ORIGINAL RESEARCH PAPER

Anaesthesiology

" DOES PREOPERATIVE GLYCOSYLATED HAEMOGLOBIN LEVELS PREDICT PERIOPERATIVE OUTCOMES IN PATIENTS UNDERGOING ON PUMP CABG SURGERY."

KEY WORDS: Diabetes mellitus, Glycosylated haemoglobin, Coronary artery bypass grafting.

Dr Dinesh Kumar* MD, DM, PDCC, FTEE., Assistant Professor, Department Of Cardiac, Thoracic And Vascular Anaesthesia, JSS Super Specialty Hospital And Medical College, JSS academy of higher education and research., Mysore-570011, Karnataka, India. *Corresonding Author

Dr. Thomas Koshy MBBS, DA, MD, PDCC, FIACTA, FTEE, Professor, Division Of Cardiothoracic & Vascular Anesthesia, Department Of Anesthesiology, Sri Chitra Tirunal Institute Of Medical Science And Technology. Trivananthapuram, Kerala-695011

ABSTRACT

Diabetes mellitus is one of the major risk factors for ischemic heart disease & atherosclerosis. It is a systemic disease involving all the systems of the body. Various studies have shown uncontrolled diabetes to be associated with many macro vascular complications like coronary artery disease, stroke & micro vascular complications like nephropathy, neuropathy, retinopathy, etc. Studies has also shown that glycosylated haemoglobin (HbA1C) level is an indicator of blood sugar control over the last 3-4 months and it predicts both micro & macro vascular complications. The optimal control of blood sugar in the perioperative period during cardiac surgery is a very controversial topic and many studies have addressed it differently. Perioperative hyperglycemia is an independent risk factor for increased morbidity & mortality during cardiac surgery. The objective of this study is to find out whether long term preoperative blood glucose control as indicated by the HbA1C (blood sugar levels over last 3-4 months) level influence the perioperative blood sugar levels, insulin requirement, inotropic requirement, the incidence of atrial fibrillation, infection rate & duration of ICU & hospital stay in patients undergoing on pump CABG surgery.

INTRODUCTION

Diabetes mellitus is one of the major risk factors for ischemic heart disease & atherosclerosis. It is a systemic disease involving all the systems of the body. Various studies have shown uncontrolled diabetes to be associated with many macro vascular complications like coronary artery disease, stroke & micro vascular complications like nephropathy, neuropathy, retinopathy, etc.[1-5] Studies have also shown that glycosylated haemoglobin (HbA1C) level is an indicator of blood sugar control over the last 3-4 months and it predicts both micro & macro vascular complications. The American diabetes association has recommended the use of HbA1C levels as a method of assessing long term glycemic control in diabetic patients. HbA1C more than 7% is an independent risk factor for micro vascular & macro vascular complications in diabetic patients. American Association of clinical endocrinologist's medical guidelines for clinical practice for the management of diabetes mellitus recommends to maintain glycosylated haemoglobin less than 7%. [13]

The optimal control of blood sugar in the perioperative period during cardiac surgery is a very controversial topic and many studies have addressed it differently. Perioperative hyperglycemia is an independent risk factor for increased morbidity & mortality during cardiac surgery. Various retrospective studies have shown that perioperative hyperglycemia is associated with the increased inotropic requirement, increased ICU & hospital stay, higher infection rate, delayed wound healing, renal failure & cerebrovascular accidents. [1-5] Van Den Berg et al had recommended tight control of blood sugar between 80-120 mg/dl in critically ill patients.[9] Finfer S, et al studied intensive versus conventional glucose management in critically ill patients & concluded that tight control is associated with increased risk of hypoglycemia & neurological complications.[10] Griesdale et al, in their meta-analysis titled 'Intensive insulin therapy and mortality among critically ill patients' reported increased risk of hypoglycemia & neurological complications with intensive insulin therapy[11] Currently Society of thoracic surgeon's guidelines recommends maintaining blood sugars less than 180mg/dl in the perioperative period.[12]

OBJECTIVES:

1. To assess whether patients with HbA1C more than 7% have higher blood sugar & insulin requirements perioperatively.
2. To evaluate whether patients with HbA1C more than 7% require higher inotropic support.
3. To assess whether a patient with HbA1C more than 7% have a higher incidence of atrial fibrillation, infections & prolonged ICU & hospital stay.

MATERIALS AND METHODS

Study design: Prospective Randomized controlled observational, single center study. Patients who were scheduled for elective coronary artery bypass grafting on cardiopulmonary bypass, who met all the inclusion criteria and did not have any exclusion criteria and were willing to participate in the study were included. The total numbers of patients were 120 as calculated by power analysis.

Inclusion criteria: Patients aged 40-80 yrs of either sex, with triple vessel diseases & ejection fraction of > 30% undergoing elective on pump CABG.

Exclusion criteria: Age < 40 yrs or > 80 yrs, emergency surgery, co- existing valvular disease, preoperative renal failure, EF < 30 %, LMCA lesion, large LA Size (> 4 cms), h/o of atrial fibrillation & those unwilling to give consent were excluded.

Conduct of the study: After the approval of technical advisory committee & institutional ethical committee this study was started. Informed written consent was taken from participants who were willing to participate in the study. Those meeting all of the inclusion criteria and did not have any of the exclusion criteria were selected. HbA1C levels were done as a part of the routine CABG work-up. Depending on HbA1C levels they were divided into two groups.

Group I: HbA1C > 7%.
Group II: HbA1C < 7%

One day prior to surgery fasting blood sugar & random blood sugars were determined. If it was more than 180 mg/dl, the patient was treated according to sliding scale as per our institute protocol. In patients with a history of DM, oral hypoglycemic drugs & insulin were stopped on the day of surgery as per institute protocols. For all patients FBS was estimated on the day of surgery and further blood sugar estimations were done in the pre CPB, CPB and post CPB periods. If blood sugar was more than 180mg/dl, patients were treated uniformly with human regular Insulin using modified Cleveland clinic protocol. Postoperatively blood sugar levels were monitored every hourly, if blood sugar levels more than 180 mg/dl; it was treated as per modified Cleveland clinic protocol for insulin dose. All patients were treated to maintain blood sugar levels less than 180 mg/dl as per society of thoracic surgeon's guidelines.[7]

Data analysis: Preoperatively demographic data like age, sex,

history of diabetes, duration of diabetes & treatment, Ejection fraction, Regional wall motion abnormality, blood sugar & HbA1C levels were recorded. Perioperatively blood sugar levels, total insulin requirement during surgery & first 48 hrs post-operatively, the inotropic requirement (according to Wernovsky inotropic score = Dobutamine (µg/kg/min) + Dopamine (µg/kg/min) + 100 X adrenaline (µg/kg/min) + 100 X nor adrenaline (µg/kg/min) + 10 X milrinone (µg/kg/min) + 10,000 X vasopressin dose (U/kg/min) [17] & any episode of atrial fibrillation were recorded. Postoperatively, patients were followed up till discharge from hospital. Superficial or deep sternal wound infections, duration of ICU & hospital stay, any episodes of atrial fibrillation, were recorded. These data were collected from the patient's charts and files in the intensive care unit (ICU) & ward. Statistical analysis was performed with SPSS 16th edition for windows. P value < 0.05 was taken as significant.

OBSERVATION AND RESULTS:

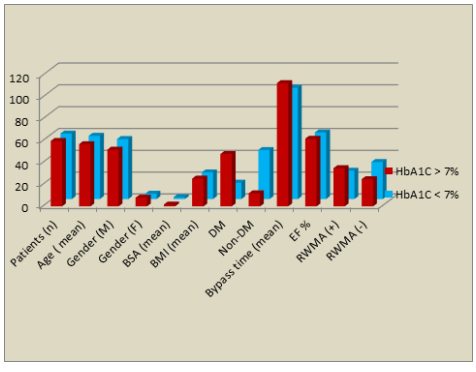
Group-I (HbA1C > 7%) included patients in the age group 57 ± 8 yrs. 52 were males & 8 females. 48 patients had diabetes, whereas 12 patients had no past h/o diabetes. Group-II (HbA1C < 7%) included patients in the age group 58 ± 8.6 yrs. 55 were males & 5 females, only 15 patients had diabetes while the rest had no h/o diabetes. Demographic variables between group-I & group-II were compared using Chi-square test for variables with a nominal scale (gender, diabetic status & RWMA) & paired T-test for variables with interval scale & normal distribution (age, BSA, BMI, EF & bypass duration). **Table-1** shows P value is > 0.05 for all variables except diabetic status, meaning both the groups are comparable with regard to demographic data. **Graph-1** shows a comparison of the demographic variables between the two groups. Preoperative, intraoperative & postoperative blood sugar levels for the first 48 hrs, intraoperative & postoperative insulin requirement were compared using the Paired T-test. **Table-2 & Graph-2 & 3** shows that perioperative blood sugar levels & postoperative insulin requirement were higher in group-I & statistically significant as compared to group-II. Intraoperative insulin requirement was not statistically significant.

Perioperative outcomes were compared using the Paired T-test (inotropic score, ICU & hospital length of stay) & Fisher's test (atrial fibrillation & infection rate). **Table-3 & Graph-4** shows that inotropic score (based on inotropic dose) was higher in group-I patients during first 48 hrs in the ICU. Six patients in group-I & four patients in group-II developed atrial fibrillation which was not statistically significant. Duration of stay in the ICU in group-I (2.8 ± 0.8 days) was longer than group-II (2.6 ± 0.4 days) but not statistically significant (p = 0.08). Length of stay in the hospital was longer in group- I (7.1 ± 3.5 days) as compared to group-II (6.2 ± 0.4) & was statistically significant. (p= 0.02). Six patients developed deep Sternal wound infection & three patients had to undergo pectoral flap surgery. All the six patients were from the group-I & had high HbA1C levels preoperatively. **Graph-5** shows the glucose variability between the two groups during pre-bypass, bypass & ICU for the first 48 hrs. Glucose variability is more in group-I as compared to group-II.

Table-1 Demographic data

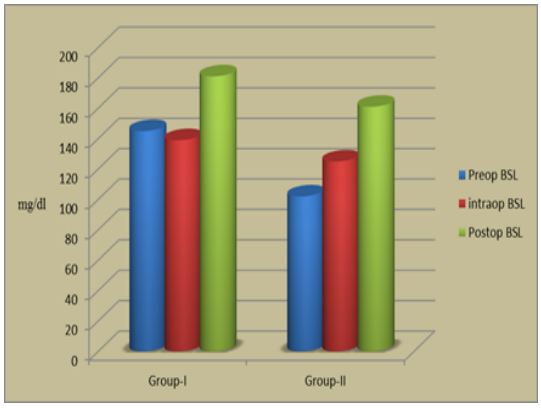
Groups	Patients (n)	Age (years)	Gender (n) (male/female)	BSA(m2) Mean ± SD	BMI(Kg/m2) Mean ± SD	Number of patients with/without diabetes	Bypass time (minutes) Mean ± SD	EF% Mean ± SD	Number of patients with/without RWMA
I (HbA1C >7%)	60	57 ± 8	52/8	1.71 ± 0.2	25.5 ± 3.5	48/12	113 ± 30	62 ± 11%	35/25
II (HbA1C <7%)	60	58 ± 8.6	55/5	1.68 ± 0.2	24.4 ± 4.8	15/45	102 ± 25	61 ±11%	26/34
P- value		0.51	0.55	0.46	0.24	0.0	0.37	0.62	0.1
Test		Paired T-test	Chi-square	Paired T-test	Paired T-test	Chi-square	Paired T-test	Paired T-test	Chi-square

BSA- body surface area, BMI- body mass index, EF- ejection fraction, RWMA- regional wall motion abnormality



Graph-1 Demographic variables

BSA- Body surface area, BMI- body mass index, DM- diabetes mellitus, EF- ejection fraction, RWMA- regional wall motion abnormality.



Graph- 2 Perioperative blood sugar levels

Group-I: HbA1c > 7 grm/dl, Group – II: HbA1c < 7 grm/dl

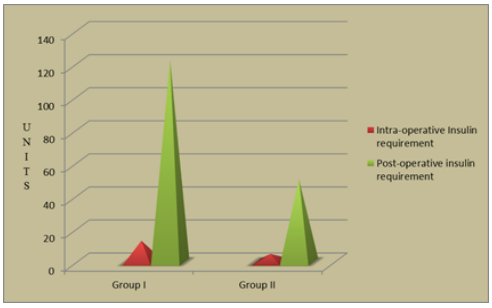
Table-2-Perioperative blood sugar levels & insulin requirement

Groups	Preoperative BSL(mg/dl) (Median±SD)	Intraoperative BSL(mg/dl) (Median±SD)	Postoperative (First48 hrs.) BSL(mg/dl) (Median±SD)	Intraoperative Insulin requirement (Units) (Mean ± SD)	Postoperative Insulin requirement (Units) (Mean ± SD)
I (HbA1C > 7%)	145 ± 49	139 ± 34	181 ± 27.5	3.2 ± 9	122 ± 89
II (HbA1C < 7%)	102 ± 20	125 ± 31	161 ± 22	1 ± 3.5	50 ± 43
P value	0.00	0.04	0.00	0.08	0.00
Test	Paired T-test	Paired T-test	Paired T-test	Paired T-test	Paired T-test

BSL-blood sugar levels

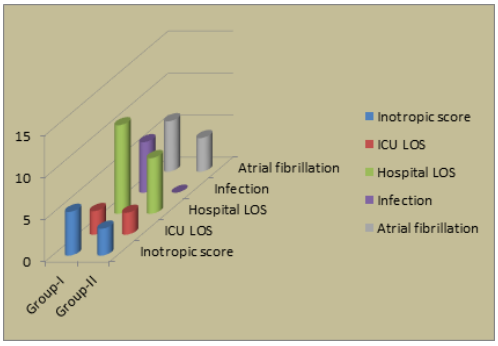
Table-3 Perioperative outcomes following on pump CABG

Groups	Inotropic Score (n) (mean ± SD)	ICU length of stay (Days) (mean ± SD)	Hospital length of stay (Days) (mean ± SD)	Infections n (percentage)	Atrial fibrillation n (percentage)
I (HbA1C > 7%)	5.2 ± 7	2.8 ± 0.8	7.1 ± 3.5	6 (10%)	6 (10%)
II (HbA1C < 7%)	3.2 ± 4.3	2.6 ± 0.4	6.2 ± 0.4	0	4 (6.7%)
P- value	0.05	0.08	0.02	0.03	0.74
Test	Paired T test	Paired T test	Paired T test	Fisher's T test	Fisher's T test



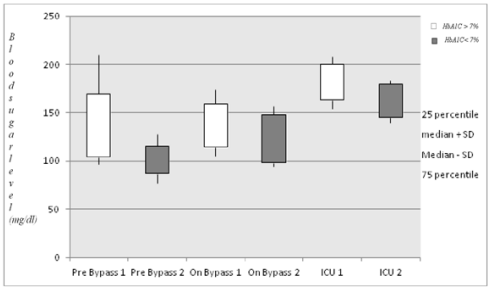
Graph-3 Perioperative insulin requirement to maintain BSL < 180 mg/dl

Group-I: HbA1c > 7 grm/dl, Group-II: HbA1c < 7 grm/dl



LOS- length of stay

Graph-4 Perioperative outcomes following on pump CABG



Graph-5 Perioperative blood sugar levels & variability

DISCUSSION:

The objective of our study was to determine whether preoperative glycosylated haemoglobin levels (HbA1C) could predict the probability of perioperative hyperglycemia, duration of stay in the ICU & hospital, inotropic requirement, the incidence of surgical site infection & atrial fibrillation in the postoperative period. During cardiac surgery there is an alteration in the glucose metabolism. Many factors like surgical stress, exposure to CPB, inotropes, insulin resistance; predispose both diabetic & non-diabetic patients to develop hyperglycaemia. Various studies have shown that perioperative hyperglycaemia & glucose variability is associated with prolonged ICU & hospital stay, increased mortality & morbidity perioperatively during cardiac surgery. Perioperative hyperglycaemia & glucose variability influence the outcome in critically ill patients. However, their extent of perioperative hyperglycaemia can only be determined afterwards, which limits their use as a clinical predictor. Identifying relevant patient characteristics that are connected to and could possibly predict intra- and postoperative hyperglycaemia is an important step toward improved medical management.

The importance of preoperative HbA1C levels, whether surgery should be delayed in patients with higher values, HbA1C levels can it be used to predict perioperative hyperglycaemia & post-operative outcomes following on pump CABG are the questions we have tried to answer from our study.

Our study had two groups with 60 patients each. Group-I (HbA1C > 7%) included patients in the age group 57 ± 8 yrs. 48 patients had diabetes, whereas 12 patients had no past h/o diabetes. Group-II (HbA1C < 7%) included patients in the age group 58 ± 8.6 yrs. 15 patients had diabetes while the rest had no h/o diabetes. Both groups were comparable with regard to demographic data, echo features & bypass duration. Group-I patients had higher blood sugars pre bypass, on bypass & in the ICU for the first 48 hrs. Group-I patients required higher insulin dose to maintain blood sugars around 180 mg/dl during perioperative period & first 48 hrs in the ICU. Inotropic score (based on inotropic dose) was higher in group-I patients during first 48 hrs in the ICU. Duration of stay in the ICU in group-I (2.8 ± 0.8 days) was longer than group-II (2.6 ± 0.4 days) but not statistically significant (p = 0.08). Length of stay in the hospital was longer in group- I (7.1 ± 3.5 days) as compared to group-II (6.2 ± 0.4) & was statistically significant. (p = 0.02). Six patients postoperatively developed deep Sternal wound infection & three patients had to undergo pectoral flap surgery. All the six patients were from the group-I & had high HbA1C levels preoperatively.Six patients in group-I & four patients in group-II developed atrial fibrillation which was not statistically significant.

LIMITATION AND STRENGTHS:

It was a small observational single center study. Inotropic score that is the maximum dose of inotrope used in the ICU during first 48 hrs was used to calculate inotropic requirement in both the groups. The duration of inotrope used couldn't be compared as there was no cardiac output monitoring postoperatively in all patients.

Compared with other studies, it was a prospective study with a homogeneous cohort from a single center. All data was manually collected; so there was no issue of data loss through automatic data collection. The blood sugar level was maintained less than 180 mg/dl in both the groups as per the present STS guidelines. Modified Cleveland clinic insulin dose protocol was used in both the groups to maintain blood sugar levels less than 180 mg/dl perioperatively.

CONCLUSION:

In summary, this prospective study proves that preoperative HbA1C levels predict the degree of perioperative hyperglycaemia, insulin requirement perioperatively & duration of stay in the hospital. Patients with higher HbA1C levels have an increased risk of infections & require higher inotropic support. In patients with higher HbA1C levels preoperatively, the risk benefit ratio to be considered before taking for surgery. In this subset of patients surgery may be delayed until the blood sugars are controlled for a better outcome.

REFERENCES:

1. Salomon NW, Page US, Okies JE, Stephens J, Krause AH, Bigelow JC. Diabetes mellitus and coronary artery bypass: short-term risk and long-term prognosis. Journal of Thoracic Cardiovascular Surgery. 1983; 85:264-271
2. Thourani VH, Weintraub WS, Stein B, et al. Influence of diabetes mellitus on early and late outcome after coronary artery bypass grafting. Annals of Thoracic Surgery. 1999; 67:1045-1052.
3. McAlister FA, Man J, Bistritz L, Amad H, Tandon P. Diabetes and coronary artery bypass surgery: an examination of perioperative glycemic control and outcomes. Diabetes Care 2003; 26:1518–1524.
4. Anderson RE, Brismar K, Barr G, Ivert T. Effects of cardio-pulmonary bypass on glucose homeostasis after coronary artery bypass surgery. European Journal of Cardiothoracic Surgery 2005; 28:425–430.

5. Gandhi GY, Nuttall GA, Abel MD, et al. Intraoperative hyperglycaemia and perioperative outcomes in cardiac surgery patients. Mayo Clinical Proceedings 2005; 80:862-866.
6. Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. Journal of Thoracic Cardiovascular Surgery 2003; 125:1007–1021
7. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. Endocrinology Practice 2004; 10(supplement 2):21-33.
8. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative out-comes and decreases recurrent ischemic events. Circulation 2004; 109:1497–1502.
9. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. New England Journal of Medicine2001; 345:1359-1367.
10. Finfer S, Chittock DR, Su SY, et al: Intensive versus conventional glucose control in critically ill patients. New England Journal of Medicine 2009; 360:1283-1297.
11. Griesdale DE, de Souza RJ, van Dam RM, et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. CMAJ 2009; 180: 821-827.
12. Harold L. Lazar, Marie McDonnell, Stuart R. Chipkin, et al. The Society of Thoracic Surgeons Practice Guideline Series: Blood Glucose Management during Adult Cardiac Surgery Annals of Thoracic Surgery 2009; 87: 663-669
13. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care 2005; 28: 4-36.
14. Halkos ME et al. Elevated preoperative HbA1C level is predictive of adverse events after coronary artery bypass surgery. Journal of thoracic & cardiovascular surgery 2008; 136 (supplement 3):631-640.
15. Moitra VK, Greenberg J, Arunajadai S, Sweitzer B et al. The relationship between glycosylated haemoglobin and perioperative glucose control in patients with diabetes. Canadian Journal of Anaesthesia 2010; 57(supplement 4):322-329.
16. Hudson CC, Welsby IJ et al. HbA1C levels & outcome in non-diabetic cardiac surgery patients. Canadian journal of anaesthesia 2010; 57(supplement 6):565-572.
17. Wernovsky G. Wypij D, Jonas RA, et al. Postoperative course & hemodynamic profile after the arterial switch operation in neonates & infants. A comparison of low flow cardiopulmonary bypass & circulatory arrest. Circulation 1995; 92:2226-2235.
18. Medhi M, Marshall MC Jr, Burke HB, et al. HbA1c predicts length of stay in patients admitted for coronary artery bypass surgery. Heart Dis 2001; 3: 77-79.