 DOI: 10.18231/2394-4994.2016.0001

Beta blocker in post cardiac surgery patients

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Abstract

The use of beta blocker drugs already widely given to patients after heart surgery. Management of post-heart surgery requires collaboration between multidisciplinary, such as surgeons, anesthesiologists, cardiologists, and intensivist. Post-cardiac surgery patients may experience some complications. Complications may include arrhythmias usually atrial fibrillation. Beta blockers can be used for the treatment of atrial fibrillation after cardiac surgery.

Keywords: Arrhythmias, Beta blockers, Cardiac surgery

Introduction

Perioperative beta-blocker therapy has the potential to reduce perioperative cardiovascular complications (myocardial ischemia, stroke, heart failure) caused by neutralization of tachycardia and cathecolamine-induced hypertension. Early beta-blocker administration for Cardio Pulmonary Bypass (CPB) or within 10 minutes after release of the aortic clamp can improve the function of ventricle.[(1)]

It has been proven that the discontinuation of beta-blockers before surgery and or early post-surgery in patients who has taken the beta blocker for long period is a strong and independent predictor of the occurrence of postoperative atrial fibrillation (Post-Operative Atrial Fibrillation / POAF) in cardiac surgery. Continued provision of beta blockers until the morning before surgery has been recommended and is currently practiced by most anesthesiologist. Although beta-blocker provision as soon as possible after surgery is usually considered the standard of care that can reduce the incidence of POAF after coronary surgery, in fact it is clinically unclear and there are no clear guidelines that specify the beta-blocker should be given to the period of early postoperative and how it should be given, As a result, the use of beta blockers after surgery vary widely among practitioners and cardiac centers.[(2)]

Population of patients undergoing coronary artery bypass surgery (coronary artery bypass surgery) or CABG increased. There are more than 300,000 CABG operations are performed each year in the United States. With the development of medical therapies and interventional cardiology, life expectancy has increased. Coronary revascularization with CABG surgery technique is the treatment of choice for patients with three vessel coronary disease and low ejection fraction (EF).

Of the 65 377 patients who underwent CABG in New Jersey from 1998 to 2007, the incidence of heart failure after CABG in patients with EF <35% increase over a period of 10 years, but no significant increase in patients with EF ≤ 35%. Mortality is still unchanged from 1998 to 2007, with an average of 1.8% in the hospital and 5.1% and 7.2% at first and second years follow-up. In general, a mortality rate is 3.5% in patients undergoing CABG surgery, and the number will increase to 50% in patients with multiple risk factors. In heart valve replacement surgery, the mortality rate as much as 5.9% on a double valve replacement (aortic and mitral), and 2.3% in aortic valve replacement.[(3,4)]

More and more patients with old age undergoing CABG surgery in Europe and America, are accompanied with poor cardiovascular status and comorbid conditions, such as smoking, type 2 diabetes, kidney disorders, hypertension and cerebrovascular diseases.[(3,4)]

Evidence shows doctors in the ICU (intensivist) has made significant changes in the care of critically ill patients, by reducing mortality by 40%, lowering the time of extubation, reduce complications, infections, and length of treatment, including in cardiac post-surgical patients.[(3,4)]

Nevertheless, it still needs teamwork between intensivist, cardiologist, anesthesiologist and cardiac surgeon in treating post cardiac surgery patients with complex of pathophysiology disorder, metabolic disorders and bleeding caused by CPB, and postoperative complications that may occur.[(3,4)]

Literature Review

Beta blockers selectively bind to the beta-adrenergic receptors and interfere with the ability of catecholamines or other beta sympathomimetic substances to elicit a response. Beta blocker drugs prevent catecholamines and sympathomimetic effects on the heart and smooth muscle of the airways and blood vessels. Beta-blocker therapy should be continued throughout the perioperative period to maintain the desired drug effects and to avoid the risk of hyperactivity of the sympathetic nervous system that is associated with abrupt discontinuation of this medication.[(5)]

Working Mechanism

1. Beta-adrenergic receptor antagonists showed selective affinity for beta-adrenergic receptors, where they act with competitive inhibition (reversible bonding so that the drug can be transferred from the receptors occupied if agonist available in large enough quantities).
2. Provision of chronic beta-adrenergic receptor antagonist associated with an increased number of beta-adrenergic receptors.[5]
3. The disadvantage of beta blockers primarily by their negative inotropic and chronotropic effect attributable to a decrase in central sympathetic outflow and suppression of renin activity, thus it can slow AV conduction and precipitate heart block therefore pacemaker backup should be available when IV beta-blocker are given.

Classification

Beta blockers have varying degrees of selectivity for the beta1 receptor. The drugs with more selective beta, 1 has a less effect on vascular and bronchopulmonar beta 2 receptor. Beta-blockers are also grouped by the number of intrinsic sympathomimetic activity (intrinsic sympathomimetic activity, ISA). Many beta-blockers have little agonist activity; although the drug would not produce a similar effect with full agonists, such as epinephrine, beta-blockers with ISA may not be as good as beta-blockers without ISA in treating patients with cardiovascular disease. In addition, beta blockers can also be classified as drugs that are eliminated by hepatic metabolism (such as atenolol or metoprolol), renally excreted without change (such as atenolol), or hydrolyzed in the blood (such as esmolol).[5,6]

Table 1: Comparative characteristics of Beta Adrenergic Receptor Antagonists

	Propranolol	**Nadolol**	**Pindolol**	**Timolol**	**Metoprolol**
Cardioselectivity	No	No	No	No	Yes
Partial agonist activity	No	No	Yes	No	No
Protein binding (%)	90-95	30	40-60	10	10
Clearance	Hepatic	Renal	Hepatic/Renal	Hepatic	Hepatic
Active metabolite	Ya	No	No	No	No
Half-life elimination (h)	2-3	20-24	3-4	3-4	3-4
First pass hepatic metabolism (%)	75	Minimal	10-15	50	60
Oral adult dose (mg)	40-360	40-320	5-20	10-30	50-400
Intravenous adult dose (mg)	1-10		0,4-2	0,4-1	1-15

	Atenolol	**Acebutolol**	**Betaxolol**	**Esmolol**
Cardioselectivity	Yes	Yes	Yes	Yes
Partial agonist activity	No	Yes	No	No
Protein binding (%)	5	25		55
Clearance	Renal	Hepatic/renal	Hepatic/renal	Plasma hydrolisis
Active metabolite	No	Yes		No
Half-life elimination (%)	6-7	3-4	11-22	0,15
First pass hepatic metabolism (%)	10	60		
Oral adult dose (mg)	5-200	20-800	10-20	
Intravenous dose adult (mg)	5-10	12,5-50		10-80 50-100 mcg/kg/mnt

Source: Stoelting[5]

Pharmacokinetics

1. The main differences in pharmacokinetics among all beta-adrenergic receptor antagonist is a short elimination half-life of esmolol (about 10 minutes) to compare with other drugs.
2. The beta-adrenergic receptor antagonists are eliminated by a few different paths and should consider renal or liver function.
3. Therapeutic plasma concentrations vary greatly between these drugs and between patients (interpatient variability). Explanations for interpatient variability include differences in tone of the basal sympathetic nervous system, dose-response curve to drugs so that changes in plasma concentration generate minimal changes in the pharmacological effects, the impact of active metabolites, and genetic differences in the beta-adrenergic receptors that affect how each patient respond to medications and plasma concentrations.[5]

Side Effects and Limitation

The side effects of beta blockers is the same for all the available drugs, although the amount may vary depending on the selectivity and the presence or absence of intrinsic sympathomimetic activity. The main

contraindication for administration of beta blockers is the atrioventricular heart block or heart failure that is not caused by tachycardia.

1. The cardiovascular system. Beta blockers produce negative inotropic and chronotropic effects. Patients with peripheral vascular disease do not tolerate either peripheral vasoconstriction associated with beta-2 receptor blockade produced by nonselective blocker. The main antidisrhytmic effect is to prevent disrhytmogenic effects of endogenous or exogenous catecholamines or sympathomimetic.
2. Interaction with anesthesia. Additive effect of myocardial depression with beta blockers and anesthetics are not excessive, and treatment with beta blockers can be safely maintained during the perioperative period (possible exception of patients treated with timolol whom profound bradycardia has been observed with the inhaled anesthetics).[5]
3. Esmolol, the ultrafast, short acting beta blocker, must be used with extreme caution when the patient is hypertensive but has a marginal cardiac output, frequently, blood pressure and cardiac output are maintained by fast heart rates at low stroke volume. Use of esmolol in this circumstance will often reduce blood pressure and cardiac output by a negative inotropic effect with little reduction in heart rate.[6]
4. Beta blocker carries non cardiac side effect as limitation of its use i.e.: brochospasm (less with cardioselective beta blockers atenolol and metoprolol), diarrhea, impotence, depression and intermittent claudication.[6]

Use of Beta Blockers

Beta blockers can prevent ventricular arrhythmias in cardiac surgery patients. Esmolol improve the success rate of the auto re-beat, decreased incidence of ventricular fibrillation after the primary re-beat, and maintain delivery and myocardial oxygen consumption balance better without extending bypass. Esmolol treatment did not increase the need for temporary pacemaker to keep the heart rate after bypass. Because it is a beta blocker with a very short duration of action, esmolol rarely reduce heart rate or contractility when administered in the early stages. Additionally, esmolol improve recovery of heart and the balance of oxygen delivery and oxygen consumption of the heart, which increases the myocardial energy storage and thus profitable in weaning process.[8]

More and more doctors tend to use beta blockers to treat a variety of arrhythmias including ventricular arrhythmias in patients with non-cardiac surgery. According to studies, beta blockers had a positive effect on recovery and ventricular arrhythmias in cardiac surgery patients, which showed a beta blocker is another alternative that is useful for rhythm control in patients Cardio Pulmonary Bypass (CPB).[9]

Use of Beta Blockers in Post Cardiac Surgery

Postoperative atrial fibrillation (Postoperative Atrial Fibrillation / POAF) are common after surgery or thoracic and cardiac surgery, and causes increased morbidity, mortality short-term and long-term, the duration of treatment in the intensive care unit (ICU), and health costs. The study reported that the written algorithm is simple and convenient to use, incremental dosage with either oral bisoprolol or intravenous esmolol achieving target heart rate and blood pressure in the ICU.[2]

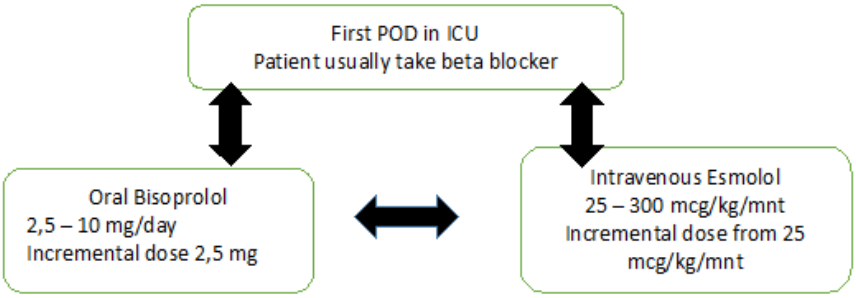

Fig. 1: Algorithm early postoperative beta blockers

Goal of therapy: heart rate 60 -90 bpm and systolic blood pressure > 100 mmHg
Source: Jean-Luc[2]

Beta blockers should be routinely used as a first choice for prophylaxis of AF in all patients undergoing cardiac surgery, unless there are contraindications (Grade A recommendation based on level studies 1a). Sotalol, betaxolol, and carvedilol may be more effective than the propranolol, metoprolol and atenolol for the prevention of AF. On the other hand, carvedilol was found to be more acceptable than other beta blockers because of its relative safety.[11] Amiodarone should be used for the prophylaxis of AF in all patients undergoing heart surgery in which the beta-blocker therapy may not be granted (Grade A recommendation based on level studies and1b 1a).

In high-risk patients who received beta-blocker therapy for the prophylaxis of AF, amiodarone can also be used as an additional prophylaxis with a fairly low incidence of complications. These patients should be protected from the complications bradycardia by placing wire pacing intra-operatively (Grade A recommendation based on level 1b studies).[10,12]

Various types of dysrhythmias may occur, caused by an atrium or ventricle. Atrial fibrillation is the most common dysrhythmia in patients after cardiac surgery. In this case, drugs may be used such as magnesium, digoxin, diltiazem, esmolol, and amiodarone. The use of the beta-blocker drugs would reduce the incidence of postoperative atrial fibrillation or atrial dysrhythmia other. Beta adrenergic receptor antagonist, such as atenolol or metoprolol can be administered on the first day of post operation in the morning.[13]

Installation of temporary pace maker can be used before or after surgery, to increase the heart rate. The incidence of arrhythmia is common in post-cardiac surgery patients, so understanding the mechanism and electrophysiological antiarrhythmic drugs is needed. The rhythm of atrial fibrillation or atrial flutter occurred in 35% of cardiac surgery patients, usually appearing on days 2 and 3 post-surgery. The aetiology is due to atrial distension, pericardial inflammation, increased sympathetic activity, trauma surgery, and unfavorable durability of atrium. To prevent atrial fibrillation, drugs known as beta blockers could be given before the operation. Other medicines (amidaron, magnesium sulfate, digoxin, steroids, diltiazem) are reported useful for postoperative atrial fibrillation.[13]

Discontinuation of beta-blocker in 24-48 hours can lead to a withdrawal syndrome characterized by hypertension (rebound hypertension), tachycardia, and angina pectoris. This effect seems to be caused by an increase in the number of beta-adrenergic receptors (up-regulation).[7] Recovery after heart surgery is very dependent on myocardial function of pre-operative and post-operative related to the anatomy of the coronary arteries. After the operation is complete, the contractility of the heart will be less than before the operation. This is influenced by the severity of chronic and ischemic dysfunction that occurs, the effectiveness and complications of invasive procedures before surgery, as well as intra-operation process. ECG and ventriculography preoperatively provide information related to ischemic processes that occur. Thrombolysis therapy, anticoagulant, anti-thrombosis, nerve and kidney function are taken into consideration for the post-operative management.[14]

Intraoperative incident was attributed to the recovery process, including the management of anesthesia, hypothermia, kardioplegia, and duration of CPB. Ejection fraction <35% and ischemia / myocardial infarction before surgery becomes essential for post-surgery. Patients with outflow obstruction due to cardiac hypertrophy associated with hypertension or aortic stenosis becomes a challenge in the post-surgery period. Early surgery in patients with heart valve surgery reduces postoperative disorder compared with late intervention after disrupted ventricular function.[14]

The management of patients in the ICU, physiological processes that occur are affected by 1) the excess pressure (pressure overload) or 2) the excess volume (volume overload). It will affect the preload, contractility, heart rate, and heart rhythm. So it is very important to optimize the left ventricular preload. In ventricular pressure overload (such as hypertrophy), required considerable volume. After the operation is complete, the myocardium would be on excess pressure due to reduced myocardial compliance. Thus the pulmonary artery pressure will be higher than the preload. In patients with fluid overload (such as mitral insufficiency), blood pressure responses and cardiac index can be used to asses preload adequacy, pulmonary artery pressure less sensitive in this case.[14]

History of the disease prior to surgery, medication therapy, surgical procedures, and medications given during the transfer to the ICU, will determine when the patient's heart rate. Heart rate fluctuation is intolerable in Cardiac hypertrophy or excess pressure patient. Excessive tachycardia reduces ventricular filling time, thus lowering the diastolic volume and cardiac output. With optimal preload, in patients with hypertrophic myocardium, the heart rate was maintained at 90-100 x / min, as well as the need of atrial "kick" for heart rhythm synchrony. Atrial "kick" is the number of extra blood that flowed into the ventricle due to increased atrial pressure when atrial contraction. Usually the number of atrial "kick" is not much, because 80% of the blood already flowed into the ventricle passively.[14]

The heart with excess fluid more tolerance toward the ventricular tachycardia and arrhythmia. Tachycardia (~ 100x / m) be a therapeutic strategy, because of sinus rhythm <77 will prolong diastolic filling, affecting ventricular.12 Preoperative ejection fraction <35%, the degree of hypothermia intra operation <35C, and a long CPB time (> 120 minutes) will affect postoperative contractility, thus requiring hemodynamic support. The decline in myocardial function, depending on the severity and duration, will increase the risk of damage to other organs. Patients with older age are more sensitive to multi-organ damage, especially if accompanied by other comorbid (central nervous system, kidneys, and lungs).[14]

Another study discusses the effectiveness of beta blockers peri-operatively to improve the outcome of patients after cardiac and non-cardiac surgery. Beta-blockers reduce perioperative arrhythmias and myocardial ischemia, but has no effect on myocardial infarction, death, or prolonged hospitalization stay.[7] Post-cardiac surgery patients typically experience hypotension, in this case it is necessary to evaluate preload, contractility, afterload, heart rate and rhythm. If adequate preload is accompanied with sinus rhythm,

hypotension caused by vasodilation or inadequate myocardial function can be given inotropic drugs.[13]

Hypertension can be caused by hypothermia, hypercarbia, hypoxemia, hypoglycemia, inadequate analgesia, and intravascular fluid overload. Could be caused by iatrogenic, such as the delivery of drugs or unnecessary vasoconstrictor. Other causes are the withdrawal symptoms of giving anti-hypertensives, such as beta blockers and α agonisr group.[13] Hypertension occurs in the early phase of post-heart surgery can be treated with rapid onset of action antihypertensive drugs given by continuous infusion. Some drugs can be used, for example nitroglycerin (NTG), which works against dilated veinsa at low dose, and affects the arterial vascular resistance only at high doses. Nevertheless, the heart rate will increase, and arterial resistance (afterload) will be reduced. NTG will reduce the propensity of the coronary arteries to vasoconstrict (spasm) and affects internal mammary artery and the radial artery blood flow. Other drug choice is nitropruside, beta-blockers rapid onset (esmolol), or nitroprusside.[15]

Table 2: Rapid onset antihypertension drug[15]

Drug	Dose	Information
Nitroglycerin	20-300 mcg/mnt or 0, 1-5 mcg/kg/mnt	Improve coronary atery spasm
Esmolol	Loading dose 500 mcg/kg, continuous infusion 50-150 mcg/kg/mnt	Rapid onset, easily titrating, caution in patient with bradycardia and Left ventricular dysfunction
Nicardipin	2, 5-15 mg/hour	Caution in heart conduction disorder, long half-life, difficult to titration
Nitroprusside	0, 1-5, 0 mcg/kg/mnt	Prolong use should be avoided beacause renal toxicity

Source: Lemmer[15]

Another study found that in patients with post-heart surgery, administration of beta-adrenergic (metoprolol) with epinephrine can improve bad memories experiences in males but not in females, while beta-blockade selectively reducing memory for the bad experience postoperative lye and symptoms of post trauma stress disorder (Post-traumatic stress disorder / PTSD) in female.[16]

Conclusion

The management of patients after cardiac surgery can be classified as pharmacological and non-pharmacological. It requires collaboration between multidisciplinary, like the surgeon, anesthesiologist, cardiologist and intensivist. The use of pharmacological in this case is the advantage of beta blocker drugs to manage post-operative atrial fibrillation. Application of the principles in accordance with the protocols used in each center of cardiac surgery is very beneficial for patient recovery and reduced maintenance costs.

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