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A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY TO DETERMINE THE ROLE OF ANTIBIOTIC PROPHYLAXIS FOR AVERTING SURGICAL SITE INFECTION AFTER CORONARY ARTERY BYPASS GRAFT

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Abstract:

Objectives: *To compare the outcomes of short-term (24-hour) antibiotic prophylaxis in patients undergoing coronary bypass surgery (CABG) and its effect on deep sternum wound infection (DSWI) / mediastinitis.*

Place and Duration: *Study was conducted at Rawalpindi Institute of Cardiology for one-year duration from May 2019 to May 2020.*

Patients and Methods: *A cross-sectional comparative study was conducted to compare the effect of short (24-hour) ABP on surgical site infections (SSI) and acquired antimicrobial resistance. The study included prospective surveillance of 200 patients undergoing isolated CABG surgery (with / without a pump) meeting the inclusion and exclusion criteria. One hundred patients receiving prophylactic antibiotics for less than 24 hours were compared with another 100 patients receiving prophylactic antibiotics for more than 24 hours. Surgical site infection (SSI) was assessed daily during the patient's stay at the Rawalpindi Institute of Cardiology. Diagnosis of the identified SSI was based on positive cultures, marked dehiscence of the sternum wound, fever, pain, redness, discharge, purulent drainage, and sternum instability. The main exposure was ABP duration and the primary endpoint was DSWI (mediastinitis).*

Results: *During the study period, 9 patients developed DSWI / mediastinitis, the infection rate was 4% in the <24 h ABP group and 5% in the> 24 h ABP group, and the difference was not statistically significant (P = 0.774). The proportion of patients with deep organ space involvement (mediastinitis) and sepsis requiring cable replacement was 3 patients (3%) after 24-hour ABP (P = 0.700). There were no differences between the groups in terms of mortality or the duration of hospitalization (preoperative hospitalization, stay in the intensive care unit, and hospitalization after surgical intervention). The isolated microorganisms showed a similar distribution in both groups. The proportion test was used and it was found that there was no difference in the percentage of infections in the two groups (p-value 0.05).*

Conclusion: *The results confirm that the prophylactic combination of antibiotics with vancomycin and 24-hour aminoglycoside is as effective as prophylaxis given for more than 24 hours in preventing surgical site infection in patients undergoing isolated CABG.*

Key words: *Antibiotic Prophylaxis, Coronary Artery Bypass Graft, Surgical Site Infections*

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INTRODUCTION:

Antibiotic prophylaxis is used to avoid surgical site infections. However, overuse of antibiotics is associated with increased costs and the development of antimicrobial resistance. There is general agreement that postoperative prophylactic antibiotics should be discontinued within 24 hours of most major surgery[1-2]. In recent years, there has been increasing interest in the potential clinical benefits of a single dose of antibiotic administration. The benefits of single dose antimicrobial prophylaxis are based on the basic microbial principles: reduced antimicrobial resistance, fewer problems with drug toxicity and super infection, and lower cost. However, most cardiac surgery departments use multi-dose antimicrobial prophylaxis that lasts between 24 and 48 hours, often until all drains are removed. There is disagreement about the type of antibiotic prophylaxis, whether to use a single or multiple dose or the duration of administration[3-4]. Superficial infections of the sternum wound are observed in approximately 2% to 6% of patients after cardiac surgery. Recent studies show that the incidence of deep sternal infections associated with cardiac surgery ranges from 0.25% to 4%. In our facility, in the case of serious infections of the sternum wound, we found methicillin-resistant staphylococci (70%), therefore we use vancomycin and amikacin for prophylaxis[5-6]. In general, in Pakistan, antimicrobial prophylaxis in heart surgery is not regulated by national or local guidelines. This problem is common to other developing countries. In view of the possibility of reducing the dose of antibiotics, a prospective randomized comparative study conducted in our facility showed that there is no need to continue antibiotic prophylaxis beyond 48 hours in patients undergoing open heart surgery[7-8]. Previous research in this area has focused on the presence of clear evidence of antibiotic abuse among the Pakistani population. In view of the lack of local or institutional guidelines for antimicrobial prophylaxis, the current study hypothesizes that 24-hour antibiotic prophylaxis is as effective as prophylaxis longer than 24 hours.

PATIENTS AND METHODS:

This study was held at Rawalpindi Institute of Cardiology for one-year duration from May 2019 to May 2020. A total of 200 patients undergoing isolated CABG surgery were enrolled in this study. A comparison of 100 patients receiving prophylactic antibiotics for less than 24 hours was compared with another 100 patients receiving prophylactic antibiotics for more than 24 hours. ICU patients due to prolonged ventilation, patients requiring long-term inotropic support, active preoperative infection were excluded from the study protocol. Patients were shaved the night before surgery and in the operating room; the skin was painted with povidone iodine for 5 minutes. 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. According to the study protocol, blood biochemistry, complete blood count, and serum creatinine were obtained before surgery and daily. No routine nasal swabs or urine cultures were collected. Just before the first incision, each patient was given prophylactic intravenous antibiotics (mainly vancomycin 1 g and Amikacin 500 mg). The study consisted of two arms: one group received prophylactic antibiotics for less than 24 hours; the second group received prophylactic antibiotics for more than 24 hours. No further intravenous or oral antibiotics were administered. All data was collected in a specially designed Performa. The sternum incision site was assessed daily during the patient's stay (5-6 days). Diagnosis of diagnosed sternal infections was based on positive cultures, marked dehiscence of sternotomy, fever, pain, redness, discharge, purulent drainage, and instability of the sternum. Operating room logs were reviewed to identify all surgical revisions. Patients were monitored for surgical site infection and any wound discharge was stained and plated using the Gram method. The cultured organisms were also susceptible to antibiotics. Each patient with a culture-confirmed wound infection received further antibiotics depending on the organism sensitivity to the antibiotic. The primary endpoint was the incidence of surgical site infection over the period studied and its impact on deep sternum wound infection (DSWI) / mediastinitis. The collected information was transferred to the SPSS (Statistical Package for Social Sciences) version 15.0 computer program and analyzed accordingly. Continuous or interval-related variables are expressed as mean + SD. The comparison of continuous variables between groups was performed using the Student's t-test. The comparison of discrete variables between groups was performed using the x2 test and Fisher's exact test. A two-specimen proportion test was used to determine the 95% confidence interval (95% CI) for the determination of surgical site infection. Independent risk factors for infection were determined using Fisher's exact test. The alternative test will be applied when the repeated measurement assumption is not met. $P \leq 0.05$ was considered to indicate a statistically significant difference.

RESULTS:

A total of 200 patients undergoing isolated CABG surgery were included in the study. A total of 100 patients received prophylactic antibiotics for less than 24 hours, and another 100 patients received prophylactic antibiotics for more than 24 hours. The mean age in both groups was 52.67 ± 6.99 and 50.95 ± 6.40 years, respectively (<24 h vs.> 24 h). The incidence of comorbidities and operative conditions was similar in both groups. During the study period, 9 patients developed DSWI / mediastinitis, the infection rate was 4% in the <24 h ABP group and 5% in the> 24 h ABP group, and the difference was not statistically significant (P = 0.774). The proportion of patients with deep organ involvement (mediastinitis) and sepsis requiring cable replacement was 3 patients (3%) for <24 hours and 4 patients (4%) in> 24 hours ABP (P = 0.700). There were no differences between the groups in terms of mortality or the duration of hospitalization (preoperative hospitalization, stay in the intensive care unit, and hospitalization after surgical intervention) (Table 1).

Postoperative 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 (Mediastinitis)	4(4%)	5(5%)	0.116	0.733
Rewiring for sternal dehiscence	3(3%)	4(4%)	0.148	0.700
Mortality	5(5%)	4(4%)	0.116	0.733

Of the 7 SSIs in <24 h, 88% were culture positive, of which 68% were S. Aureus isolated. Similarly, 85% of positive cultures were observed at> 24 hrs. ABP, 76% of S. Aureus was isolated. It is worth noting that other rare microorganisms are: Coagulase negative S. Aureus, Enterococci and Gram negative. Pseudomonas aeruginosa were the most important gram-negative organisms obtained in wound cultures. The isolated microorganisms showed a similar distribution in both groups. Both groups were comparable in terms of age (p = 0.05), sex (p = 0.816), surgery performed (p = 0.214), diabetes (p = 0.376) and re-exploration for bleeding (p = 0.326). The proportion test was used and it was found that there was no difference in the percentage of infections in the two groups (p-value 0.05).

DISCUSSION:

Antimicrobial prophylaxis in cardiac surgery has been shown to reduce the incidence of surgical site infections (SSIs). Inappropriate antimicrobial prophylaxis, such as inappropriate antimicrobial selection or inappropriate duration / dosing regimen, may increase the incidence of antibiotic-resistant strains, extend hospital stay, cause side effects, and negatively impact the institution's pharmacy budget for antibiotics[7-9]. In developing countries such as Pakistan, where the role of clinical pharmacists is still in its infancy, the first step in establishing an organized clinical pharmacy service is to evaluate current practice to identify the need for improvement. The routine administration of prophylactic antibiotics to patients undergoing cardiac surgery is a well-established assumption in modern practice; however, the length of time for which antibiotics should be administered is far from the established. The rationale for extending the duration of antibiotic prophylaxis in cardiac surgery is the pharmacokinetic / pharmacodynamic changes due to the bypass process, hypothermia and blood loss. However, longer duration of antibiotic use is associated with the risk of drug toxicity, the emergence of resistant organisms, and increased costs. It is clear that antibiotic resistance is a growing problem with serious clinical implications[10]. It is less clear that the problem is directly related to the long-term use of prophylactic antibiotics in cardiac surgery. The purpose of prophylactic use of antibiotics is to prevent contamination during work; therefore, timely and appropriate administration is more important than long-term use of antibiotics. Moreover, long-term use of prophylactic antibiotics not only raises concerns about increased drug side effects and an increased risk of developing infections from drug-resistant pathogens, but also increases the cost of treatment[11-12]. In a prospective observational study, Harbarth et al. Reported that long-term use of prophylactic antibiotics [greater than 48 hours after coronary artery bypass graft (CABG)] is significantly associated with increased antimicrobial resistance from clinical samples such as resistant Enterobacteriaceae and Enterococcus[13-14]. Taking all this into account, further evidence for the use of extended prophylactic regimens in cardiac surgery comes from another systematic review recently published by Mertz et al. This review also concluded that perioperative prophylactic regimens of at least 24 hours are more effective in preventing SSI in cardiac surgery. However, the 2011 American College of

Cardiology Foundation / American Heart Association guidelines for coronary artery bypass surgery still only recommend preoperative antibiotic prophylaxis, with further intraoperative doses in the event of prolonged surgery[15]. There are no special recommendations for the subsequent duration of prophylaxis. Overall, the study found no association between the higher dose and longer duration of antibiotic prophylaxis and lower DSWI rates. In the era of increasing antimicrobial resistance and the spread of highly virulent strains, the need for continued postoperative prophylaxis should be carefully considered.

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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