Original Article

Comparison of the Effectiveness of Continuous versus Intermittent Cefazolin for the Prevention of Infection after Off-Pump Coronary Artery Bypass Graft

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Received 05 August 2013; Accepted 18 April 2014

Abstract

Background: *Surgical site infection is known as a common complication after cardiac surgery, and Cefazolin is the best prophylactic antibiotic to prevent this complication. The goal of this study was to evaluate the effect of continuous and intermittent Cefazolin for the prevention of superficial surgical site infection following off-pump coronary artery bypass (OPCAB).*

Methods: *This prospective randomized clinical trial study was conducted on 141 patients candidated for OPCAB and divided into two groups. This study was performed between February 2011 and February 2012 in the Iranian city of Yazd. Patients in both groups received 2 g of Cefazolin as a starting dose and at 30 minutes before incision. Definition of surgical site infections was according to the Centers for Disease Control and Prevention Criteria (CDC-criteria). In the continuous infusion group (n = 74), 3 g of Cefazolin was infused over a 24-hour period after surgery. In the intermittent group (n = 67), 1 g of Cefazolin was administered at 3, 11, and 19 hours after the starting dose. Hyperlipidemia, diabetes, hypertension, smoking, history of heart disease, and incidences of superficial infection were compared between the two groups. Duration of follow- up was 4 weeks.*

Results: *The mean age of the patients was 60.49 ± 10.63 years. The patients were 30.5% female and 69.5% male. There were no significant differences in age, body surface area, duration of operation, number of distal grafts, number of proximal grafts, and duration of hospital stay before heart surgery between two groups. The incidence of infection in intermittent group was (7.5%) and in continuous groups was (2.7%). There was no significant difference in the incidence of infection between the two groups (p value = 0.26).*

Conclusion: *Our findings in this study showed no significant differences between continuous and intermittent Cefazolin for the prevention of superficial surgical site infections after OPCAB.*

J Teh Univ Heart Ctr 2014;9(3):120-123

This paper should be cited as: Forouzannia SK, Karimi-Bondarabadi AA, Bagherinasab M, Sarebanhassanabadi M. Comparison of the Effectiveness of Continuous versus Intermittent Cefazolin for the Prevention of Infection after Off-Pump Coronary Artery Bypass Graft. J Teh Univ Heart Ctr 2014;9(3):120-123.

Keywords: *Cefazolin • Infection • Coronary artery bypass, off -pump*

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Introduction

Cardiac surgery is known as an invasive and complex operation. Patients candidated for off-pump coronary artery bypass (OPCAB) are at risk of surgical site infection.[1] Infection after cardiac surgery is mostly related to sternotomy and vein graft harvesting site incisions.[2] Reported incidence rate of postoperative infection in cardiac surgery varies from 7% to 18%, and deep sternal wound infection has a reported incidence rate of 1% to 3%.[3] These complications can cause mortality rates of up to 30%. Prophylactic antibiotics are recommended in cardiac surgery because of high mortality in patients with infections. The benefit of prophylactic antibiotics in cardiovascular surgery has been shown in some studies.[4-5] Staphylococci are the most common organisms that exist in the vein harvesting site and chest wound infections.[6] Cefazolin is the mainstay of prophylaxis in cardiac surgery thanks to its low toxicity and extensive microbial coverage.[7] Today in cardiac surgery, Cefazolin is administered intermittently as an intravenous bolus with a dose of 1 - 2 g before anesthesia induction and repeated after the onset of cardiopulmonary bypass or at wound closure and then two to three doses every 8 hours.[7] Cefazolin has a short elimination half time.[8] Accordingly, in this study, Cefazolin was used as a continuous infusion in order to counteract this effect. It is clear that a continuous infusion of Cefazolin after a bolus dose can provide continuously higher serum levels of Cefazolin compared to a bolus injection.[8] It is, therefore, expected that a continuous infusion can be more effective as a prophylactic antibiotic therapy in cardiac surgery. However, some studies have shown no differences between the continuous and intermittent methods for the prevention of superficial surgical site infection.[9]

The aim of the present study was to compare bolus and continuous prophylactic Cefazolin injections in OPCAB candidates.

Methods

This prospective randomized clinical trial study, performed between February 2011 and February 2012 in the Iranian city of Yazd, recruited 141 patients candidated for OPCAB. The study was approved by the Ethics Committee of the Cardiovascular Research Center of Shahid Sadoughi University of Medical Sciences. This study was approved by Iranian Registry of Clinical Trial with IRCT-code: 2014041917026N1. All patients gave informed consent to participate in this study. The study population was divided into two groups through simple randomization: continuous and intermittent groups. Both groups received the same anesthesia and perioperative management and received 2 g of Cefazolin as a starting dose 30 minutes before incision. In the continuous infusion group (n = 74), 3 g of Cefazolin was continuously infused over a 24-hour period. In the intermittent group (n = 67), 1 g of Cefazolin was administered at 3, 11, and 19 hours after the starting dose. Definition of surgical site infections was according to the Centers for Disease Control and Prevention criteria (CDC-criteria). In this study, the evaluation of infections was based on the superficial type of the surgical site infection. Patients with a history of antibiotic therapy during the 72-hour period before surgery, severe renal and liver failure, and pregnancy were excluded from the study. Duration of follow-up was 4 weeks. Data were analyzed using the chi-squared and t-tests.

Results

This prospective randomized clinical trial was conducted on 141 patients at a mean age of 60.49 ± 10.63 years. Demographic data are presented in Table 1. Hyperlipidemia, diabetes mellitus, hypertension, smoking, and history of heart disease had no statically significant differences between the two groups (Table 1).

The t-test analysis revealed no significant differences in terms of age (p value = 0.9), body surface area (p value = 0.77), surgery time (p value = 0.7), number of distal grafts (p value = 0.14), number of proximal grafts (p value = 0.36), and bedding time before heart surgery (p value = 0.33) between the two groups. Also, there was no significant difference in the incidence rate of postoperative infection between the two groups (p value = 0.26) (Table 2).

Table1. Characteristics of the two groups*

Variable	Intermittent Group (n=67)	Continuous Group (n=74)	Total (n=141)	P value
Age (y)	62.83±13.57	58.15±12.14	60.49±14.63	0.923
Gender				
Male	41 (61.2)	57 (77.1)	98 (69.5)	0.051
Female	26 (38.8)	17 (22.9)	43 (30.5)	
Hyperlipidemia	42 (62.7)	45 (60.8)	87 (61.7)	0.819
Diabetes	40 (59.7)	41 (55.4)	81 (57.4)	0.663
Hypertension	34 (50.7)	32 (43.2)	66 (46.8)	0.373
Smoking	45 (67.2)	49 (66.2)	94 (66.7)	0.905
History of heart disease	38 (56.7)	47 (63.5)	85 (60.3)	0.410

*Data are presented as mean±SD or n (%)

Table 2. Incidence of infection between the two groups*

Superficial infection	Bolus (n=69)	Continuous (n=74)	Total	P value
No	62 (92.5)	72 (97.3)	134 (95.0)	0.264
Yes	5 (7.5)	2 (2.7)	7 (5.0)	

*Data are presented as n (%)

Discussion

Surgical site infection is one of the most important complications after surgery and is known as a second most common cause of nosocomial infections.[10] Wound infection can even lead to an increased financial burden by prolonging hospitalization.[11] Risk factors that increase the incidence of postoperative wound infection include obesity, diabetes mellitus, use of internal mammary artery graft, advanced age, male gender, chronic obstructive pulmonary disease, smoking, and preoperative hospital stay of more than 5 days.[12] Some studies have suggested that diabetes mellitus can contribute to a more severe surgical site infection.[13] On the other hand, smoking is thought to exert no significant effect on the rate of surgical site infection.[14]

Overall, it is clear that an effective prophylactic antibiotic should be an appropriate antibiotic with a peak blood level before skin incision and an adequate level during surgery and the early postoperative period.[15] Cefazolin has a time-dependent killing feature; this means that the maximal effect of this antibiotic requires exposure to antibiotic concentrations above the minimum inhibitory concentration (MIC) to have the maximum efficacy.

In a study conducted by Zanetti G et al.,[16] the results demonstrated that intermittent Cefazolin could reduce surgical site infection by more than 16% in patients with prolonged (more than 240 minutes) surgical procedures. Waltrip T et al.[17] indicated that beta-lactam antibiotics, when infused continuously, might be more effective than intermittent dosing in perioperative prophylaxis against wound infection. Kasiakou SK et al.[18] reported that there was no difference in mortality and nephrotoxicity between their two study groups of continuous and intermittent intravenous administration. A systematic review, performed by Roberts et al. [19] showed that a continuous infusion of beta-lactam antibiotics had no potency to change the mortality rate statistically. In our study, the mortality rate was zero. In the Roberts et al.[19] study, a continuous infusion of beta-lactam antibiotics did not influence the status of clinical cure; the authors, however, suggested that a continuous infusion had the same effect as a higher dose of a bolus administration. Zeller V et al.[20] demonstrated that the administration of a continuous infusion of Cefazolin to treat bone and joint infection was practical, efficient, safe, and available. Harbath S et al.[21] concluded that prolonging prophylaxis for more than 48 hours did not reduce the incidence of surgical site infection in cardiac surgery but it could increase resistance to microorganisms. Douglas A et al.[22] suggested that 2 g of bolus Cefazolin 30 minutes prior to surgical incision could provide acceptable plasma and interstitial fluid concentrations for microorganisms in patients candidated for abdominal aortic aneurysm open repair surgery. Finkelstein R et al.[23] indicated that Vancomycin and Cefazolin had similar effects for preventing surgical site infection in open heart surgery; nevertheless, the authors reported that the side effects of Vancomycin included hypotension and resistance to microorganisms. Consequently, in the present study, we chose to utilize Cefazolin as the best prophylactic antibiotic in cardiac surgery. In previous studies, no significant differences were found in terms of the length of hospital stay and intensive care unit stay between the continuous infusion and the bolus injection of beta-lactam antibiotics.[24] In a study by Admebri et al.,[9] no patient had developed surgical site infection at 30 days after surgery. Furthermore, the authors found that a continuous infusion of Cefazolin after bolus Cefazolin administration provided better Cefazolin serum levels without increased costs and higher total dose. In our study, 7 patients acquired infection; the difference between the two groups, however, did not constitute a statistical significance.

Conclusion

In light of the findings of the present study, there seem to be no significant differences between continuous and intermittent infusions of Cefazolin for the prevention of superficial surgical site infection after OPCAB. Nonetheless, further studies with more patients and longer follow-up periods are recommended.

Acknowledgments

This study was approved and supported by Shahid Sadoughi University of Medical Sciences. The authors are indebted to all the physicians, nurses, and patients who participated in this research.

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