Outcome of Tight Versus Standard Glycemic Control in Coronary Artery Bypass Patients

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Abstract

Objectives: To compare the outcome of tight versus standard glycemic control and its impact on post operative morbidity and short term mortality in patients undergoing Coronary Artery Bypass Grafting (CABG).

Patients and Methods: A prospective surveillance of 124 patients undergoing isolated CABG surgery (on pump) was included in the study, 62 patients in each group were randomly assigned to tight and standard glucose control group. The main exposure was insulin in respect to level of blood glucose and the primary outcome measures were Sternotomy wound infection, Leg wound infection and new Myocardial Infarction. Surgical Site infection was assessed on a daily basis during the patient's stay in the Department of Cardio-

thoracic Surgery, Sheikh Zayed Hospital, Lahore or within 30 days of operation prompting the patient to return to the hospital. Chi-square test or χ^2 test was used to identify the significance of various short term morbidities and mortality.

Results: In this study, 12 patients in the standard group and 4 patients in the tightly controlled group developed Sternal wound infection (p value 0.046). Similarly, 9 versus 2 patients in the standard and tight group respectively developed Leg wound infection (p-value 0.035). Test of proportion was applied and it was found that there was significant difference in the proportion of infection in the two groups (p value 0.05). However, there were no significant differences in other morbidities and the short term mortality.

Conclusion: Study confirmed that tight glucose control post operatively in CABG patient's results in reduced sternal and leg wound infection rates; however, there was no effect on other morbidities and short term mortality.

Key words: Glycemic control, Coronary artery bypass grafting, Surgical Site Infections.

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Introduction

It is well known that a marked inflammatory response occurs after cardiopulmonary bypass resulting in increased levels of stress hormones such as the corticosteroids, Anti-diuretic hormone, catecholamines, growth hormone etc. The hyperglycemia thus developed is pro-inflammatory and perpetuates itself. At a cellu-

lar level it causes an increase in pro-inflammatory transcription factors which induce production of pro-inflammatory cytokines TNF – alpha, IL_1, IL_2, IL_6, IL_8 and IL_{18}.[1,2] This leads to worsening of the hyperglycemia. One of the resultant effects is an increase of blood glucose levels even in non diabetics and more so in Diabetics.

Although previous studies have shown a beneficial effect of controlling blood glucose levels, there is conflicting evidence about the exact level of control that remains to be defined.

Materials and Methods

A total of 124 patients undergoing isolated CABG surgery (on pump) were included in this study conducted at tertiary health care centre. Patients were divided equally (62 in each group) and randomized to each group on the basis of serial numbers issued prior to the commencement of the study. Patients in ICU for prolonged Ventilation, Patients who require prolonged inotropic support, active preoperative infection and impaired preoperative Creatinine function were excluded from the study protocol. Diabetic patients were

Table 1: Intensive Care Unit Insulin Protocol for Tight Glucose Control (TGC).

Group Begin protocol for BG > 110 mg/dL			
BG (mg/dL)	Infusion Rate	Bolus	
110 – 125	1 Unit/h	1 unit	All patients D5W infusion At 10 ml/hr
126 – 150	2 Units/h	2 units	
151 – 200	3 units/h	3 units	
201 – 250	5 units/h	5 units	
251 – 350	10	10 units	

ICU Protocol for Patients in the Standard Glucose Control (SGC) Group			
BG (mg/dL)	Infusion Rate	Bolus	
110 – 125	0 Unit/h	0 unit	All patients D5W infusion At 10 ml/hr
126 – 150	0 Units/h	2 units	
151 – 200	1 units/h	2 units	
201 – 250	5 units/h	5 units	
251 – 350	10 units/h	10 units	

optimized before and during surgery with insulin infusion according to hospital protocol regardless of their preoperative oral hypoglycemics medication.

Continuous Insulin Infusion was used in both groups with addition of insulin boluses according to individual response (Table 1).

Our aim was to regulate Blood Glucose levels within **90 – 130** mg/dl in the TGC group and **131 – 190** mg/dl in the SGC group in first **48 hours** after surgery. Blood Glucose was measured at hourly intervals for the first 12 hrs, 2 hourly for the next 12 hrs and 4 hourly in the next 24 hrs. Venous blood glucose was checked using "Dimension RX" machine and Capillary blood glucose was checked by "On Call Plus" glucometer, which was calibrated after every 10 readings using standard glucose solution. Patients with hypoglycaemic episode were rechecked frequently and administered 25% D/W.

Diagnosis of identified Sternal or leg wound infection were based on positive cultures, clear dehiscence of the sternotomy wound, fever, pain, redness, secretion, purulent drainage, and sternal instability; during hospital stay or within 30 days of operation. In hospital mortality was considered for the purpose of this study. Table deaths and emergency CABG were excluded.

Comparison of discrete variables between groups was done using Chi-square test or x^2 test and P≤0.05 was considered to indicate a statistically significant difference.

Results

Between august 2011 through September 2012, a total of 124 patients undergoing isolated CABG surgery were included in this study. The mean age was 51.27 ± 4.45 and 53.15 ± 4.21 years (TGC versus SGC), respectively, in the two groups. The incidence of co-morbid conditions as well as operative conditions was simi-lar between the groups. During the study period 12 patients (18%) developed Sternal wound infection in the SGC group and 4 patients (6%) in the TGC group; differences were statistically significant (P=0.046). Similarly, 9 patients (14%) developed Leg wound infection in SGC group and 2 patients (3%) in TGC group, values being statistically significant (p-value 0.035).

1.5% mortality was observed in each group, both during ICU stay, one had ventilator associated pneumonia and the other developed new anterior wall myo-

Table 2:

	Tight Glycaemic Control	Standard Glycaemic Control	χ^2-value	p-value
Sternal Wound Infection	4	12	4.00	0.046
Leg Wound Infection	2	9	4.45	0.035
Atrial Fibrillation	10	12	0.18	0.670
Stroke	2	1	0.33	0.564
Time on Ventilator (Minutes)	423	437	0.23	0.633
New Myocardial Infarction	2	3	0.20	0.655
Mortality	1	1	0.00	1.000

cardial infarction not responding to inotropes or Intra aortic Balloon pump. However, there were no significant differences in other morbidities and the short term mortality (Table 2).

Comment

Cardiopulmonary Bypass is known to be a source of great stress to the body resulting increased levels of stress hormones such as corticosteroids, Catecholemines, growth hormone eventually leading to Hyperglycemia. Hyperglycemia has been found to adversely affect leukocyte function in many ways such as reduction in bactericidal capacity, reduced phagocytosis, chemotaxis and adherence to bacteria. Interestingly leukocyte function has an inverse relationship to the extent of hyperglycemia.[3] Recently, improved glucose control has been shown to reduce infection rates and mortality in hospitalized diabetic patients.[4-6] Most observational and retrospective studies have shown a longer hospital and ICU stay and a higher mortality as a result of hyperglycemia regardless of the diabetic status of the patient.[7-9] This may be due to a substantial number of patients who are not formally labeled as diabetics but understandably developing the same complications. There is growing evidence that hyperglycemia developing as a result of stress due to medical or surgical illness is not a benign condition but results in a worse clinical outcome and possibly increased mortality.[10,11]

A retrospective study by Zerr and colleagues aiming to establish the efficacy of subcutaneous versus continuous insulin in controlling blood glucose levels after cardiac surgery showed that apart from continuous insulin infusion being better at glucose control, increased levels within 48 hours of surgery were an independent risk factor for deep sternal wound infection.[12] A chart review of diabetic patients undergoing CABG showed a substantial increase in the rates of pneumonia, urinary tract infections and surgical site infections if the blood sugar levels were higher than 200mg/dl.[13]

It is worth mentioning that although many studies show the deleterious effects of hyperglycemia, one retrospective study in CABG patients did not find any significant increase in either surgical site or noscomial infections.[14] However only 35% of patients in the forementioned study were diabetics.

Our study sought to define the value below which the glucose level results in the reduction in a variety of morbidities and short term mortality. We found that maintaining Blood Glucose level < 130 mg/dl a majority of the time in the 1st 48 hrs after CABG in the ICU results in a significant reduction in the incidence of sternal and leg wound infection.There was no significant change in the occurrence of Stroke, Atrial Fibrillation, Time spent on ventialtor, new Myocardial Infection and short term mortality.

Conclusion

The results indicate that tight glucose control post operatively in CABG patient's results in reduced sternal and leg wound infection rates; however, there was no effect on other morbidities and short term mortality.

Limitations

This study was limited in the time scale for long term effects. Further studies are needed to define the effect of Blood Glucose levels on long term morbidity and

mortality. Large scale Multicenter studies are needed before the adoption of these results internationally.

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