総 説 (Review)

Anesthesia and Coronary Artery Disease

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The incidence of coronary artery disease and its diagnosis is increasing particularly in well developed countries. It is estimated that 40 million adults in North America have some degree of coronary artery disease. The annual number of patients suffering acute myocardial infarction exceeds 1.5 million and death attributed to CAD exceeds 550,000. Among 25 million operations performed in the United States every year, there are 400,000 cardiac surgeries and it is estimated that 1 milion non cardiac surgery patients have confirmed CAD and 2 or 3 million patients are at a higher risk of CAD. The main risk of anesthesia and surgery in patients with CAD is perioperative myocardial ischemia which is estimated to be about 10% in patients above 65 years old and 5% in patients above 45 years old. The incidence of perioperative MI is definitely related to the age of myocardial infarction. Mortality rate complicating perioperative MI is much higher than mortality rate complicating reinfarction in coronary care units. Perioperative MI is frequently silent and usually occurs during the first three postop days.

Risk Factors

The risk of perioperative MI is related to severity of CAD, left main coronary artery lesion above 50%, presence of congestive heart failure, age above 65 years old and emergency surgery. There is also a high risk of perioperative myocardial infarction in patients who are not previously diagnosed to have CAD as these patients can suffer silent myocardial ischemia and can be asymptomatic during daily life. As patients who have peripheral vascular disease present a very high risk of perioperative MI. It is estimated that over 90% of symptomatic patients with peripheral vascular disease suffer significant CAD and between 50-70% of asymptomatic patients suffer CAD. Generalized atherosclerosis, diabetes and hypertension are very common in patients with PVD and these are significant predisposing factors for CAD.

Perioperative MI occurs with the balance between myocardial oxygen supply and demand becomes negative during anesthesia and surgery. The main determinants of myocardial oxygen consumption includes tachycardia, hypertension, increased ventricular wall tension and increased intraventricular pressure. Tachycardia not only increases myocardial oxygen consumption but also decreases the diastolic filling time and decreases delivery of myocardial blood supply.

Anesthesia management for patients with heart disease should assure continuous myocardial protection by maintaining a positive balance between myocardial oxygen supply and demand, and minimizing myocardial depression to maintain adequate cardiac output for vital tissue perfusion.

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Changing Epidemiology of Patients with CAD

Age

In the last decade, the percentage of patients over the age of 70 undergoing open heart surgery has increased from 0.2% in the early seventies to about 10% in the early eighties and appears to be headed to 30% or more in the 1990s.

As age increases, hepatic blood flow decreases. Hepatic clearance of opioids is flow dependant and clearance of fentanyl approximates hepatic blood flow. In the elderly, microsomal enzyme activity is also decreased. We have observed longer time to extubation in octogenarians after either fentanyl or sufentanil anesthesia. (Ref SCA 1989, Higgins) Increased age attenuates elasticity of blood vessels and barorecepter reflex. The characteristics of the endothelial linings of the blood vessels and the vasoactive substance they secretes are changed. Therefore, it is also expected that the hemodynamics may be less stable during induction of anesthesia as there are more blood pressure fluctuations and a possibility of hypotension.

Reoperations

The percentage of reoperations recently exceeded 20% of all coronary and heart valve surgeries at our institution and similar referral centers. These patients usually have a higher incidence of preoperative ischemia, impaired ventricular function and are of relatively older age groups. The magnitude and duration of surgery is higher than first time surgery. Such higher risk patients with limited reserves mandate ultimate hemodynamic stability to prevent ischmia.

Preop Drug Therapy

Currently, in the last decade, patients who have CAD are receiving new therapeutic modalities, including nitroglycerin, long-acting and short-acting beta blockers and calcium channel blockers.

Beta Blockers

These drugs help to minimize the hemodynamic changes during induction of anesthesia and surgery and lowers the risk of perioperative myocadial infarction. Indeed it is noticed that patients come to the operating rooms with relatively slower HR and don't react to stressful stimuli by much increase in HR and BP should these patient's haven't been receiving their beta blocker therapy. It is our policy to continue beta blocker therapy until the time of surgery. Allow the patient to receive their morning dose and beta blokers can also be used introperatively for treatment of hypertension associated with tachycardia alone particularly in the presence of signs of myocardial ischemia.

Since potent opioids alone are insufficient to protect the myocardium adequately from autonomic sympathetic responses, many anesthesiologists use propranolol, labetalol and esmolol which have been shown effective in preventing heart rate increases during induction and surgical stimulation.

Calcium Channel Blockers

Calcium channel blockers can be potent myocardial depressants as well as peripheral vasodilators, mainly arteriolodilators while having little effect on skeletal muscles. Calcium channel blockers decrease SVR, MAP and myocardial contractility. However, different calcium channel blockers affect these parameters and heart rate to variable degrees.

Verapamil, which is a potent local anesthetic, blocks both the fast and the slow channels and is a potent myocardial depressant and can cause a variable degree of AV block. Diltiazem has negative chronotropic effects and can reduce the HR by up to 10%. Both verapamil and

diltiazem can cause sinus arrest in patients with SA node disease. Nifedipine, and to a lesser degree varapamil, can cause reflex increase in the HR particulary with acute administration. Verapamil and dilitiazem have more negative inotropic effects than nifedipine which is a potent peripheral vasodilator. However, our clinical experience and that of others is that chronic administration of calcium channel blockers is safe in patients receiving anesthesia for open heart surgery.

We also recommend the continuation of calcium channel blockers until the day of surgery but we don't advocate its routine intraoperative use as this may be accompanied by significant hypotension. Should hypotension occur in patients receiving calcium channel blockers it is better to they will require relatively larger doses of vasopressor to restore the BP back since calcium channel blocker can antagonize the alpha 2 effect of the vasopressors. We also recommend continuation of antihypertensive therapy until the day of surgery.

Combined Beta Adrenergic and Calcium Entry Blockade Therapy

This combination has gained favor in the therapy of angina pectoris in patients who are unresponsive to a single agent alone. This combination therapy has been associated with severe conduction disorders (bradycardia, asystole) when anesthesia is induced with potent narcotics. The reflex increase in HR in response to vasodilation produced by calcium channel blockers can increase CO and may maintain MAP. If beta blockers are added that reflex increase in the heart rate will be obtunded. Therefore, the beta blocked patient will also be more vulnerable to hypotension.

Effective blockade by either calcium channel or beta blockers in cardiac patient may be tested by determining the degree of suppression of the cardiac rate response to the "hand-grip" manuver or by the vasodilation and fall in pressure induced by either isoproterenol or sodium nitroprusside. Clinically, the hand grip test can be applied to most patients preoperatively. A modified test is to ask the patient to hold a tight fist, using only the muscles of the forearm, for a period of 1-3 minutes and record any changes of heart rate. Less than a 10% increase in HR indicates a significant degree of blockade.

Clonidine: is an antihypertensive agent and a central alpha 2 adrenergic agonist or antagonist. It modulates efferent sympathetic vasomotor tone, but preserves the sympathetic mediated reflex control of BP. These central sympathetic inhibitory effects result in decreased HR, SVR, CO and BP. In addition to the central sympathetic effects of clonidine, the drug has been shown in animals to have some analgesic properties and to reduce the amount of halothane required for anesthesia. Clonidine interacts centrally with opioid analgesics. Preoperative treatment with clonidine is effective in blocking the cardiovascular reflexes to intubation, more than the combination of lidocaine and fentanyl. Preoperative administration of clonidine reduces the amount of fentanyl required for intubation by 45% and the sufentanil requirement by 40%.

Clonidine treated patients resumed spontaneous ventilation and were extuabated earlier than the non clonidine treated patients. However, there may be a higher incidence of bradycardia that will require treatment. Also, clonidine treatment may be risky in patients with poor ventricular function that is dependant upon a high sympathetic drive.

Advantages of opioid anesthetics for patients with heart disease include decreased heart rate, lack of myocardial depressant effects, maintained "perfusion pressure," attenuated responses to sympathetic stimulation, and minimum changes in heart rate and blood pressure.

Morphine: In the late 60's morphine in large

doses was reintroduced as the main anesthetic agent for patients undergoing heart surgery, mainly for valve replacement. Patients anesthetized with large dose morphine frequently developed hypertension during endotracheal intubation, at skin incision and during the postoperative period, and venodilatation hypotension which required increased volume administration precipitating increased intravascular volume.

This hypotension is related to the rate of administration (10 mgm/minute), histamine release, venodilation, or decrease in SVR. However, morphine anesthesia is not associated with myocardial depression. Morphine anesthesia was also complicated by a high incidence of awareness, prolonged postoperative amnesia and prolonged respiratory depression.

When nitrous oxide was added to morphine anesthesia significant bradycardia, and significant decrease in MAP, CI, LVSW1, and SVR were noted in patient with either valve or coronary artery disease.

Fentanyl: Fentanyl is 60-80 times as potent as morphine. It is a safer and better anesthetic. Fentanyl, like all other opioids, has a negative chronotropic effect and it reduces neural, endocrine and metabolic responses to stimuli. Large dose fentanyl anesthesia (50-75 mcg/kg), with 100% oxygen has no significant effect on ventricular function. All parameters of myocardial function were well preserved with fentanyl anesthesia. Only in vitro can very large doses of fentanyl anesthesia depress myocardial contractility.

Bradycardia caused by fentanyl anesthesia is usually not severe, responds to treatment with anticholinergic drugs and it may not be apparent clinically when vagolytic muscle relaxants such as pancuronium bromide are used. However, the use of pancuronium bromide with fentanyl anesthesia can even result in significant tachycardia and hypertension, particularly in patients not receiving beta or calcium channel blocker therapy.

Fentanyl anesthesia is rarely complicated by hypotension which can be due to severe impairment of ventricular function, blocker therapy or dehydration. With fentanyl anesthesia hypertension of reflex origin has been frequently reported during and after sternotomy. It is a sign of light levels of anesthesia, but increasing the doses of fentanyl do not control the rise in blood pressure ("ceilling effect") and hypertension requires treatment by vasodilators or inhalational anesthetics.

The addition of nitrous oxide to fentanyl resulted in ventricular depression, tachycardia, decreased CO and increased SVR. The addition of diazepam does not block the sympathetic cardiovascular reflexes but may cause vasodilation.

Sufentanil: Between 1980 and 1981 our group studied and compared sufentanil/pancuronium. We reported significant increase in heart rate and blood pressure when metocurine was substituted for pancuronium using the same dose of sufentanil in the prior study there was a lower incidence of tachycardia and hypertension.

In our very early clinical experience with sufentanil/vecuronium, we reported 3 cases of severe bradycardia, even sinus arrest complicating the induction of anesthesia. These patients were receiving both calcium channel and beta blockers. Both sufentanil and muscle relaxant were administered over a short period of time. These incidents emphasized that preoperative drug therapy, the choice of muscle relaxant, and the rate of administration determine the hemodynamic changes observed during sufentanil induction.

This was related to the use of pancuronium and mainly in patients with good ventricular function, not treated by either beta or calcium channel blockers. Unlike fentanyl, hypertension related to sufentanil anesthesia can be minimized or treated by increasing the doses

and by further supplements of sufentanil since there is no ceiling effect.

Due to the short duration of action of sufentanil, patients receiving small doses of sufentanil may have a higher incidence of postoperative hypertension due to early emergence from anesthesia and require blood pressure control by peripheral vasodilators such as sodium nitroprusside.

Currently our clinical experience emphasizes that slow administration of sufentanil for induction, over 2-3 minutes, and the appropriate choice of muscle relaxant produce hemodynamic stability with sufentanil anesthesia.

Muscle Relaxants and Cardiac Surgery

Pancuronium does not cause histamine release or hypotension. Pancuronoium has strong vagolytic chronotropic effects as it tends to increase the heart rate, cardiac output and BP. Tachycardia was less significant when succinylcholine was used to facilitate intubation and only small doses of pancuronium were used to maintain muscle relaxation. Prevention or treatment of tachycardia can minimize the incidence of ischemia.

Vecuronium, Atracurium, Pipecuronium and Doxacurium

Studies by our group and others using different muscle relaxants reaffirmed that they did not cause tachycardia as observed with pancuronium.

Anesthesia management for patients with CAD can be summarized as "myocardial protection." The term myocardial protection emphasizes the need of protecting the myocardium against ischemia and further weakening of heart function. Therefore, it is essential that management of anesthesia does not cause any increase in myocardial oxygen consumption or decrease in myocardial oxygen delivery. This entails maintaining adequate cardiac output that provides optimal myocardial perfusion at minimium cost of myocardial oxygen consumption. Myocardial preservation and protection starts preoperatively and continues into the postoperative period. Both premedication and inducing agents have to be selected very carefully to suit the hemodynamic condition of the patient. There is no single anesthetic agent or regimen that can be used as a standard for all patients. Premendication should provide adequate amnesia and sedation to the patient without affecting or causing a drop in the BP. Inducing agents should be matching between the inducing agent and the muscle relaxant that is used for facilitation of intubation. Usually a combination that provides minimum hemodynamic changes is the best for the patient. Multiple inducing agents are currently available such as opioids, barbiturates, ketamine, propofol, etc. Also there are several muscle relaxants, some of them claim to have no hemodynamic effect such as vecuronium or doxacurium or pipecuronium and pancuronium that increase the HR. A selection of an inducing agent and muscle relaxant that suites the hemodynamic condition of the patient is best choice.

Anesthesia Management

Our anesthesia management for patients with heart disease can be summarized as follows.

All patients presenting to surgery are advised to maintain beta and calcium channel blocker therapy and other antihypertensive treatment to the day of surgery and the morning dose of beta blockers. Preoperative medication consists of a strong analgesic such as morphine sulphate, and an amnesic such as scopolamine in doses adjusted according to the age and clinical condition. Routinely, all coronary artery patients receive transdermal nitroglycerin patches which have effect for 12-24 hours. Induction of anesthesia is usually smooth, with minimal hemodynamic changes and minimal in-

cidence of ischemia as detected by continuous EKG monitoring with ST measurements.

All patients have comprehensive hemodynamic monitoring which includes arterial blood pressure, all parameters that can be obtained from pulmonary artery catheters such as CVP, PCWP, CO, SVR and other calculated indices. Pulse oximetry and temperature changes are also continuously monitored. We continuously display two EKG leads, one of them a chest lead, preferably V5, though practically the leads may be at either V6 or V7. Transesophageal echo can add some advantages in early detection of ischemia particularly in reoperations which require more dissection and manipulation of the heart.

As a guideline to facilitate endotracheal intubation, we use vecuronium bromide for patients with a heart rate >60 beats/min; for slow heart rates, <60 beats/min, we use pancuronium bromide. For induction of anesthesia we use 6-10mcg/kg of sufentanil or up to 50-70mcg/kg of fentanyl. We prefer sufentanil in hyperdynamic patients with high BP or HR. However, due to the extreme variability in ventricular function, blood volume, baroreceptor function, the effect of beta and calcium channel blockade, blood pressure and heart rate fluctuations during induction and anesthesia are not uncommon. Therefore vasoactive drugs such as vasopressors, vasodilators and beta blockers should be available for immediately use during induction and thereafter to immediately adjust any undesirable hemodynamic changes and to prevent any episodes of ischemia.

Anesthesia is supplemented by sufentanil 1-2 mcg/kg every 30-45 minutes or by 5-10 mcg/kg fentanyl every half hour and as needed. Vasodilators are frequently used during surgery to control the BP during dissection of the internal mammary arteries to minimize bleeding, to prevent or control the increase in SVR and to prevent or minimize the incidence of postoperative hypertension. Nitroglycerin is used deliberately in the presence of any signs of ischemia and for control of moderate degrees of hypertension. However, sodium nitroprusside is used more to lower SVR and control hypertension, particularly at the end of surgery.

Neither muscle relaxants nor opioids are reversed at the end of surgery. Their effects are allowed to dissipate while the patient is mechanically ventilated. Over 60-70% of patients do not require ventilatory support after the first 12 hours postoperatively and can be extubated when they are hemodynamically stable. A similar percentage of patients are usually discharged from the ICU on the first postoperative day. Occasional patients who awaken suddenly are treated with additional narcotics, if hemodynamic stability or other reasons proscribe early extubation.

Outcome after cardiac surgery continues to improve, and we believe opioid anesthesia has contributed to the improvement. Further work needs to be pursued into the role of continuing opioid anesthesia and analgesia in the early postoperative period to ameliorate the stress response. The future holds exciting possibilities with the advent of short acting opioids, muscle relaxants and sedative-hypnotics that can be administered by continuous intravenous infusion, allowing the anesthesiologist to precisely time awakening.