ORIGINAL ARTICLE

Antibiotic Prophylaxis for Preventing Surgical Site Infection after Coronary Artery Bypass Graft: Prospective Randomized Comparative Study

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ABSTRACT

Objectives: To compare the outcome of short-term (<24 hours) versus longer-term (>24 hours) antibiotic prophylaxis in patients undergoing coronary artery bypass graft (CABG) surgery and its impact on deep Sternal Wound Infection (DSWI) / Mediastinitis.

Patients and methods: To compare the effect of short (<24 hours) versus prolonged (>24 hours) ABP on surgical site infections (SSIs) and acquired antimicrobial resistance, Cross sectional comparative study was conducted. Prospective surveillance of 200 patients undergoing isolated CABG surgery (on pump/off pump) fulfilling the inclusion and exclusion criteria were included in the study. Comparison were made between 100 patients receiving less than 24 hours of prophylactic antibiotics with another 100 patients receiving more than 24 hours of prophylactic antibiotics. Surgical Site infection (SSI) was assessed on a daily basis during the patient's stay in the Department of Cardiac Surgery, Mayo Hospital/KEMU, Lahore. Diagnosis of identified SSI were based on positive cultures, clear dehiscence of the sternotomy wound, fever, pain, redness, secretion, purulent drainage, and sternal instability. The main exposure was the duration of ABP, and the primary outcome measure was DSWI (Mediastinitis).

Results: During the study period 9 patients developed DSWI/Mediastinitis, the infection rates were 4% in the group < 24 h of ABP and 5% in the group receiving >24 h of ABP therapy, and the difference was statistically non-significant (P=0. 774). The proportion of patients with deep-organ-space involvement (mediastinitis) and sepsis requiring rewiring were 3 patients (3%) for <24 hours and 4 patients (4%) in >24 hours of ABP (P=0.700). There were no differences between groups for mortality or duration of hospitalization (preoperative hospitalization, intensive care unit stay, and hospitalization after surgical intervention). The microorganisms isolated showed a similar distribution in both groups. Test of proportion was applied and it was found that there was no difference in the proportion of infection in the two groups (p value 0.05).

Conclusion: Findings confirm that a prophylactic Antibiotic combination using Vancomycin and an aminoglycoside of 24 hours duration is as effective as prophylaxis administered for longer than 24 hours regimen for preventing surgical site infection in patients undergoing isolated CABG.

Key words: Antibiotic Prophylaxis, Coronary artery bypasses grafting, Surgical Site Infections

INTRODUCTION

Antibiotic prophylaxis is used to avoid Surgical site Infections. However, the overuse of antibiotics is associated with increased costs and the development of antimicrobial resistance[1, 2]. There is emerging general agreement that post-operative prophylactic antibiotics should be stopped within 24 h of most major surgical procedures.[3-6]

In recent years, there has been increased interest in the potential clinical benefits of administering the antibiotic in a single dose. The benefits of single-dose antimicrobial prophylaxis are based on microbial first principles: reduced antimicrobial resistance, fewer problems with drug toxicity and super infections, and reduced cost. However, most cardiac surgery units use multiple-dose antimicrobial prophylaxis that continues for 24 to 48 hours and often until all the drain tubes are removed.[7] There is no consensus on the type of antibiotic prophylaxis, whether a single dose or multiple doses should be used, or the duration of administration[7,8].

Superficial sternal wound infections are seen in approximately 2% to 6% of patients after cardiac surgery.[9-11] Recent studies show that the incidence of deep sternal infections associated with cardiac surgery ranges between 0.25% and 4%[11,12]. The in hospital mortality associated with mediastinitis ranges from 7% to 20%[8] and the mortality in patients with

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superficial sternotomy infections may be in excess of 5%[9]

The primary prophylactic antibiotic for adult cardiac surgery is recommended to be a first-generation cephalosporin, which is usually cefazolin in populations that do not have a high incidence of methicillin-resistant Staphylococcus aureus (MRSA).[8] In our Institution, serious sternal wound infections had methicillin resistant staphylococcus aureus (70%), so we are using vancomyycin and amikacin for prophylaxis[13].

In Pakistan in general, antimicrobial prophylaxis in cardiac surgery is not governed either by national or by local guidelines. This problem is typical of other developing countries. With a view of possible reduction in antibiotic dosage, prospective randomized comparative trials performed in our institution showed that there is no need to continue antibiotic prophylaxis for more than 48 hours in patients undergoing open-heart surgery. Previous research in this topic area focused on the presence of a clear evidence of antibiotic misuse among the Pakistani population.[13] In light of this absence of local or institutional antimicrobial prophylaxis guidelines, the current study hypothesize that, Antibiotic prophylaxis of 24 hours duration is as effective as prophylaxis administered for longer than 24 hours.

PATIENTS AND METHODS

From February 2010 through April 2012, a total of 200 patients undergoing isolated CABG surgery were included in this study and conducted at tertiary health care centre. Comparison was made between 100 patients receiving less than 24 hours of prophylactic antibiotics with another 100 patients receiving more than 24 hours of prophylactic antibiotics. Patients in ICU for prolonged Ventilation, Patients who require prolonged inotropic support, Active preoperative infection were excluded from the study protocol. Patients were shaved the night before surgery and in the operating room; skin was painted with povidone iodine for 5 min. None of the patients received topical antibiotics at the time of surgical wound closure. The wounds were painted with povidone iodine ointment and covered with a sterile dressing. Per study protocol, blood chemistries, complete blood counts and serum creatinine were obtained pre-operatively and every day. No routine nasal swab or urine cultures were taken. Shortly before the first incision, prophylactic intravenous antibiotics (principally vancomycin 1 g and Amikacin 500mg) were administered to each patient. The study had two arms: one group received prophylactic antibiotics for less than 24 h; the other group received prophylactic antibiotics for more than 24 h. No further intravenous or oral antibiotics were administered.

All the data were collected in specifically designed Performa. Sternal incision site was assessed on a daily basis during the patient's stay (5–6 days). Diagnosis of identified sternal infections was based on positive cultures, clear dehiscence of the sternotomy, fever, pain, redness, secretion, purulent drainage, and sternal instability. Operating room logs were reviewed to identify all surgical revisions. The patients were monitored for surgical site infection and any wound discharge was subjected to Gram's stain and culture. The antibiotic susceptibility of organisms grown was also noted. Any patient having culture-proven wound infection received further antibiotics according to the antibiotic susceptibility of the organism grown. The primary outcome was the incidence of surgical site infection within the study period and its impact on deep sternal wound infection (DSWI)/Mediastinitis.

Collected information was transferred to SPSS (Statistical Package for the Social Sciences) version 15.0 computer software programme and analyzed accordingly. Continuous or interval-related variables are expressed as mean+SD. Comparison of continuous variables between groups was done using the Student's t-test. Comparison of discrete variables between groups was done using the x2 test and Fisher's exact test. A two-sample test of proportion was applied to determine the 95% confidence interval (95% CI) to determine surgical site infection. Independent risk factors for infection were determined using Fisher's exact test. An alternative test will be used when the assumption for repeated measurement will not fulfil. $P \leq 0.05$ was considered to indicate a statistically significant difference.

RESULTS

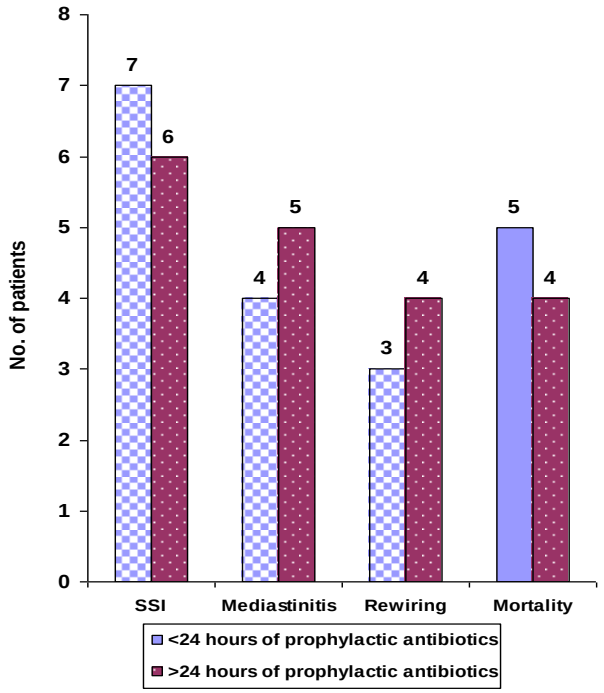
Between february 2010 through April 2012, a total of 200 patients undergoing isolated CABG surgery were included in this study. Total of 100 patients received less than 24 hours of prophylactic antibiotics with another 100 patients received more than 24 hours of prophylactic antibiotics. The mean age was 52.67±6.99 and 50.95±6.40 years (<24 h versus prolonged >24 hours), respectively, in the two groups. The incidence of co-morbid conditions as well as operative conditions was similar between the groups. During the study period 9 patients developed DSWI/Mediastinitis, the infection rates were 4% in the group <24 h of ABP and 5% in the group receiving >24 h of ABP therapy, and the difference was statistically non-significant (P=0. 774). The proportion of patients with deep-organ-space involvement (mediastinitis) and sepsis requiring rewiring were 3 patients (3%) for <24 hours and 4 patients (4%) in

>24 hours of ABP (P=0.700). There were no differences between groups for mortality or duration of hospitalization (preoperative hospitalization, intensive care unit stay, and hospitalization after surgical intervention) (Table 1, Fig.1).

Table: Distribution of patients according to post-operative SSI and Mediastinitis

Post-operative finding	<24 hrs of prophy-lactic antibiotics (n=100)	>24 hrs of prophy-lactic antibiotics (n =100)	Chi sq value	P value
SSI	7(7%)	6(6%)	0.082	0.774
DSWI (Medias-tinitis)	4(4%)	5(5%)	0.116	0.733
Rewiring for sternal dehiscenc e	3(3%)	4(4%)	0.148	0.700
Mortality	5(5%)	4(4%)	0.116	0.733

Fig.1: Distribution of patients according to SSI, mediastinitis, rewiring and mortality



Among 7 SSIs in <24 h, 88% were culture positive from which 68% S. Aureus was isolated. Similarly, 85% culture positive seen in >24h of ABP, 76% S. Aureus was isolated. It is noteworthy that other organism infrequently encountered were Coagulase negative S. Aureus, Enterococci and Gram Negative. Pseudomonas aeruginosa were the most prominent Gram-negative organisms obtained in wound cultures. The microorganisms isolated showed a similar distribution in both groups. The two groups were comparable for age (P=0.05), gender (p=0.816), procedure done (P= 0.214), diabetes mellitus (p=0.376), and re exploration for bleeding (p=0.326). Test of proportion was applied and it was found that there was no difference in the proportion of infection in the two groups (p value 0.05).

DISCUSSION

Antimicrobial prophylaxis in cardiac surgery has been demonstrated to lower the incidence of surgical site infection (SSI). Inappropriate antimicrobial prophylaxis, such as inappropriate selection of the antimicrobial agent or inappropriate duration/dosing regimen, can increase the prevalence of antibiotic resistant strains, prolong hospital stay, cause adverse reactions, and negatively affect an institution's pharmacy budget for antibiotics. In developing countries such as Pakistan, where the role of clinical pharmacists is still in its primary stages, the first step in establishing an organized clinical pharmacy service is the evaluation of current practice to determine the need for improvement. Routine administration of prophylactic antibiotics to patients undergoing cardiac surgery is a well-accepted tenet of contemporary practice; however, the duration for which the antibiotics should be administered is far from settled.

The rationale given for prolonging the duration of antibiotic prophylaxis in cardiac surgery includes the pharmacokinetic/pharmacodynamic changes caused the bypass process, hypothermia and loss of blood.[7] The longer duration of antibiotic use is, however, associated with the risk of drug toxicity, emergence of resistant organisms and increased cost.[14] It is clear that antibiotic resistance is a progressive problem with serious clinical implications. It is less clear that the problem is directly linked to prolonged use of prophylactic antibiotics in cardiac surgery.

The aim of prophylactic antibiotic use is to prevent contamination while operating; therefore, timely and adequate administration is more important than prolonged use of antibiotics. Furthermore, prolonged use of prophylactic antibiotics not only provokes the worry of increased drug side effects and increased risk for developing infections due to drug-resistant pathogens, but also increases medical costs. In a prospective observational study, Harbarth et al[15] have reported that prolonged use of prophylactic antibiotics [beyond 48 hours after coronary artery bypass graft (CABG)] is significantly associated with increased antimicrobial resistance from clinical specimens, such as resistant Enterobacteriaceae and Enterococcus.

Taking all of this into account, further evidence for the use of prolonged prophylactic regimens in cardiac surgery comes from another systematic review published recently by Mertz et al.[16] This review also concluded that perioperative prophylactic regimens of at least 24 h duration are more effective in preventing SSI in cardiac surgery. However, the 2011 American College of Cardiology Foundation/ American Heart Association guideline for coronary artery bypass graft surgery still only gives recommendations for preoperative antibiotic prophylaxis, with further intra-operative doses for prolonged surgery. No specific recommendation is made with regard to subsequent duration of prophylaxis.[17]

In summary, study could not demonstrate an association between higher dose and longer duration of antibiotic prophylaxis and lower DSWI rates. In an era of increasing antimicrobial resistance and spread of hyper virulent strains , further consideration should be given to the need for continued prophylaxis after surgery.

CONCLUSION

The results indicate that Antibiotic prophylaxis of 24 hours duration is as effective as prophylaxis administered for longer than 24 hours. Continuing ABP beyond 24 hours after CABG surgery is still widespread; however, this practice is ineffective in reducing SSI, increases antimicrobial resistance, and should therefore be avoided.

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