

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended to serve as a general statement regarding appropriate patient care practices based upon the available medical literature and clinical expertise at the time of development. They should not be considered to be accepted protocol or policy, nor are intended to replace clinical judgment or dictate care of individual patients.

HYPERTENSION MANAGEMENT

SUMMARY

Hypertension is commonly encountered in the surgical patient. Although most commonly related to inadequate pain relief, a variety of other etiologies for either systolic or diastolic hypertension may be seen. An algorithm for hypertension management is presented.

RECOMMENDATIONS

- There is insufficient data to support recommendations on this subject.

INTRODUCTION

Hypertension (HTN) is defined as a systolic blood pressure (SBP) ≥ 140 mmHg or a diastolic blood pressure (DBP) ≥ 90 mmHg. *Hypertensive emergencies* are situations that require immediate reduction in blood pressure secondary to the presence of end-organ dysfunction. *Hypertensive urgencies* require reduction over hours to days. *Hypertensive crisis* is often used to refer to either of these situations.

In general, patients with a history of hypertension should be maintained on appropriate perioperative antihypertensives in anticipation of perioperative exacerbation of their hypertension. Patients in shock who are likely to exhibit inadequate systemic perfusion should have their usual antihypertensives medications held until their hemodynamic status is more stable. Acute hypertension in the postoperative period, in the absence of prior history, is almost always related to pain, anxiety, agitation, or abnormalities of gas exchange or pH.

The acute management of isolated systolic, isolated diastolic, and combined systolic and diastolic hypertension differ. Generally, diastolic hypertension is more clinically important and should be treated first. The primary determinants of systolic blood pressure (SBP) are left ventricular contractility, stroke volume, and Great vessel compliance. The primary determinants of diastolic blood pressure (DBP) are systemic vascular resistance, peripheral run off, and diastolic time interval (heart rate). As coronary perfusion pressure is determined by the difference between DBP and pulmonary artery occlusion pressure (PAOP), overzealous treatment of systolic hypertension with vasodilators may result in a fall in coronary perfusion pressure and development of myocardial ischemia, especially in the elderly patient with coronary artery stenosis. In such patients, it is frequently safer to observe higher systolic pressures in order to ensure adequate myocardial oxygen delivery given the morbidity and mortality of perioperative myocardial ischemia.

Vasodilator infusions should be titrated to mean arterial pressure (MAP) as the dynamic response artifacts of intra-arterial pressure monitoring systems least affect this parameter.

ANTIHYPERTENSIVE MEDICATION REVIEW

Direct vasodilators include nitrates and peripheral vasodilators. The nitrates, sodium nitroprusside (SNP) and nitroglycerin (NTG), have a direct effect on the venous and arterial smooth muscle resulting in smooth muscle relaxation. While SNP exerts this effect equally, NTG has a greater effect on venous tone. Hemodynamic effects include afterload reduction (decreased SVR) and increased cardiac output (CO) in the presence of adequate preload. Preload reduction occurs due to a decrease in venous tone and reduced aortic and left ventricular impedance. A beta blocker is often needed to blunt the baroreceptor response and associated reflex tachycardia. A concept to remember when using SNP is that its degradation products are cyanide and thiocyanate. SNP obtains a sulfhydryl group donated from erythrocytes to form cyanide. This is converted in the liver to thiocyanate, which is eliminated by the kidneys. Hepatic and/or renal failure can lead to accumulation of these breakdown products.

Peripheral vasodilators include hydralazine and minoxidil. The mechanism of action of minoxidil is similar to nitrates, causing venous and arterial smooth muscle relaxation. Hydralazine is a direct arterial vasodilator and effects DBP more than SBP. Both decrease SVR and cause reflexive tachycardia. Minoxidil has a pronounced baroreceptor response and resultant reflexive tachycardia for which beta-blockers may be needed. In hypertensive emergencies, hydralazine may be given intramuscularly in patients without intravenous access.

Beta blockers represent a second class of antihypertensives. Although the exact mechanism by which they is not fully understood, several theories exist. First, CO is reduced through negative chronotropic and inotropic effects on the heart. One can reason that a lower CO lowers blood pressure because blood pressure is the product of CO x peripheral vascular resistance (PVR). A second theory is based on the presence of both alpha and beta adrenergic receptors in the brain. Alpha blockade reduces sympathetic outflow from the brain, reducing blood pressure. It is plausible that beta blockade of adrenergic receptors located on the surface membranes of juxtaglomerular cells reduces renin release. Attenuation of the renin-angiotensin-aldosterone system should reduce blood pressure.

Beta-blockers can be further classified based on cardioselectivity and intrinsic sympathomimetic activity (ISA). Cardioselective agents preferentially block beta-1 receptors. Beta-1 receptors, found on the heart and kidneys, increase heart rate, contractility, and renin release. Beta-2 receptors are found on the lungs, liver, pancreas, and arteriolar smooth muscle. Stimulation causes bronchodilatation and vasodilation. At low doses metoprolol, atenolol, bisoprolol, and acebutolol are cardioselective and safe for us in patients with asthma, chronic obstructive pulmonary disease, peripheral vascular disease, and diabetes mellitus. Beta selectivity is lost at higher doses. Beta-blockers with ISA maintain normal basal sympathetic tone by acting as partial beta agonists. Theoretically, they have an advantage in patients with borderline congestive heart failure, sinus bradycardia, and peripheral vascular disease. This however has not been clinically proven. The major disadvantage of this category is that, unlike the other beta blockers, they do not offer protection in patients suffering acute myocardial infarction. Beta blockers without ISA have been shown in numerous trials to reduce mortality and the incidence of nonfatal reinfarction.

Beta blockers have several adverse effects. Beta-1 blockade of the myocardium may lead to bradycardia, AV conduction abnormalities, or worsening of CHF. Beta 2 blockade of the lung may lead to acute bronchospasm in asthma or COPD patients. Beta 2 blockade in the arteriolar smooth muscle may aggravate intermittent claudication or Raynaud's phenomenon.

Abrupt discontinuation of beta-blockers may produce rebound hypertension, unstable angina, and death. It is prudent to gradually taper the dose over several weeks before discontinuing. In patients without coronary artery disease, abrupt discontinuation may be associated with reflex tachycardia, increased sweating, and generalized malaise. Beta-blockers may also induce glucose intolerance by inhibiting insulin secretion and generating insulin resistance.

Combined alpha and beta blockers, such as labetalol, antagonize alpha, beta 1, and beta 2 receptors. The hemodynamic effect of labetalol is SVR reduction. Due to beta blockade, there is limited reflexive tachycardia and therefore little effect on CO. Labetalol's onset of action is five minutes and its average duration is six hours. The ratio of beta to alpha blockade is 7:1. Labetalol is useful in patients with pheochromocytoma, dissecting aortic aneurysm, cocaine-induced hypertension, alcohol withdrawal, and post-operative hypertension.

Central alpha agonists, such as clonidine, stimulate alpha 2 adrenergic receptors in the brain. This leads to a reduction in sympathetic outflow from the vasomotor center in the brain and an associated increase in vagal tone. As a consequence of reduced sympathetic activity and some enhancement of parasympathetic activity, heart rate, CO, SVR and renin are decreased. In addition, baroreceptor reflexes are blunted. Adverse effects include sodium and fluid retention, rebound hypertension with abrupt withdrawal, sedation, and dry mouth. Clonidine is useful as an adjunct in the treatment of alcohol and tobacco withdrawal.

Peripheral alpha-1 blockers include doxazosin, terazosin, and prazosin. Hemodynamic effects include arterial and venous vasodilatation, resulting in decreased SVR and reflex tachycardia. Adverse effects

include sodium and fluid retention at higher doses. They cross the blood brain barrier and may cause CNS effects such as lassitude, vivid dreams, and depression. An interesting side effect is the so-called “first-dose phenomenon”, characterized by transient dizziness or faintness, palpitations, and syncope occurring within one to three hours after the first dose. These effects are associated with orthostatic hypotension and are minimized by dosing at bedtime. This class of drugs is useful for treatment of refractory hypertension.

Angiotensin converting enzyme (ACE) inhibitors block the conversion of angiotensin I to II. ACE is present in several different cell types. Its principle location is in endothelial cells, making blood vessels the major site for angiotensin II production. Angiotensin II is a potent vasoconstrictor and stimulator of aldosterone secretion. ACE inhibitors also block the degradation of bradykinin and stimulate the synthesis of other vasodilating substances including prostaglandin E2 and prostacyclin. The major hemodynamic effect of ACE inhibitors is the decreased SVR due to increased compliance of large arteries. By increasing large vessel compliance, ACE inhibitors also help prevent and/or decrease left ventricular hypertrophy. ACE inhibitors may induce acute renal failure in patients with bilateral renal artery stenosis or unilateral stenosis with a single functioning kidney. In this population, glomerular filtration is dependent upon the vasoconstrictive effect of angiotensin II on the efferent arteriole.

Calcium channel blockers (CCBs) cause relaxation of cardiac and smooth muscle by blocking voltage sensitive calcium channels thereby reducing the entry of extracellular calcium into the cells. Vascular smooth muscle relaxation leads to vasodilatation and a reduction in blood pressure. CCBs are classified as dihydropyridines and non-dihydropyridines. Non-dihydropyridines include verapamil and diltiazem. These agents slow atrio-ventricular conduction and may result in bradycardia and heart block.

Fenoldopam is a post-synaptic dopaminergic (D1) agonist. It decreases SVR and causing naturesis. Fenoldop-am increases renal blood flow similar to renal dose dopamine but is up to six times more potent in producing renal vasodilatation. The cost of a 48-hour infusion (3mcg/kg/min) exceeds \$1000, as compared to SNP at less than \$15. For this reason Fenoldopam should be reserved for patients with severe HTN with renal failure.

ANTIHYPERTENSIVE INDICATIONS

+ Indicated - Contraindicated

	Labetalol	Enalapril	Hydralazine	ACE-1	SNP	NTG	Beta blocker	Calcium channel blocker	Diazoxide	Minoxidil	Loop Diuretic	Methyropa	Clonidine	Esmolol
Postop HTN	+	+	+											
CrCl < 60	+	+	+	-	-									
Acute MI	+		-			+	+	+	-	-				
Cardiac Insufficiency		+	-			+	-		-					
Hyperactive Airway Disease	-	+				+	-	+						
Pulmonary Edema						+				-	+	-		
Cerebral Infarct	+					-	-	-	-	-		-	-	
TBI	+		-	+	-	-		-				-	-	+
Cocaine Withdrawal	+					+	-							
EtOH Withdrawal													+	
Tobacco Withdrawal													+	

LITERATURE REVIEW

There is insufficient data to support recommendations on this subject.

REFERENCES

1. Erstadt BL., Barletta JF. Treatment of hypertension in the perioperative patient. *Ann Pharmacother* 2000;34:66-79.
2. McKindley DS., Boucher BA. Advances in pharmacotherapy: Treatment of hypertensive crisis. *Journal of Clinical Pharmacy and Therapeutics* 1994;19:163-180.

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