Postoperative Hypertension

Kyle A. Weant, PharmD; Jeremy D. Flynn, PharmD; Kelly M. Smith, PharmD

Postoperative hypertension is a significant complication following surgery that can result in significant complications if left untreated.

Postoperative hypertension is a significant complication that can occur following various types of surgeries and may have significant adverse sequelae. Patients with postoperative hypertension have an increased incidence of neurologic deficits and operative mortality. Postoperative hypertension has an arbitrary definition but can be defined as systolic blood pressure (BP) >190 mmHg or diastolic BP ≥100 mmHg on two consecutive readings following surgery that requires pharmacologic control.

Who’s At Risk?
More than half (60%) of those who exhibit postoperative hypertension have some form of hypertension prior to surgery. Preoperative hypertension is the single most important determinant in the development of postoperative hypertension, increasing the incidence by >20%. Patients can also have a variety of responses following surgery, as data from 100 consecutive endarterectomies demonstrated three different postoperative blood pressure responses including a hypotensive (28), hypertensive (19), and normotensive response (53). Although each patient can present differently, it remains well-established that the hypertensive patient is at greater risk of postoperative hypertension, which is associated with increased morbidity and mortality. This highlights the importance of restarting home medications in all patients, especially in those taking blood pressure lowering medications as they are at increased risk for postoperative hypertensive complications.

Pathophysiology
Postoperative hypertension can be due to a variety of causes. Some of these include pain (30%), anxiety (16%), hypercarbia (15%), hypercapnia, hypothermia, volume overload, and bladder distension. Postendarterectomy hypotension and hypertension appear to represent transient baroreceptor dysfunctions. A significant elevation in epinephrine has been noted just before treatment, with a subsequent decrease within 30 minutes following treatment with antihypertensives. Others have found an elevation in plasma epinephrine and norepinephrine concentrations, suggesting an enhanced sympathetic response to surgery. Studies have found an increase in peripheral vascular resistance and unchanged cardiac output within one hour after surgery. Plasma renin activity was depressed in patients in the hypertensive group, therefore activation of the renin-angiotensin system was not important in the pathogenesis of this postoperative hypertension. This evidence points to a sympathetic trigger in the development of postoperative hypertension.
ative hypertension and therefore poses an ideal target for therapy.6

TREATMENT OPTIONS

The patient should first be assessed for other treatable causes of hypertension such as pain control and anxiety, as well as ensuring that the foley catheter is appropriately posi-

Several oral and parental options exist for therapy. The ideal agent has a moderate duration of activity, rapid onset, and an oral conversion form.

ESMOLOL

Esmolol is a cardioselective beta-receptor antagonist that has a short duration of activity and rapid onset. It has a unique pathway of metabolism that does not rely on renal or hepatic mechanisms. It produces a reduction in systolic blood pressure, mean arterial pressure, as well as heart rate. The typical dose of esmolol is a bolus injection of 500 μg/kg followed by an infusion of 25-300 μg/kg/min.8,9

Labetalol

Labetalol is a medication with mixed sympathetic activity, having both alpha-1-receptor and nonselective beta-receptor antagonism. However, the ability of the drug to result in beta-receptor block-ade far exceeds its alpha receptor antagonism. These differential effects result in its use as an agent that can not only decrease afterload and cause vasodilation, but that also does not result in tachycardia. It has a rapid onset of action, but has a half-life of up to 8 hours, making it less desirable in the treatment of short-lived conditions. Its typical use is at an initial dose of 10-20 mg every 10 minutes up to a maximum dose of 40 mg.8,10

Clonidine

Clonidine is a unique option in that it is available both as an oral and transdermal formulation. It is a centrally acting alpha-2-adrenergic-receptor agonist that reduces sympathetic-nervous-system activity, subsequently decreasing both blood pressure and heart rate.11 Clonidine has a rapid onset of action, approximately 30 minutes to 2 hours, with a duration of 6-8 hours. As yet, no studies have been published on the use of clonidine in postoperative hypertension. The recommend-ed dosage of clonidine for hypertensive crisis is 0.1-0.2 mg orally repeated every hour as needed until a maximum dose of 0.6 mg is reached. The use of the transdermal patch is limited by a delayed onset of action by up to 48-72 hours. It is also important to note that the use of this medication should not be stopped abruptly as this may result in rebound hypertension.11,12

Nicardipine

Nicardipine is a dihydropyridine calcium-channel blocker. This medication has been extensively used in the treatment of postoperative hypertension.13 The dihydropyridine class of medications is selective for vascular smooth muscle and has little effect on cardiac conduction or inotropic activity. The pre-dominant hemodynamic effect is vasodilation of arteri-al resistance vessels, eventually leading to a reduction in vascular resistance and mean arterial pressure.11,14 The typical intravenous dose used is an initial infusion of 10 mg/hr increased by 2.5 mg/hr every 5 minutes to a maximum of 15 mg/hr or until the target blood pressure is achieved. When steady-state is achieved with this medication, often the maintenance dose can be decreased to 2.5 mg/hr.3,13 Although this medication has an oral conversion form, its usefulness is limited by cost, and patients may be converted to another calcium-channel blocker, often amlodipine. Other calcium-channel blockers that have been evaluated for use in postoperative hyperten-sion include oral and sublingual nifedipine. Such use for postoperative hypertension should be avoided as it can result in excessive reduc-tions in blood pressure.15

Nitroprusside

Sodium nitroprusside is an agent that causes vasodilation of both the venous and arterial vasculature. This vasodilatory action results from the metabo-lism of nitroprusside to nitric oxide, a potent vasodilator.16 The onset of action of the drug is rapid and it has a short dura-tion of action.17 One drawback of this medication is that its metabolism results in the for-mation of cyanide, which over time, or in patients with renal dysfunction, can accumulate and cause toxicity.18 The usual starting dosage is 0.25-0.5 μg/kg/min and is increased by 0.5-1.0 μg/kg/min every 5-10 min for more than a few minutes because of the increased risk of cyanide toxicity even in those with normal renal function. In addition, an increased risk of tachyphylaxis exists with this medication and therefore almost constant titration is necessary with its use.8

Fenoldopam

A unique mechanism of action separates fenoldopam from other available options. Approved for the treatment of acute hypertension, fenoldopam is a dopamine-1-receptor agonist that increases renal
blood flow resulting in increased diuresis and nature-
sis. It has been shown to decrease mean arterial pres-
sure, systolic blood pressure, diastolic blood pressure, and systemic vascular resistance. Fenoldopam should be started at an initial dose of 0.1 µg/kg/min and titrated at increments of 0.05–0.01 µg/kg/min to a maximum dose of 1.6 µg/kg/min.

HYDRAZINE

Hydralazine causes prefer- ential dilation of arteriolar smooth muscle. It results in a decrease in mean arterial, sy- stolic and diastolic blood pres-
sure, but has a negative impact on the myocardium by causing an increase in heart rate, car-
diac output, and myocardial contractility. Although this medication exists as a treat- ment option for postoperative hypertension, it should not be used as a first-line agent and should be used with caution in patients with primary cardiac abnormalities. The initial dose is 5–10 mg intravenously and should not exceed 20 mg at any given time.

THE BOTTOM LINE

Postoperative hypertension is a serious complication fol-
lowing surgery that can result in significant complications if left untreated in susceptible patients. The causes of this complication vary but are likely the result of increased sympathetic outflow due to surgery. Several agents exist for the treatment of this condition, including esmolol, clonidine, nicardipine, nitroprusside, and fenoldopam. Esmolol is a rapid acting agent that directly blocks sympathetic activation of the myocardium and results in a decrease in both blood pressure and heart rate. Clonidine is advantageous due to its oral formulation and central activity. Nicardipine, nitroprusside, and fenoldopam are short-acting intravenous formulations that can be rapidly titrated and decrease blood pressure without decreasing heart rate. Longer acting agents that include labetalol and hydralazine may be less desirable secondary to their longer duration of action.

REFERENCES

1. Hogenson KD. Acute postoper- ative hypertension in the hyper-
parison between intravenous nicardipine and sodium nitro-
5. Bove EL, Fry WJ, Gross WS, Stanalod JC. Hypotension and hypertension as consequences of baroreceptor dysfunction following carotid endarterecto-
8. Oates JA, Brown NJ. Antihypertensive agents and the drug therapy of hyperten-
9. Gray RJ, Bateman TM, Czer LS, Conklin C, Matloff JM. Comparison of esmolol and nitroprusside for acute post-car-
13. IV Nicardipine Study Group. Efficacy and safety of intra-
14. Singh BN, Josephson MA. Clinical pharmacology, phar-
15. Grossman E, Messerli FH, Grodzicki T, Kowey P. Should a moratorium be placed on sublin-
16. Geniton DJ. A comparison of the hemodynamic effects of labelalol and sodium nitroprus-
18. Patel CB, Laboy V, Venus B, Mathru M, Wier D. Use of sodi-
20. Varon J, Marik PE. The diagno-
sis and management of hyper-