10,11] Despite these unfavorable results, investigations continued into the use of prophylactic antibiotics in orthopaedic surgery.[6] Orthopaedic Surgeons in Nepal believe in using prophylactic antibiotics but there are discrepancies in the choice of antibiotics. Available literature recommends cephazolin as the prophylactic antibiotic. Though the infection rate among patients who received cephazolin was higher than those who received ceftriaxone, it was statistically insignificant (p value 0.083). Similar study comparing cephazolin vs ceftriaxone was done in abdominal hysterectomy surgery by Natacha Phoolcharoenin et al. in Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. They also concluded that there is no difference between the use of single-dose preoperative ceftriaxone and cefazolin in preventing infectious morbidity among patients undergoing hysterectomy.[12]

Factors like: duration of surgery, associated medical illness, preoperative haemoglobin status, preoperative serum albumin level, amount of blood loss during surgery and preoperative admission days would be expected to influence the incidence of infection. Malnutrition is a known risk factor for deep infection after a variety of orthopaedic surgical procedures.[13,14] A serum albumin level of less than 3.5 g/dl has been associated with an increase in wound complications.[15] In our study, 11% of the patients had serum albumin less than 3.5 g/dl. We found only the duration of surgery had a statistical association with the incidence of infection. Longer the duration of surgery, more was the chance of surgical site infection. Perhaps our sample size was not large enough. The mean infection rate in our study was 6.1% which must be considered

high. We do not know the infection rate of other institutions in Nepal. The infection rate in a study by Pavel et al.[8] in which the patients received cephaloridine was 2.85% and the study by Henley et al.[16] in which the patients received cefamandole was 1.6%. Postoperative infection has been estimated to occur following 1% to 2% of all total hip arthroplasties and 2% to 4% of all total knee arthroplasties in the United States.[17,18] In our study, there was no statistical difference between the rate of infection among those who received cephazolin and those who received ceftriaxone. This shows the futility of administering expensive antibiotics (ceftriaxone) instead of cheaper one e.g. cephazolin. The use of cheaper antibiotics like cephazolin instead of ceftriaxone for 48 hours saves Rs 30,00,000 per 10,000 patients.

Conclusion

We conclude that in clean elective orthopaedic surgeries, there is no difference in the rate of infection among patients who received cefazolin and those who received ceftriaxone in our setting.

References

1. Nicholas F, D.Mitri S, Marschall BB, WilliamTO. Prevention of perioperative infection. J Bone Joint Surg Am. 2007; 89: 1605-18.
2. Zimmerli W. Antibiotic prophylaxis. In: Ruedi TP, Buckley RE, Moran CG. (eds.) AO Principles of Fracture Management. Volume 1- Principles. 2nd ed. Clavadelerstrasse, AO publishing; 2007. p. 424-33.
3. Harkess JW, John R, Crockarell Jr. Arthroplasty of hip. In: Canale ST, Beaty JH. (eds.) Campbell's operative orthopaedics. Volume 1. 12th ed. Philadelphia, Elsevier Mosby; 2013. p. 250.
4. Prokuski L. Prophylactic antibiotics in orthopaedic surgery. J Am Acad Orthop Surg. 2008; 16: 283-93.
5. Li JT, Markus PJ, Osmon DR, Estes L, Gosselin VA, Hanssen AD. Reduction of vancomycin use in orthopedic patients with a history of antibiotic allergy. Mayo Clin Proc. 2000; 75: 902-6.
6. Oishi CS, Carrion WV, Hoaglund FT. Use of parenteral prophylactic antibiotics in clean orthopedic surgery. A review of the literature. Clin Orthop Relat Res. 1993; 296: 249-55.
7. Bratzler DW, Houck PM. Surgical Infection Prevention Guidelines Writers Workgroup: Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004; 38: 1706-15.

8. Pavel A, Smith RL, Ballard A, Larsen IJ. Prophylactic antibiotics in clean orthopaedic surgery. J Bone Joint Surg Am. 1974; 56: 777-82.
9. Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ. The impact of surgical-site infections following orthopaedic surgery at a community hospital and a university hospital: adverse quality, excess length of stay, and extra cost. Infect Control Hosp Epidemiolo. 2002; 23: 183-9.
10. Tachdjian MO, Compere EL. Postoperative wound infections in orthopedic surgery: Evaluation of prophylactic antibiotics. J Int Coll Surg. 1957; 28: 797-805.
11. Olix ML, Klug TJ, Coleman CR, Smith WS. Prophylactic antibiotics in elective operations on bones, joints, and tendons. Surg Forum. 1960; 10: 818-9.
12. Phoolcharoena N, Nilgateb S, Rattanapuntamaneec O, Limpongsanuraka S, Chaithongwongwatthana S. A randomized controlled trial comparing ceftriaxone with cefazolin for antibiotic prophylaxis in abdominal hysterectomy. International Journal of Gynecology & Obstetrics. 2012; 119(1): 11-3.
13. Dreblow DM, Anderson CF, Moxness K. Nutritional assessment of orthopedic patients. Mayo Clin Proc. 1981; 56: 51-4.
14. Greene KA, Wilde AH, Stulberg BN. Preoperative nutritional status of total joint patients: Relationship to postoperative wound complications. J Arthroplasty. 1991; 6: 321-5.
15. Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults: scientific review. JAMA 2002; 287:3116-26. Erratum in: JAMA. 2002; 288: 1720.
16. Henley MB, Jones RE, Wyatt RWB, Hofmann A, Cohen RL. Prophylaxis with cefamandole nafate in elective orthopedic surgery. Clin Orthop Relat Res. 1986; 209: 249-54.
17. An YH, Friedman RJ. Prevention of sepsis in total joint arthroplasty. J Hosp Infect.1996; 33: 93-108.
18. Berbari EF, Hanssen AD, Duffy MC,Steckleberg JM, Ilstrup DM, Harmsen WS, Osmon DR. Risk factors for prosthetic joint infection: case control study. Clin Infect Dis.1998; 27: 1247-54.