Arterial hypertension is not an independent risk factor in cardiovascular complications in noncardiac surgery. Nevertheless, preoperative evaluation is necessary and includes estimation of arterial hypertension grade and possible damage of target organs. In patients with first and second grade of arterial hypertension postponement of elective intervention is not necessary, only optimization of therapy. On the other hand, patients with third level arterial hypertension have benefit if intervention is postponed till the reduction of arterial pressure. There is no indication that any of the antihypertensive drug groups has advantage in the preoperative treatment of hypertension.

Unlike arterial hypertension pulmonary hypertension increases the risk of cardiac morbidity and mortality in the perioperative period. In patients with pulmonary hypertension, anesthesia and surgery may be complicated with heart failure, hypoxia and arrhythmias. Preoperative and postoperative treatments include calcium channel blockers, prostanoids, endothelin receptor antagonists and inhibitors of phosphodiesterase type 5.

Key words: arterial hypertension, pulmonary hypertension, preoperative preparation, non-cardiac surgery.

INTRODUCTION

Cardiovascular causes of morbidity and mortality are very common in patients referred for elective surgery. Besides detection of cardiovascular disease preoperative cardiac evaluation also includes the risk assessment and preoperative preparation in order to reduce the risk for peri- and postoperative cardiovascular complications. This manuscript will present the risk assessment and preoperative preparation in patients with systemic and pulmonary hypertension.

PREOPERATIVE PREPARATION OF PATIENTS WITH ARTERIAL HYPERTENSION

Arterial hypertension is found in one billion people worldwide. In recent decades its prevalence has increased due to increasing number of young and middle-aged patients with metabolic syndrome which often includes arterial hypertension, as well as a growing number of elderly whose pressure is increased in more than 60%1. Arterial hypertension is the major risk factor of coronary artery disease, heart failure, renal and cerebrovascular disease and dementia1-5. The importance of hypertension as a risk factor is best illustrated by the fact that any increase in systolic pressure for 20mmHg and diastolic pressure for 10mmHg from baseline value of 115/75mmHg to 185/115mmHg, in people aged 40 to 70 years doubles the risk of cardiovascular diseases5.

Is hypertension a risk factor for cardiovascular complications in noncardiac surgery?

The answer to this question is not easy at all. According to Goldman et al. arterial hypertension is found in about a quarter of patients who are sent to the surgery6. The first report on the impact of hypertension on the increase of perioperative risk dates back to 1929. In a series of 75 patients with arterial hypertension Sprague et al. showed that the third died in the perioperative period, and about half of them died due to cardiovascular complications7. Since then, numerous studies have been published about this issue8-10. Meta analysis of 30 observational studies that examined the correlation between arterial hypertension and perioperative cardiac risk in patients referred to noncardiac surgery have shown that hypertension increases the risk of cardiovascular events for 1.36 fold compared to normotensive patients11. However, the authors of this meta-analysis concluded that the relationship was statistically but not clinically significant. They found that there was little correlation between pressure values less than 180mmHg for systolic and 110mmHg for diastolic
Preoperative evaluation of patients with arterial hypertension

The first step in the evaluation involves determining whether the patient with high blood pressure values during the preoperative period and who does not know for earlier hypertension actually has hypertension or not. During the initial evaluation of the patient, we can not exclude influence of fear, anxiety and pain on increase in arterial pressure. It is important to identify a possible existence of white coat hypertension. It is defined as a persistent increase in blood pressure during conventional measurements in clinical conditions since the values obtained by the 24-hour ambulatory blood pressure monitoring, and those measured in home conditions are normal. About 15% of the population has this form of hypertension. Cardiovascular risk in these patients is lower than in those with persistent hypertension, but there is evidence that patients with this health problem have higher prevalence of target organ damage and metabolic disorders than normotensive subjects.

Transient increase in blood pressure on admission to hospital for surgical intervention does not require specific therapy in preparation for the upcoming intervention. This also applies to patients who are referred to more serious intervention because invasive (intraarterial) monitoring is possible during these interventions. This monitoring begins immediately before induction of anesthesia and is available in the early postoperative period. This method of arterial pressure measuring is far more precise than the conventional one, especially in the elderly in whom it is sometimes impossible to accurately determine blood pressure due to vascular rigidity. Recently (since 2007), we went a step further, and now we have opportunity for very precise noninvasive continuous measurement of arterial blood which is also used in our country.

The existence of hypertension requires identifying whether this hypertension is primary or secondary. Secondary hypertension is relatively rare but some forms could have serious implications for peri- and postoperative course. This primary refers to pheochromocytoma which is seen in 0.1-1% of newly diagnosed hypertension. It can provoke serious complications during surgery. In patients with pheochromocytoma pharmacological and physical stimuli during and after anesthesia could lead to serious fluctuations of blood pressure which are difficult to control and which may be complicated by myocardial ischemia, heart failure or stroke. Prolonged exposure to excess catecholamine cause vasoconstrictive hypovolemia that is difficult to detect and which can complicate adequate fluid balance. If there is suspicion of pheochromocytoma non-urgent surgical procedures should be postponed until this possibility is excluded. The evidence of pheochromocytoma implies surgical removal whenever it is possible and surgical intervention thereafter. The other possibility is optimal, longer usage of alpha blockers, although in those circumstances it is difficult to predict whether the absolute prevention of blood pressure fluctuations is achieved.

Arterial hypertension is a usual finding in patients with Conn’s syndrome and has been found in more than 80% of patients with Cushing’s syndrome. Two types of hypertension could be differed according to the values of blood pressure, typically systolic blood pressure in Conn’s syndrome is <160mmHg and diastolic blood pressure is >100mmHg, while Cushing’s syndrome systolic blood pressure is >160mmHg and diastolic pressure is mostly <100mmHg. Common to both syndromes is the presence of hypokalemia and possible metabolic alkalosis which should be promptly corrected (especially in the preoperative treatment) in order to reduce the risk of cardiac arrhythmias. A therapy is also different in these two syndromes. Usage of aldosterone antagonists is characterized for Conn’s syndrome, while there is no specific therapy for Cushing’s syndrome. Previous diagnosis of these forms of hypertension may facilitate the application of appropriate preventive measures.

The risk assessment is crucial to determine the severity of hypertension. It is based on the average value of at least two independent measurements. As previously mentioned, in patients with first and second level arterial hypertension, without metabolic and cardiovascular abnormalities, the routine preoperative evaluation is done and there is no reason for further examinations and intervention postponements. In contrast, in patients with third level hypertension, additional examinations are needed because there are evidences that they are at higher risk of target organ damage. Patients with dominant or isolated increase of systolic blood pressure also have a higher risk of postoperative cardiovascular complications. One reason is that systolic hypertension by increase in pulse pressure significantly damages target organs. The other reason lies in the fact that is mostly seen in the elderly where comorbidities are frequent (e.g. pulmonary and renal diseases). Routine preoperative evaluation of newly and previously diagnosed patients with arterial hypertension includes taking data on earlier values of blood pressure and treatment, as well as data that might include a subclinical target organ damage and early cardio, cerebrovascular and renal disease and examination. The tests included in the evaluation are: ECG, chest X-ray, electrolyte levels (especially in patients who have diuretics in therapy), ura
Preoperative preparation of patients with arterial or pulmonary hypertension in noncardiac surgery

and creatinine level for evaluation of renal function and basal hematocrit. When associated diseases - cardio and cerebrovascular and renal - exist, additional evaluation is required. Thus, in suspected coronary artery disease (stable angina pectoris) a stress test should be done (and stress or pharmacologic echocardiographic test in hospitals where it is possible), and coronary angiography when it is necessary (in the case of reduced coronary reserve proven by these methods, unstable or postinfarction angina). When there is suspicion or signs and symptoms of heart failure, an additional test is echocardiography. With suspected or proved cerebrovascular disease, in addition to carotid arteries duplex scan in some situations it is necessary to do the MRI or CT scan. These tests are conducted to determine whether hypertension mediated diseases exist, whether these comorbidities are adequately treated and to adjust therapy for surgical treatment and postoperative recovery.

Postponement of intervention until the correction of pressure values is necessary in patients with third level hypertension, in patients with acute coronary syndrome, decompensated heart failure, serious arrhythmias and severe valvular disease.

Changes in arterial blood pressure during anesthesia and surgery

Chronic increase of arterial pressure is maintained by increased systemic vascular resistance, increased preload, by activation of the sympathetic nervous system and the renin-angiotensin system, baroreceptor denervation, rapid changes in volume, excessive production of serotonin. All of these mechanisms in different ways and to a different degree are included during anesthesia and surgery.

Sympathetic activation during induction of anesthesia may cause increased blood pressure 20 to 30mmHg and heart rate of 15 to 20 beats/minute in normotensive persons. This response to the beginning of anesthesia may be more visible in patients with uncontrolled hypertension. Thus, systolic pressure can rise by 90mmHg and the heart rate by 40 beats/min.

With the progression of anesthesia there is a tendency of a decrease of mean arterial pressure due to the direct effects of anesthetics, reduced tone of sympathetic nervous system, loss of baroreceptor blood pressure control. The result can be the episodes of intraoperative hypotension. In patients with hypertension significant fluctuations in the values of arterial blood pressure may occur which can consequently lead to myocardial ischemia. Significant reduction in blood pressure more than 50% or less than 33% during surgery in the period of 10 minutes is an independent predictor of perioperative adverse events.

Strong sympathetic response during induction of anesthesia which is followed by sinus tachycardia and a significant increase in arterial blood pressure can be seen if the tracheal intubation is difficult or prolonged. Difficult intubation is common in some interventions such as thyroid gland surgery.

Also, chronic hypertension resets autoregulation of cerebral circulation which could cause fluctuations of the arterial pressure and consequently intraoperative and postoperative cerebral ischemia. The level of blood pressure and heart rate in recovery from anesthesia are gradually increasing. In patients with arterial hypertension that increase can be rapid and drastic. It can also cause increase of the risk of cardiovascular and cerebrovascular diseases.

Each operation is associated with stress response. This response is initiated by tissue damage and mediated by neuroendocrine factors, which can induce an increase in arterial pressure and sinus tachycardia. These changes together with fluids changes, in some operations, participate in the development of imbalance between myocardial supply and demand. Surgery also causes changes in the balance of prothrombotic and fibrinolytic factors which may predispose coronary artery thrombosis (increased fibrinogen and other coagulation factors in platelet activation and reduced fibrinolysis). These changes are proportional to the duration of the intervention. All these changes, in high risk patients, may lead to the ischemia and heart failure.

The essence of prevention of adverse cardiovascular and cerebrovascular events in hypertensive patients during anesthesia and surgery is the maintenance of perioperative arterial pressure between 70 and 100% of baseline value and prevention of tachycardia.

Preoperative patient management

Beta blockers: basic mechanism of this group of drugs is the correction of imbalances between myocardia oxygen supply and demand caused by sympathetic stimulation. In addition to favourable negative chronotropic and inotropic effects these drugs also lead to redistribution of coronary subendocardial flow, atherosclerotic plaque stabilization and prevent the occurrence of serious cardiac arrhythmias. However, data on the importance of beta blockers preoperatively are controversial. Two studies have shown mortality reduction in patients at risk of postoperative complications who received beta blockers preoperatively. In contrast, the POISE study has proven the reduction of risk of acute coronary events, but not of stroke and total mortality.

The results of meta-analysis of the benefit of perioperative use of beta blockers are not consistent. Discrepancy in the findings on the benefit of pre- and perioperative use of beta blockers could be due to different types of intervention, differences in the applied beta blocker agent and the way of their application. Despite controversies, the high-risk patients with ischemic heart disease, who have already been on beta blocker therapy, do not stop this therapy and the dose should be titrated according to values of heart rate and arterial pressure level. For those who are unable to take oral medication it is necessary to continue with parenteral beta blockers because termination of this therapy can provoke a rebound reaction. It is also necessary to continue with beta blockers even after the intervention.
In high risk patients referred to vascular surgery, beta-blocker therapy should start at least seven days before the surgery and titrate the dose according the heart rate and arterial pressure\textsuperscript{1,2}.

The advantage is given to the use of beta blockers without intrinsic sympathomimetic activity, with long half-life as bisoprolol\textsuperscript{1,2}. It is necessary to avoid initiation of beta blockers in higher doses on the day of the intervention\textsuperscript{23}. There is no certain evidence about the advantage of these drugs in patients referred to intermediate or low risk surgery.

**Angiotensin converting enzyme inhibitors and angiotensin 1 receptor blockers**: independent of their anti-hypertensive effects these drugs prevent the target organ damage. They repair endothelial function, have anti-inflammatory effect and interfere in atherogenesis\textsuperscript{1}. In spite of these findings, their application in the perioperative period is called into question because of the potential effects on central vagal effects. Application of these drugs alone or in combination with another drugs may cause moderate hypotension and bradycardia 30 min of anesthesia induction, especially when they withdraw less than 10h prior to surgery\textsuperscript{23}. In some patients this may be associated with a reduction in intravascular volume. Thus, it would be perfect to use this kind of therapy constantly until one day before the operation, and not on the day of intervention. Continuation of the therapy after surgery is possible when the patient is euvolemic with low risk of postoperative deterioration of renal function\textsuperscript{2}.

**Diuretics**: thiazide diuretics are commonly used drugs in the treatment of arterial hypertension. Commonly, they are used in a low dose while their effectiveness is moderate\textsuperscript{1}. It is necessary to stop taking these drugs on the day before the intervention because of possible interaction with anesthetic and subsequent loss of volume and hypokalemia. Hypokalemia can cause cardiac arrhythmias and potentiate the effects of muscle relaxants\textsuperscript{1,2}.

**Calcium channel blockers**: in addition to antihypertensive effects non-dihydropyridine may have favourable effect on the balance between supply and myocardial oxygen consumption. Meta analysis of 11 randomized studies that examined the effectiveness of calcium channel blockers (diltiazem, verapamil and nifedipine) found that the use of these drugs in patients referred to non-cardiac intervention reduced the number of episodes of myocardial ischemia and PSVT\textsuperscript{26}.

It is specially emphasized the advantage of using diltiazem. The use of sublingual nifedipine is contraindicated because of the well-known risk of stroke, acute myocardial infarction and death\textsuperscript{1}.

During intervention in the control of blood pressure we can use vasodilators such as nitroglycerin or nitroprusside in addition to deep sedation. Nitroglycerin is given in low dose reduces preload and in high dose reduces afterload. It is also known as the first choice in patients with peri- or postoperative acute coronary events, heart failure and pulmonary edema.

**PREOPERATIVE MANAGEMENT OF PATIENTS WITH PULMONARY HYPERTENSION**

Pulmonary hypertension can be idiopathic or secondary (due to congenital heart defects, in the collagen vascular diseases etc). It occurs in chronic obstructive pulmonary disease and as complication of pulmonary thromboembolism. Since this is a low prevalent disease (15 to 50 cases per 1 million adults), the experience of the potential risks of non-cardiac interventions is poor\textsuperscript{1,2}. Potential perioperative complications of pulmonary hypertension include increased incidence of right heart failure, persistent postoperative hypoxia and arrhythmias and increased mortality.

Patients with pulmonary hypertension are often advised to avoid elective surgery because of the risk of early postoperative sudden death.

In a sample of 2066 patients with pulmonary hypertension referred to bypass surgery it has been shown that the mean pulmonary arterial pressure greater than 30mmHg was an independent predictor of mortality\textsuperscript{27}. Ramakrishna et al. in their study which included 145 patients with pulmonary hypertension who had been referred to non-cardiac intervention found that early mortality (30 days of intervention) was 7% and the incidence of postoperative morbidity was 42%\textsuperscript{29}. The most common causes of early mortality were respiratory failure and right heart failure. The most common were respiratory failure (28%) (pneumonia, hypoxia which required prolonged oxygen therapy or intubation), then arrhythmias (12%) and heart failure (11%).

As predictors of morbidity after non-cardiac interventions the most important are NYHA class II and hig-her, surgical intervention with intermediate and high risk, previous pulmonary embolism, and duration of anesthesia over 3 hours. Independent predictors of mortality in these patients were right ventricul hypertrophy, the ratio between systolic pressure in the right ventricle and systolic blood pressure greater than 0.66 and the Tei index of the right ventricle greater or equal to 0.75.

In a small retrospective study Mina et al. found that the mortality of patients with pulmonary hypertension who had been referred to non-cardiac intervention was 18% and that the failure of the right ventricle occurred in 19% of patients\textsuperscript{29}.

Routine preoperative evaluation of patients with previously proven pulmonary hypertension included ECG and echocardiography.

Generally, the goal of the therapy for pulmonary hypertension is the reduction of symptoms, improvement of stress tolerance and right ventricular function. The therapy includes the use of calcium channel blockers (in patients who have positive acute vasoreactive response), prostanooids, endothelin receptor antagonists and inhibitors of phosphodiesterase type 5. Before the intervention hemodynamic balance should be improved, but the specific therapy should be discontinued 12 hours before the procedure\textsuperscript{22}. In the case of post-operative occurrence or worsening of right heart failure it is necessary to add or increase the dose of administered diuretics and use inotropic support (dopamine) when necessary. In case of inadequate response NO or epoprostenol can be applied. The use of
new specific therapy in the postoperative period did not show benefit12.

CONCLUSION

Satisfying peri-operative evaluation and treatment of cardiac patients referred to non-cardiac intervention requires the collaboration of anesthesiologists, surgeons and cardiologists. In elective surgery an adequate evaluation of the arterial hypertension level, target organ damage and pulmonary hypertension level provide an adequate decision on a possible postponement of intervention and premedication for intervention, which significantly reduces post-operative cardiovascular risk.

SUMMARY

PREOPERATIVNA PRIPREMA BOLESNIKA SA ARTERIJSKOM ILI PLUČNOM HIPERTENZIJOM ZA NEKARDIJALNE OPERACIJE


Za razliku od arterijske hipertenzije plućna hipertenzija povećava rizik od srčanog morbidity i mortaliteta u perioperativnom periodu. Kod pacijenata sa plućnom hipertenzijom, anestezija i hirurgija mogu biti komplikovane srčanom insuficijencijom, hipoksijsjom i poremećajima ritma. Preoperativno i postoperativno lečenje podrazumева primenu blokatora kalcijskih kanala, prostanoida, antagonistа endotelin receptora i inhibitorа fosfodiesterazе tip 5.

Ključne reči: preoperativna priprema, arterijska hipertenzija, plućna hipertenzija, nekardijalne operacije.

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