Intensive hyperglycemia control reduces postoperative infections after open heart surgery

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ABSTRACT: **Background:** Diabetes mellitus increases the risk of infections in patients undergoing cardiac surgery. We hypothesized that intensive perioperative hyperglycemia control by intravenous insulin infusion reduces postoperative infections in all patients undergoing open heart surgical procedures.
Methods: Sixty diabetics patients who underwent CABG operation (Group 1) were compared with fifty-five patients who underwent other cardiac surgery (Group 2) between January 2004 and March 2005. A continuous infusion of insulin was used in all these patients.
Results: There were no 30-day mortalities in either group. There was no difference in the incidence of infections between the two groups: in Group 1, 3 (5%) patients were diagnosed to have postoperative infection (superficial sternal wound infections in 1 (1.66%) and lung infection in 2 (3.33%) patients); postoperative infection occurred in only 2 patients (3.63%) in Group 2, 1 superficial sternal wound infections (1.81%) and 1 lung infection (1.81%).
Conclusions: Our analysis indicates that continuous intravenous insulin infusion improves outcome and reduces postoperative infections in patients undergoing CABG as well as those undergoing other cardiac surgery procedures. (Heart International 2006; 2: 49-53)

KEY WORDS: Hyperglycemia, Infections, Heart surgery

INTRODUCTION

The incidence of infection in cardiac surgery remains a potential cause of morbidity and mortality and the most important step in the management of this problem is prevention and this is best done by identifying the risk factors. Diabetes mellitus is an independent predictor of morbidity and/or mortality in patients undergoing coronary artery bypass grafting (CABG)(1). However, there is a growing body of clinical and experimental evidence that diabetes increases the risk of infections and may actually be a causal factor in the development of these infections also in patients undergoing other cardiac surgery procedures. The severity of infections may range from minor, superficial wound infection to fulminate mediastinitis with involvement of the sternum, heart and great vessels (2, 3) but also lung infections and urinary tract infections. The sternum is the most common infection site, it also accounted for >70% cases of severe infection. The most commonly isolated organism at the sternal site is methicillin sensitive *Staphylococcus epidermidis* followed by methicillin resistant *Staphylococcus aureus.* We hypothesized that intensive pherioperative hyperglycemia control by intravenous insulin infusion reduces postoperative infections in all patients undergoing open heart surgical procedures.

SUBJECTS AND METHODS

Patients with diabetes mellitus undergoing primary open heart surgery between January 2004 and March 2005 at St. Andrea Hospital were included in the study. The exclusion criteria were reoperations and history of allergy to penicillin/cephalosporins. Sixty diabetic patients who underwent CABG operation (Group 1) were compared with fifty-five patients who underwent other cardiac surgery (Group 2) in the same period. The preoperative base-line characteristics of the patients are summarized in Table I. There were no changes in antibiotic protocols during this time and procedures were performed by the same surgical group. On the day prior to surgery and on the day of surgery patients were advised to take a bath with 4% chlorhexidine which was applied to the whole body and retained for at least 5 minutes before taking a bath. Operative site was prepared using 10% povidone-iodine scrub solution (Betadine) for disinfection. In this one hundred fifteen patients we aimed to maintain the blood glucose levels perioperatively between 90-120 mg/dL. During the hospital stay, patients were evaluated daily preoperatively and postoperatively from the third day onward. In addition, all these patients were seen by an endocrinologist during their admission. The insulin-dependent diabetics should receive their regular dose of insulin the evening before the operative day. Insulin dose infusion starts in operating room: 2-4 U/h is the rule during operation. In the postoperative period the patients' blood glucose levels were prospectively monitored every 1 or 2 hours through fingerstick or arterial line drop sample. A continuous infusion of insulin (50 IU of Actrapid HM in 50 mL of 0.9% sodium chloride) with the use of a pump (Fresenius, Brezins, France) was started only if the blood glucose level exceeded 120 mg/dL and the infusion was adjusted to maintain the level at a value between 90 to 120 mg/dL. We didn't use a precise protocol because the dose of insulin administered was adjusted according to patient's compliance. Daily mean blood glucose levels were then calculated by averaging all glucose levels obtained clinically during the day of operation and each of the first through third postoperative days. Blood cultures were obtained whenever the central body temperature exceeded 37.5°C. Patients were then screened for postoperative infectious complications or readmission for the same reason.

Definition of infectious complications

Definitions for deep and superficial sternal wound infection followed the guidelines of the Centers for Disease Control and Prevention (4).

Deep sternal wound infection (DSWI): isolation of an organism from culture of the mediastinal tissue or fluid, visual evidence of mediastinitis, chest instability, or fever associated with the presence of purulent drainage.

TABLE I - BASE-LINE CHARACTERISTICS OF THE PATIENTS

	Group 1 (n = 60)	Group 2 (n = 55)	p value
Age (years)	63.8 ± 1.3	68.2 ± 1.5	ns
Male-no.(%)	40 (66.6%)	37 (67.2%)	ns
BMI (kg/m^2)	25.8 ± 4.7	26.1 ± 4.3	ns
Smoking-no.(%)	47 (78.3%)	42 (76.3%)	ns
Hypertension-no. (%)	53 (88.3%)	47 (85.4%)	ns
Renal failure-no. (%)	23 (38.3%)	20 (36.3%)	ns
Admission glucose-no.(%):			
> 110 mg/dL	23 (38.3%)	19 (34.5%)	ns
> 200 mg/dL	7 (11.6%)	6 (10.9%)	ns
Preoperative diabetic medication (%):			
Insuline alone	30.8	29.5	ns
Oral hypoglycemic(s) alone	57.7	58.1	ns
Diet alone	5.4	4.8	ns
None	1.2	1.5	ns

BMI = body mass index; ns = not significant

Superficial sternal wound infection (SSWI): when purulent discharge was not associated with involvement of sternal or mediastinal tissues.

RESULTS

Between January 2004 and March 2005 at St. Andrea Hospital one hundred fifteen diabetics patients under-

TABLE II - CARDIAC SURGICAL PROCEDURES CARRIED OUT IN GROUP 1 AND GROUP 2

Group 1 (n = 60)	
CABG on pump (%)	90
CABG off pump (%)	10
One IMA (%)	89
Two IMA (%)	11
Group 2 (n=55)up 2 (n=55)	
MVR (%)	61
AVR (%)	30
MVR + AVR (%)	6
Bentall Technique (%)	3

CABG = coronary artery bypass grafting; IMA = internal mammary artery; MVR = mitral valve replacement; AVR = aortic valve replacement

went primary open heart surgery. Sixty diabetic patients who underwent CABG operation (Group 1) were compared with fifty-five patients who underwent other cardiac surgery (Group 2) in the same period. The two groups of patients were comparable with respect to preoperative, intraoperative and postoperative variables. There were no significant differences with respect to age, sex, body mass index; the majority of all diabetic patients were on oral hypoglycemic agents; the cardiac procedures performed in this diabetic cohort included, for Group 1, 90% CABG on pump and 10% CABG off pump and, for Group 2, 61% mitral valve replacement (MVR), 30% aortic valve replacement (AVR), 6% MVR + AVR and 3% Bentall technique (Tab. II). Cross-clamp (81.3 ± 1.5 minutes Group 1 versus 85.4 ± 2.5 minutes Group 2; p=*ns*) and cardiopulmonary bypass time (90.4 ± 2.5 minutes Group 1 versus 98.2 ± 2.7 minutes Group 2; p=*ns*) were similar between groups (Tab. III). Insulin dose infusion started in the operating room and was adjusted based on serial glucose measurements. Mean glucose levels of diabetic patients in postoperative 1st day (116.5 ± 3 mg/dL Group 1 versus 114.4 ± 5 mg/dL Group 2) in postoperative 2nd day (117 ± 5 mg/dL Group 1 versus 118 ± 7 mg/dL Group 2) and in postoperative 3rd day (115 ± 2 mg/dL Group 1 versus

TABLE III - INTRAOPERATIVE VARIABLES

	Group 1 (n = 60)	Group 2 (n = 55)	p value
Mean CPB time (min)	90.4 ± 2.5	98.2 ± 2.7	ns
Mean aortic cross-clamp time (min)	81.3 ± 1.5	85.4 ± 2.5	ns
Operative status (%):			
elective	94	96	ns
urgent	4	3	ns
emergent	2	1	ns

CPB = cardiopulmonary bypass; ns = not significant

TABLE IV - GLUCOSE LEVEL AFTER OPERATION

	Group 1 (n = 60)	Group 2 (n = 55)	p value
Postop 1st day (mg/dL)	116.5 ± 3	114.4 ± 5	ns
Postop 2nd day (mg/dL)	117 ± 5	118 ± 7	ns
Postop 3rd day (mg/dL)	115 ± 2	116 ± 4	ns

ns = not significant

TABLE V - POSTOPERATIVE OUTCOMES

	Group 1 (n = 60)	Group 2 (n = 55)	p value
Death	0	0	ns
DSWI	0	0	ns
SSWI	1 (1.66%)	1 (1.81%)	ns
Urinary tract infection	0	0	ns
Lung infection	2 (3.33%)	1 (1.81%)	ns

DSWI = deep sternal wound infection; SSWI = superficial sternal wound infection; ns = not significant

116 ± 4 mg/dL Group 2) were also similar between groups (Tab. IV). No cases of symptomatic hypoglycemia occurred in either group of patients. There were no 30-day mortalities in either group. In Group 1, three (5%) patients were diagnosed to have postoperative infection (SSWI in 1 (1.66%) and lung infection in 2 (3.33%) patients). Postoperative infection occurred in only 2 patients (3.63%) in Group 2, 1 SSWI (1.81%) and 1 lung infection (1.81%) (Tab. V). *Staphylococcus aureus* was cultured in 3 patients (lung infections) and *Staphylococcus epidermidis* in 2 patients (SSWI).

DISCUSSION

Diabetes is a well-known risk factor for perioperative medical complications. Poor glucose control is a independent risk factor for surgical site infections (5,6) in a range of surgical procedures like cardiac surgery. Hyperglycemia impairs the function of complement and antibodies, reducing the opsonic potential of these factors and impairing phagocytosis, further reducing barriers to infection (7). These abnormalities develop when blood glucose levels exceed 11 mmol/L and do improve *in vitro* with glycemic control (8); so improving glucose control can improve immunologic function and reduce the incidence of infections (9). The findings of this investigation demonstrate that intensive perioperative hyperglycemia control by intravenous insulin infusion reduces postoperative infections in all patients undergoing open heart surgical procedures. The perioperative hyperglycemia control was implemented by nurses in the surgical intensive care unit and warm and involved routine consultation and follow-up by an endocrinologist. The mean glucose value the first three postoperative days after open heart operation was found to be the most important factor for wound infection. Aggressive glucose control in the perioperative period can be achieved using a continuous intravenous insulin infusion. Between January 2004 and March 2005 at St. Andrea Hospital, the nursing staff monitored fingerstick or arterial line drop of blood sample glucose measurements and adjusted the infusion rate intended to maintain serum glucose between 90-120 mg/dL. In our study we consecutively included all diabetic patients being operated on, and follow-up was 100% complete. The exclusion criteria were reoperations and history of allergy to penicillin/cephalosporins. The personnel, equipment, surgical techniques and use of prophylactic antibiotics were similar throughout the study period. The aim of our study was to find differences in infection incidence in two group of diabetic patients treated with continuous intravenous insulin infusion: Group 1 (n=60) who underwent CABG operation and Group 2 (n=55) who underwent other cardiac surgery in the same period. There was no difference in the incidence of infections between the two groups: in this study infection after heart surgery occurred in only 5 of 115 patients (4.34%): 3 (5%) in Group 1 and 2 (3.63%) in group 2. *Staphylococcus aureus* was the most common pathogen isolated in patients with infection after cardiac surgery, both in our study and in cases reported in the literature (10). Reports of increased risk with use of the internal mammary artery have differed and occasionally conflict among institutions (11). Our experience suggests that, in the diabetic patient population, perioperative hyperglycemia control may obviate also the infectious risk of bilateral internal mammary artery grafts. A balanced diet is also essential for the uneventful postoperative metabolic status. Van-den-Berghe et al recently reported that maintaining blood glucose levels between 80 mg/dL and 110 mg/dL significantly re-

duced morbidity and mortality in a cohort of surgical intensive care unit patients where 63% of the population were postoperative cardiac surgery patients (12). We urge surgeons and all concerned physicians not to ignore the potentially harmful and costly effect of perioperative hyperglycemia in patients undergoing heart surgery. In summary, our analysis indicates that continuous intravenous insulin infusion improves outcome and reduces postoperative infections in patients undergoing CABG as well as those undergoing other cardiac surgery procedures.

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