ß-BLOCKER THERAPY IN CORONARY ARTERY BYPASS SURGERY: OUR EXPERIENCE AT QUEEN ALIA HEART INSTITUTE

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ABSTRACT

Objective: The objective of the study was to look at the effect of using ß-blockers perioperatively in patients undergoing coronary artery bypass graft surgery at Queen Alia Heart Institute.

Methods: This is a retrospective analysis of all patients who underwent coronary artery bypass graft surgery between April 2005 and September 2006 at Queen Alia Heart Institute. The data collected included the patients' demographic characteristics, risk factors for coronary artery disease, history of myocardial infarction, renal dysfunction, history of prior cardiac surgery and the nature of coronary artery disease. We assessed operative mortality, rate of stroke, atrial or ventricular arrhythmias, duration of ventilatory support and Intensive Care Unit stay. Inclusion criteria were adult patients who were admitted for coronary artery bypass graft surgery, excluding patients who had valvular surgery, aneurysmectomy and off pump bypass surgery.

Results: We had a total of 916 patients. Four hundred and ten patients were on β-blockers while the rest were not. The two groups did not differ in their characteristics. The mean age was 60.0 ± 11 years, with 24% females. The mean Intensive Care Unit stay was 1.8 ± 0.5 days for the β-blockers group and 2.0 ± 0.6 days for the non-β-blockers group (P=0.001). Patients who had β-blockers had a rate of atrial or ventricular arrhythmias of 26% compared to 38% in the non-β-blockers group (P=0.001). The mean post-operative hospital stay for patients who received β-blockers was 7.2 ± 3 days compared to 8.4 ± 3.2 days in the non-β-blockers group (P<0.001). In-hospital mortality was 4.2% in the β-blockers group and 5.3% in the non-β-blockers group (P=NS). Stroke was seen in 2.1% in the first group compared to 3.3% in the non-β-blockers group (P=NS). Ventilatory support for more than 24 hours was seen in 7.1% compared to 6.9% in the non-β-blockers group (P=NS). Intra-Aortic Balloon Pump support was used in 4.9% compared to 5.2% in the non-β-blockers group (P=NS).

Conclusion: Perioperative β-blockers use is associated with significantly lower incidence of arrhythmias, shorter hospital stay and non-significant lower in-hospital mortality. They had no effect on ventilatory support or the use of intra-aortic balloon pump support.

Key words: Coronary artery disease, Coronary bypass, Jordan.

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Introduction

ß-Blockers are one of the oldest and most commonly used drugs for the treatment of ischemic heart disease.[1] They have been shown to improve acute outcomes and long term prognosis in ischemic heart disease[2-4] and to reduce perioperative events among high risk patients undergoing major non-

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cardiac and vascular surgery.[5-8] Prior ß-blocker therapy has also been shown to have a cardio-protective effect in limiting CK-MB release and lower intermediate term mortality rate following percutaneous coronary interventions.[9] Interest is now concentrating on exploring this beneficial effect in patients undergoing Coronary Artery Bypass Graft (CABG) surgery. Most of the evidence comes from extrapolations of the cardioprotective benefits of β-blockers from major noncardiac and vascular surgery. Operating on a ß-blocked heart is controversial with concerns arising about the negative inotropic effect of ß-blockers and complications of ß-blockade like bronchospasm.[10-13] Accordingly, many cardiac surgeons have not considered use of β-blockers perioperatively in their CABG patients.

The aim of this study was to quantify the effect of preoperative β-blocker therapy continued to the day of surgery and postopeatively on outcome, morbidity and mortality following coronary artery bypass grafting in the patient population at Queen Alia Heart Institute (QAHI).

Methods

This was a retrospective analysis of all patients who had CABG surgery between April 2005 and September 2006 at Queen Alia Heart Institute. The data collected included the patients' characteristics, risk factors for coronary artery disease (CAD), history of myocardial infarction (MI), renal dysfunction, and history of prior cardiac surgery and the nature of CAD. We assessed operative mortality, rate of stroke, atrial and ventricular arrhythmias (atrial fibrillation, flutter, ventricular tachycardia or ventricular fibrillation), duration of ventilatory support, use of intra-aortic balloon pump (IABP) support and Intensive Care Unit (ICU) stay.

Inclusion criteria were adult patients who were admitted for CABG surgery, excluding patients who had valvular surgery, aneurysmectomy, off pump bypass and those who had concurrent carotid endarterectomy.

Electrocardiographic monitoring was done continuously during ICU stay and at least daily ECG or more often upon the discretion the treating surgeon once the patient was back on the ward. Definition of risk factors was similar to criteria set in the Euro Heart Survey of patients with Acute Coronary Syndromes.[14] Current smoking was defined as smoking up to one month before surgery. Hypertension was defined as prior diagnosis, current use of antihypertensive medications or blood pressure readings of > 140 mmHg systolic or > 90 mmHg diastolic on more than two occasions. Diabetes was defined as prior diagnosis or current use of hypoglycemic medications. Hypercholesterolemia was defined as total cholesterol of > 200 mg/dl, or current use of cholesterol lowering treatment. Renal dysfunction was defined as creatinine of > 1.5 mg/dl.

Perioperative β-blocker was defined as the use of β-blocker preoperatively on admission that was continued post-op either intravenous or orally upon the discretion of the treating surgeon up to hospital discharge.

Statistical methods included the use of Office Excel and Student t test to calculate the various variables and statistical significance.

Results

We had a total of 916 patients. Four hundred and ten patients were on β-blockers (45%), while the rest were not (Fig. 1).

Table I shows patients' and disease characteristics based on preoperative use of ß-blocker. The two groups did not differ in their characteristics. The mean age was 60.0 ± 11 years, 59.0 ± 11.6 years for males and 63.1 ± 9.6 years for females (P = 0.001). Females accounted for 24% of our study population (Fig. 2). 31% had previous MI, 40.8% had diabetes mellitus and the same percentage was hypertensive. Almost two thirds (61%) were smokers. Hypercholesterolemia was present in 29.4% of patients. Fig 3 shows the prevalence of the various risk factors for coronary artery disease. The prevalence of risk factors was 95% for at least one risk for CAD to be present. Two risk factors were present in 28% and three risk factors were present in 20%. Three percent had renal dysfunction. More than 85% had three vessel diseases and 12.5% had significant left main disease. 3.8% had prior CABG surgery.

The mean ICU stay was significantly shorter for the β-blocker group at 1.8 ± 0.5 days compared to 2.0 ± 0.6 days for the non-β-blockers group (P=0.001). Patients who had β-blockers had a rate of atrial or ventricular arrhythmias of 26% compared to 38% in the non-β-blockers group (P=0.001). The mean cross clamp time was 45 minutes and a mean bypass time of 90 minutes, without a significant statistical difference between the two groups. The mean post-operative hospital stay for patients who received β-blockers was 7.2 ± 3 days compared

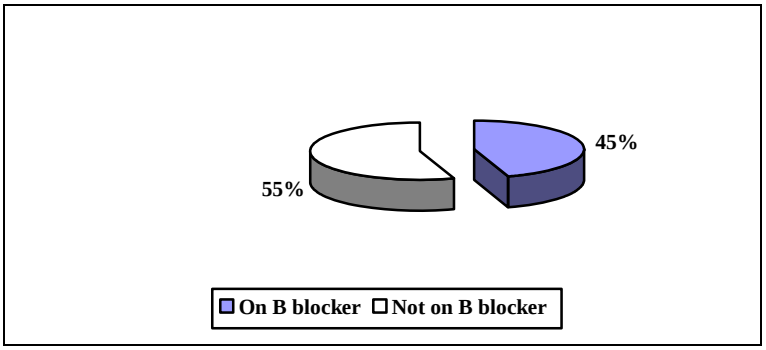

Fig. 1. Percentage of patients using B blockers

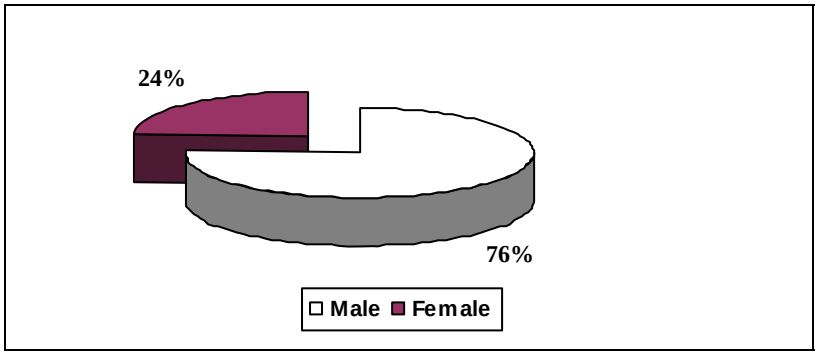

Fig. 2. Gender distribution

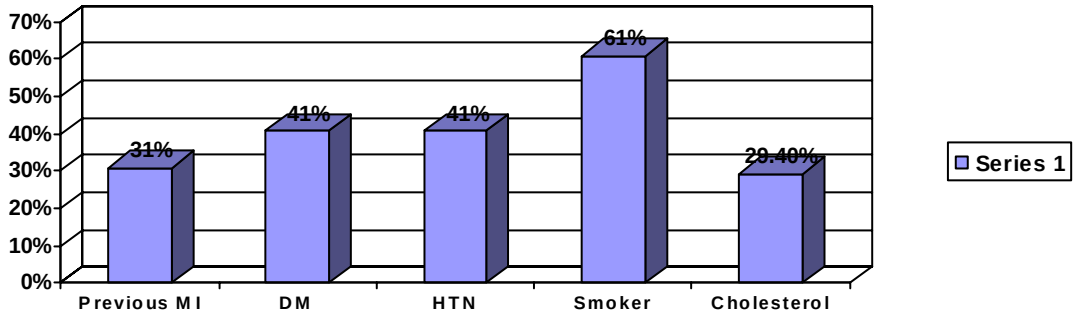

Fig. 3. The prevalence of the various risk factors for CAD

to 8.4 ± 3.2 days in the non-β-blockers group (P<0.001). In-hospital mortality was 4.2% in the β-blockers group and 5.3% in the non-β-blockers group, 20% reduction of hospital mortality (P=NS). Stroke was seen in 2.1% in the first group compared to 3.3% in the non-β-blockers group (P=NS). Ventilatory support for more than 24 hours was seen in 7.1% compared to 6.9% in the non-β-blockers group (P=NS). Intra-Aortic Balloon Pump (IABP) support was used in 4.9% compared to 5.2% in the non-β-blockers group (P=NS).

Discussion

Patients requiring CABG surgery usually have severe coronary artery disease (CAD) and the perioperative course is characterized by surgical stress and hemodynamic changes. Also, many of the regular medications are discontinued or interrupted, thus exposing the patient to their withdrawal effects.

The high prevalence of risk factors reported here is similar to those reported by similar studies in Jordanian patients and international studies.[15,16] Recommendations for a national campaign fo cessation of smoking and measures to reduce the prevalence and control of diabetes and hypertension are warranted.

To our knowledge this analysis is the first at our centre and nationally. To date, there have been no randomized trials evaluating preoperative β-blockade in CABG surgery.

Table I. Patients' characteristics in the two groups

	ß-Blocker group	Non-ß-Blocker group	P value
Age	60.3 ±10.9	59.8 ±11.1	NS
Female gender %	24		
Previous MI %	31.7	30.6	NS
Current smoker %	62	60	NS
Diabetes %	40	41.5	NS
Hypertension %	40.2	41.3	NS
Hypercholesterolemia %	28.5	30	NS
Renal dysfunction %	3.1	2.9	NS
Three vessel disease %	85	86	NS
Left main stenosis %	12	13	NS
Prior cardiac surgery %	3.9	3.8	NS
Emergency procedure %	2	2.2	NS
Number of grafts per patient	3.5	3.4	NS
LIMA use %	90	89.5	NS

NS = non-significant

Table II. In-hospital outcome

	ß-Blocker users	Non-ß-blocker users	P Value
Mean ICU stay (days)	1.8 ± 0.5	2.0 ± 0.6	0.001
Post operative arrhythmias %	26	38	0.001
Mean hospital stay (days)	7.2 ± 3	8.4 ± 3.2	0.001
In-hospital mortality	4.2	5.3	0.50
Stroke (%)	2.1	3.3	0.371
Ventilation >24 h (%)	7.1	6.9	0.50
IABP support (%)	4.9	5.2	0.50

In our study 44.8% had preoperative β-blocker therapy that was continued postoperatively. This figure is less than that quoted in international studies of 65%.[13] We have shown the beneficial effect of preoperative β-blockers that is continued postoperatively, on ICU stay, rate of atrial arrhythmias, postoperative hospital stay and a statistically non significant reduction of hospital mortality (20%). Investigators have suggested improved survival with the use of β-blockade perioperatively.

Ferguson *et al.*[13] have looked at outcomes after cardiac surgery in a large multi-centre observational study in North America. Their analysis shows that preoperative ß-blockade improved operative survival in all patients who underwent coronary artery surgery except in those with poor left ventricular function (<30%). It has also been shown that these patients also have significantly lower rates of stroke, renal failure, and prolonged ventilation. The literature reports a rate of 5-40% incidence of atrial arrhythmias post CABG surgery.[17]

Several studies have shown that initiation of β-blocker therapy preoperatively reduces the incidence of atrial fibrillation in CABG patients.[18,19] Lower stroke rate is attributed to having a high lipid solubility, thus crossing the blood brain barrier and reduction of ischemia by shifting the oxygen-haemoglobin dissociation curve to the right resulting in increased oxygen dissociation to brain tissues.[17] The high levels of circulating catecholamines result in desensitization and reduction in the density of β-adrenoceptors. This leads to abnormal response to epinephrine and norepinephrine and compounding ischemia.[20,21] Other postulated mechanisms are membrane stabilization and local anaesthetic effects of β-blockers. Ferninger *et al.*[22] identified a lower heart rate at the time of anaesthesia induction for CABG to predict perioperative events and suggested that the potential benefit of β-blocker therapy to be due to its autonomic effects. Chen *et al.*[23] reported that elderly CABG patients discharged receiving β-blockers had improved one year adjusted survival rates compared with those not receiving β-blockers.

Other postulated mechanisms suggest that catecholamines instigate and perpetuate vascular injury by promoting endothelial dysfunction, platelet aggregation, endovascular adhesion molecule

release, hypercoaguability, hypertension and direct myocyte toxicity. β-adrenergic blockade, experimentally and epidemiologically, can reverse many of these effects.[24]

Conclusion

Our analysis provides evidence that use of β-blockers is safe and effective in CABG surgery patients. Peri-operative β-blockers use is associated with significantly lower incidence of arrhythmias, shorter hospital stay and non-significantly lower in-hospital mortality. They had no significant effect on ventilatory support or the use of IABP support.

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