

# Should the duration of Antibiotics Prophylaxis be Prolonged in Diabetes patients with Isolated Coronary Artery Bypass Grafting?

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## ABSTRACT

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

**Patients and method:** We performed a cross sectional comparative study in 160 Diabetic patients undergoing CABG from October 2010 through April 2012. Comparison was made between 80 diabetic patients receiving less than 24 hours of prophylactic antibiotics with another 80 diabetic patients receiving more than 24 hours of prophylactic antibiotics undergoing isolated CABG. 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 fever, pain, redness, secretion, purulent drainage, positive cultures, clear dehiscence of the sternotomy wound.

**Results:** In-hospital incidence of Deep Sternal Wound Infection (DSWI)/Mediastinitis was 7.50% in the group <24h of ABP and 1.25% in the group receiving >24 h of ABP therapy, and the difference was statistically significant (P=0.042). The proportion of patients with deep-organ-space involvement (mediastinitis) and sepsis requiring rewiring were 7 patients (8.75%) for <24 hours and 1 patients (1.25%) in >24 hours of ABP (P=0.030). Similar results were observed in terms of mortality (8.75% Vs 1.25%). However, the microorganisms isolated showed a similar distribution in both groups. Morbidity, infections and the composite outcomes occurred more commonly in diabetic patients.

**Conclusions:** Diabetes mellitus is an important risk factor for mortality and morbidity among those undergoing CABG. This study documents the higher incidence of deep Sternal Wound Infection (DSWI) / Mediastinitis associated with less than 24h of ABP therapy, suggesting the need for prolonged ABP in Diabetic patients undergoing CABG.

**Keywords:** Antibiotic prophylaxis, coronary artery bypasses grafting, diabetes, surgical site infections.

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## INTRODUCTION

Sternal wound dehiscence is a serious and potentially life-threatening complication after median sternotomy, especially among diabetic patients<sup>1</sup>. It is associated with an increased duration of hospitalization, hospital costs and need for surgical re-intervention<sup>2,3</sup>. The risk of acquiring an infection is about 6 times higher in patients with diabetes mellitus, is increased by 30% for every day on mechanical ventilation, is about 9 times higher in patients readmitted to the CVICU and is about 20 times higher in patients who presented other complications, irrelevant to infection<sup>4</sup>.

Several pre and intra-operative risk factors have been associated with an increased incidence of DSWI. Superficial sternal wound infections are seen

in approximately 2% to 6% of patients after cardiac surgery<sup>5,6,7</sup>. Recent studies show that the incidence of deep sternal infections associated with cardiac surgery ranges between 0.25% and 4%<sup>5,6,7</sup>. The in hospital mortality associated with mediastinitis ranges from 7% to 20% and the mortality in patients with superficial sternotomy infections may be in excess of 5%<sup>6</sup>.

Antibiotic prophylaxis is used to avoid SSIs. However, the overuse of antibiotics is associated with increased costs and the development of antimicrobial resistance<sup>8</sup>. There is emerging general agreement that post-operative prophylactic antibiotics should be stopped within 24h of most major surgical procedures<sup>9</sup>.

The longer duration of antibiotic use is, however, associated with the risk of drug toxicity, emergence of resistant organisms and increased cost<sup>10</sup>. 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.

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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)<sup>11</sup>. In our Institution, majority of serious sternal infections (70%) had methicillin resistant staphylococcus aureus, so we are using vancomycin and amikacin for prophylaxis<sup>12</sup>.

The optimal duration of antibiotic prophylaxis for adult's diabetic patients undergoing CABG is unknown and guideline recommendations are inconsistent. In light of this absence of local or institutional antimicrobial prophylaxis guidelines, we performed Prospective randomized comparative trail to compare the outcome of short-term (<24 hours) versus longer-term (>24 hours) antibiotic prophylaxis (ABP) in diabetic patients undergoing coronary artery bypass graft (CABG) surgery and its impact on in-hospital incidence of deep Sternal Wound Infection (DSWI) / Mediastinitis.

## PATIENTS AND METHODS

**Setting:** Tertiary healthcare centre.

**Study population:** From October 2010 through April 2012, a total of 160 diabetic patients undergoing CABG were included in this study. Diabetes mellitus was defined as the need for oral medication or insulin before CABG. Patients without a previous diagnosis of DM who had preoperative HbA1c  $\geq 6.5\%$  were also included. Comparison was made between 80 diabetic patients receiving less than 24 hours of prophylactic antibiotics with another 80 diabetic 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.

**Intervention:** Preoperatively, diabetic patients were started on a standard sliding scale subcutaneous insulin injection. We aimed at maintaining the blood glucose levels in diabetic patients between 120 and 160 mg/dl. For Patients with blood glucose more than 160 in the operating room and in the ICU, they received continuous intravenous insulin infusions. They were then switched back to the sliding scale subcutaneous insulin injection until discharge, even after the resumption of their preoperative glucose control regimen. For non-diabetic patients, the use of sliding scale insulin infusion was triggered by blood glucose levels greater than 180mg/dl.

Patients were shaved the night before surgery and in the operating room skin was painted with povidine iodine for 5 min. 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. 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. 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.

**Assessment:** 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.

**Outcome parameters:** The primary outcome measure was in-hospital incidence of deep Sternal Wound Infection (DSWI) / Mediastinitis.

**Statistical analysis:** Collected information was transferred to SPSS (Statistical Package for the Social Sciences) version 16.0 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  $\chi^2$  test and Fisher's exact test. An alternative test was used when the assumption for repeated measurement was not fulfilled.  $P \leq 0.05$  was considered to indicate a statistically significant difference.

## RESULTS

The mean age was  $51.62 \pm 3.62$  and  $50.05 \pm 4.24$  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. The two groups were comparable for age ( $P=0.05$ ), gender ( $p=0.816$ ), procedure done ( $P=0.214$ ), choice of antibiotics ( $p=0.499$ ) and re exploration for bleeding ( $p=0.326$ ). During the study period 11 patients developed Surgical Site Infection (SSI), the infection rates were

11.25% in the group < 24h of ABP and 2.5% in the group receiving >24h of ABP therapy, and the difference was statistically significant (P=0.029).

In-hospital incidence of deep Sternal Wound Infection (DSWI) / Mediastinitis was 7.50% in the group <24 h of ABP and 1.25% in the group receiving >24 h of ABP therapy, and the difference was statistically significant (P=0.042). The proportion of patients with deep-organ-space involvement (mediastinitis) and sepsis requiring rewiring were 7

patients (8.75%) for <24 hours and 1 patients (1.25%) in >24 hours of ABP (P=0.030). Similar results were observed in terms of mortality, 7 patients (8.75%) for <24 hours and 1 patients (1.25%) in >24 hours of ABP (P=0.030). However, the microorganisms isolated showed a similar distribution in both groups. Morbidity, infections and the composite outcomes occurred more commonly in diabetic patients.

Table: Diabetes associated morbidity and mortality in CABG

Diabetic patients	<24 hours of prophylactic antibiotics (n=80)		>24 hours of prophylactic antibiotics (n=80)		P value
SSI	9	11.25%	2	2.50%	0.029
DSWI/Mediastinitis	6	7.50%	1	1.25%	0.042
Rewiring	7	8.75%	1	1.25%	0.030
Mortality	7	8.75%	1	1.25%	0.030

## DISCUSSION

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 in diabetic patient is not fully settled.

The duration of a prophylactic antibiotic regimen is directly related to the probability of developing resistant microorganisms. And thus the duration of antibiotic regimen should be limited to the shortest period of time required to effectively minimize the probability of post operative infection<sup>5</sup>. In addition, cardiac surgery patients invariably leave the operating room with indwelling chest catheters and central venous and arterial lines that can be potential routes for bacterial entry and increase the risk of infection. Furthermore, post-operative mediastinitis carries very high hospital mortality and is also associated with reduced long-term survival<sup>30</sup>.

Diabetes is associated with a higher rate of DSWI, in accordance with some studies<sup>13</sup>. It is well known that patients with DM who undergo CABG have worse early and late outcomes than CABG patients without DM<sup>14</sup>. Also, it has been shown that intraoperative and postoperative blood glucose (BG) control has a significant effect on complications such as infection and mortality<sup>14</sup>. Compared with nondiabetic individuals, diabetic patients undergoing coronary CABG have worse outcomes, including higher mortality, and higher rates of morbidity in the forms of deep sterna instability, wound infection, stroke, renal dysfunction, and respiratory problems<sup>15</sup>. Moreover, longer intensive care unit and hospital stays, poorer postoperative physical functioning, and lower quality of life are evident<sup>15</sup>.

Glucose control during CABG is another controversial issue. A recent randomized trial showed a significantly higher stroke rate and a non-significantly higher mortality rate with intensive glucose control, targeting normoglycemia (100mg/dl), during CABG<sup>16</sup>. The prevalence of diabetes and glucose intolerance and thus habitual hyperglycemia is higher among patients undergoing CABG (37% in our cohort) compared to critically ill patients assessed in trials that showed an advantage to intensive glucose control<sup>17</sup>. As most of our patients comply poorly with medical management of diabetes and do not take oral hypoglycaemic or insulin regularly unless they are hospitalized, this probably contributes to higher rate of diabetes related complications<sup>18</sup>.

The data suggest that the risk for poor outcomes is higher for those with Diabetic Mellitus undergoing CABG. The significance of this is yet unknown, but supports further investigation. This evidence, along with numerous other related recent studies, warrants the initiation of large prospective trials evaluating duration of antibiotic prophylaxis for diabetic patient undergoing CABG.

## CONCLUSION

The data provides evidence that higher incidence of deep Sternal Wound Infection (DSWI) / Mediastinitis associated with less than 24h of ABP therapy, suggesting the need for prolonged ABP in diabetic patients undergoing CABG.

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