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Beta-Blockers and Non-Cardiac Surgery

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Morbidity and mortality resulting from cardiac ischaemia are a major cause of severe complications in patients undergoing non-cardiac surgery. Peri- and postoperative ischaemia are most likely caused by an increase in myocardial oxygen demand in patients with coronary heart disease and those in whom coronary plaque ruptures may be triggered. Increased catecholamine levels and prothrombotic tendencies play an important role in these events. The perioperative risk is highest among patients with coronary heart disease, prior myocardial infarction, congestive heart failure, arterial hypertension and diabetes mellitus. Since beta-blockers directly inhibit the effects of catecholamines they should be given to patients undergoing non-cardiac surgery that have one of these risk factors but no major contraindications. Even if the drugs cause complications they usually can be tolerated during the perioperative period. *J Clin Basic Cardiol 2001; 4: 21–23.*

Key words: beta-blocker, surgery, mortality

Cardiac adverse events are a major cause of morbidity and mortality in patients undergoing non-cardiac surgery [1]. The risk is highest among patients with a history of myocardial infarction, angina pectoris, congestive heart failure, arterial hypertension or diabetes mellitus, particularly in the elderly and in patients with unstable symptoms, and the effects of these risk factors appear to be additive. On the other hand, among patients undergoing vascular surgery who have none of these features, the combined incidence of perioperative myocardial infarction or death is less than 3%. Peri- and postoperative ischaemia or myocardial infarction are most likely due to an increase in myocardial oxygen demand in patients with coronary obstructions and those in whom coronary plaque ruptures may be triggered leading to thrombosis. Increased catecholamine levels and prothrombotic tendencies that accompany the physiologic stress of surgery play an important part in these events that usually occur in the early postoperative phase [2]. Since beta-blockers directly inhibit the effects of catecholamines thereby reducing myocardial oxygen demand, cardiac arrhythmias, arterial blood pressure and shear stress, they might be particularly helpful in order to prevent cardiovascular complications accompanied with surgical interventions.

The present review discusses the role of beta-blockers in patients suffering from ischaemic heart disease and arterial hypertension that undergo non-cardiac surgery.

Beta-Blockers and Perioperative Myocardial Ischaemia

It has been shown in patients with coronary heart disease or at high risk for it that postoperative myocardial ischaemia may lead to a 2.8-fold increase of all adverse cardiac outcomes and to a 9.2-fold increase of an ischaemic event [1]. Therefore, the authors of this study suggested special attention be focused on the prevention and/or therapy of postoperative ischaemia. As a consequence, two major studies on the effects of beta-blockers on perioperative morbidity and mortality were performed and published.

Atenolol and non-cardiac surgery [3]

This randomised, double-blind trial in 200 patients compared the efficacy of atenolol to that of placebo. Patients undergoing non-cardiac surgery were enrolled when they either had presence of coronary heart disease (CHD), indicated by previous myocardial infarction, typical angina and/or a posi-

tive stress test, or risk for CHD, indicated by at least two of the following risk factors: age > 65 years, hypertension, current smoking, serum cholesterol > 240 mg/dl, diabetes mellitus. Patients received in a randomised, double-blind fashion 30 min before entry into the operating room intravenously either 5 mg atenolol or placebo when heart rate was > 55 beats/min, systolic blood pressure > 100 mmHg, no congestive heart failure, no third-degree AV-block and no acute bronchospasm. When 5 min following the intravenous administration of the first dose of the study drug these criteria were still met the same amount was infused again. Immediately after surgery the study drug was given again in the same way. Starting in the morning of the first postoperative day and each day thereafter until discharge from the hospital, patients received 50 mg atenolol or placebo orally twice daily when heart rate was > 65 beats/min and systolic blood pressure > 100 mmHg. When heart rate was between 55 and 65 beats/min and blood pressure > 100 mmHg one single oral dose of 50 mg atenolol or placebo was given daily. When heart rate was < 55 beats/min or blood pressure < 100 mmHg no study drug was given. All patients underwent operations with general anaesthesia with endotracheal intubation and received complete perioperative standard care and treatment.

192 of the patients were followed for 2 years. Twenty-one patients in the placebo group and 9 in the atenolol group died during the two-year follow-up period, representing a reduction in mortality by atenolol by 55% ($p < 0.02$). The principal effect of atenolol occurred during the first 6 to 8 months after surgery, after 8 months there was no additional substantial difference between the two groups but the existing difference was fully preserved at two years. All cardiac events were decreased in the atenolol group after one year (–67%, $p < 0.01$) and after two years (–48%, $p < 0.01$). Patients with diabetes mellitus had a 4-fold higher risk of death during the two-years follow-up after non-cardiac surgery. However, atenolol reduced this risk by 75% so that the risk of patients with diabetes in the atenolol group was similar to that of patients without diabetes in the placebo group.

More than 85% of patients tolerated the administration of atenolol, and more than 60% received the maximum doses of 10 mg intravenously and 100 mg orally. The oral administration of atenolol was not associated with an increased incidence of hypotension, bradycardia or other events, and the authors emphasised the efficacy and safety of beta-blockade even for patients with heart failure and pulmonary disease.

Based on their observations, the authors calculated that the overall cost per life-year saved with atenolol in patients with CHD undergoing non-cardiac surgery is about USD 2500.

Figure 1 shows event-free survival for two years after non-cardiac surgery in the atenolol and in the placebo group (83 versus 68 %, $p < 0.01$).

Bisoprolol and non-cardiac surgery [4]

This randomised, placebo-controlled trial in 112 patients compared the efficacy of bisoprolol to that of placebo. Patients undergoing vascular surgery (aorta abdominalis or infrainguinal arteries) were enrolled when they were considered at high risk defined by one of the following cardiac risk factors: age > 70 years, angina, prior myocardial infarction, compensated congestive heart failure, current treatment for ventricular arrhythmias, or diabetes mellitus, in addition to a positive result on dobutamine echocardiography. Exclusion criteria were asthma, left main CHD, severe three-vessel CHD, or running therapy with beta-blockers.

Treatment with oral administration of 5 mg bisoprolol or matching placebo once daily was started at least one week before surgery and continued for 30 days postoperatively. The dose of bisoprolol was increased to 10 mg once daily when resting heart rate remained > 60 beats/min. Bisoprolol was withheld when resting heart rate fell < 50 beats/min or systolic blood pressure < 100 mmHg.

The study was interrupted by the safety committee after the first planned interim analysis because of the clear benefit of bisoprolol over placebo which was not attributable to differences between the two groups.

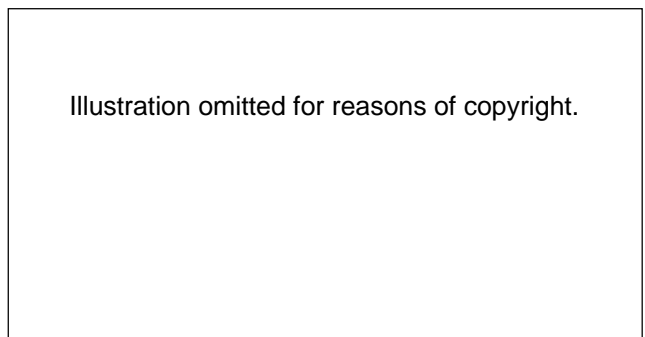


Figure 1. Event-free survival two years after non-cardiac surgery among patients who survived hospital discharge. Atenolol reduced the risk by 48 % ($p = 0.008$), $n = 192$. Reprint with permission from [3]. Copyright © 1996 Massachusetts Medical Society

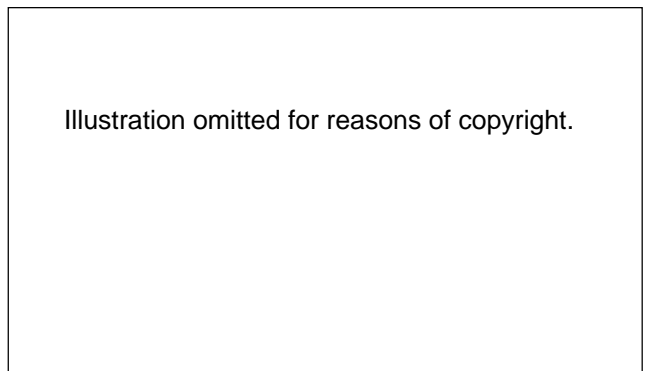


Figure 2. Cumulative percentages of patients who died of cardiac causes or had a non-fatal myocardial infarction during the postoperative period. Bisoprolol reduced the risk by 91 % ($p < 0.001$), $n = 112$. Reprint with permission from [4]. Copyright © 1999 Massachusetts Medical Society

The combined primary end point, death from cardiac causes or non-fatal myocardial infarction, occurred in 34 % of patients in the standard-care group as compared with 3 % in the bisoprolol group, representing a relative risk reduction of 91 % ($p < 0.001$) (Figure 2). 17 % of patients in the standard-care group and two patients in the bisoprolol group died in the perioperative period ($p = 0.02$). 17 % of patients in the standard-care group and none in the bisoprolol group had a non-fatal myocardial infarction ($p < 0.001$). The incidence of the combined primary end-point of this study with bisoprolol, 3 %, appears so low that it even seems likely that the same cumulative morbidity and mortality from three sequential procedures (coronary angiography, coronary revascularization, and then a surgical vascular procedure) would be higher than 3 %. Therefore, the role of coronary angiography and coronary revascularization before non-cardiac surgery might be greatly diminished, particularly since there are currently no data available demonstrating that this strategy improves outcomes [5].

Furthermore, there were additional studies published by several authors using similar protocols with different beta-blockers that revealed beneficial results similar to those in the two studies with atenolol and bisoprolol mentioned above [6–8].

Beta-Blockers and Perioperative Arterial Hypertension

Blood pressure of 180/110 mmHg or higher is associated with an increased risk for perioperative ischaemic events. Therefore, whenever possible, surgery should be delayed until blood pressure has been brought to lower levels. Since surgery is frequently accompanied by stress, and the perioperative risk is, particularly in patients with hypertension, highly related to the adrenergic arousal before, during, and after surgery, it is recommended that patients without prior antihypertensive treatment (and without contraindications) should be best treated with a cardioselective beta-blocker before, during and after surgery. On the other hand, surgical candidates with a currently adequately controlled blood pressure should remain on their regimen [9, 10].

Conclusions

Since cardiac events are a major cause of morbidity and mortality in patients undergoing non-cardiac surgery, and peri- and postoperative ischaemia (including myocardial infarction) is most likely caused by an increase in myocardial oxygen demand due to increased catecholamine levels in the perioperative phase, beta-blockers appear particularly suitable to prevent the deleterious effects of increased catecholamines since these effects are directly inhibited by these drugs. Indeed, during the last years it has been shown repeatedly that beta-blockers are able to decrease the incidence of perioperative cardiac adverse events. Latest results even suggest that it might be appropriate to refrain from interventions of coronary revascularisation (PTCA or CABG) before surgery in patients with proven coronary heart disease, particularly when they have a clear indication for an urgent surgical intervention such as a malignant tumor or an infectious focus which might cause sepsis. In this case the time needed for revascularisation itself as well as pharmacological therapy following these interventions, particularly inhibitors of platelet aggregation such as aspirin, clopidogrel or ticlopidine, might unnecessarily delay surgery and herewith cause disadvantages to patients. As a worthwhile alternative, revascularisation might be performed only after surgery, and instead, beta-

blockers might be used during the complete perioperative phase in order to prevent cardiac adverse events. However, it is clear even in patients with coronary heart disease who undergo non-cardiac surgery that beta-blockers always have to be used with proper care and only when they are really indicated.

References

1. Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. *N Engl J Med* 1990; 323: 1781–8.
2. Eagle KA, Froehlich JB. Reducing cardiovascular risk in patients undergoing noncardiac surgery. *New Engl J Med* 1996; 335: 1761–3.
3. Mangano DT, Layug EL, Wallace A, Tateo I. Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *New Engl J Med* 1996; 335: 1713–20.
4. Poldermans D, Boersma E, Bax JJ, Thomson IR, van de Ven LLM, Blankensteijn JD, Baars HF, Yo TI, Trocino G, Vigna C, Roelandt JRTC, van Urk H. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. *N Engl J Med* 1999; 341: 1789–94.
5. Lee TH. Reducing cardiac risk in noncardiac surgery. *N Engl J Med* 1999; 341: 1838–40.
6. Wallace A, Layug B, Tateo I, Li J, Hollenberg M, Browner W, Miller D, Mangano DT. Prophylactic atenolol reduces postoperative myocardial ischemia. *Anesthesiology* 1998; 88: 7–17.
7. Zaugg M, Tagliente T, Lucchinetti E, Jacobs E, Krol M, Bodian C, Reich DL, Silverstein JH. Beneficial effects from beta-adrenergic blockade in elderly patients undergoing noncardiac surgery. *Anesthesiology* 1999; 91: 1674–86.
8. Urban MK, Markowitz SM, Gordon MA, Urquhart BL, Kligfield P. Postoperative prophylactic administration of beta-adrenergic blockers in patients at risk for myocardial infarction. *Anest Analg* 2000; 90: 1257–61.
9. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VI). *Arch Intern Med* 1997; 157: 2413–46.
10. Kaplan NM. *Clinical hypertension*, 7th edition. Williams & Wilkins, Baltimore, USA, 1998: 248.

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