

# Routine Use of Periprocedural Anticoagulation

The increased safety and efficacy of today's anticoagulants have resulted in regular, often routine, use of anticoagulation during endovascular procedures.

BY GERALD ZEMEL, MD

**T**he emergence of catheter-based interventions as a first-line therapy for an increasing number of arterial and venous disease patients has resulted in a paradigm shift within the medical specialties dedicated to treating these diseases. This shift has required us to rethink and revise some of our previously held standards of care, in obvious ways such as is the case with obtaining advanced training in new skill sets or purchasing dedicated imaging equipment, but also in more subtle areas such as the different pharmacological requirements inherent with new approaches.

In recent years, we have been fortunate to witness the introduction of advanced medications capable of providing patients increased safety before, during, and after their procedures. One example is anticoagulation. The introduction of foreign bodies (eg, catheters, balloons, stents, and other devices) into the vasculature during an interventional procedure increases the thrombotic potential. This thrombotic potential is further increased in procedures during which anything is left behind in the vessel, such as is the case with stenting. To compound matters, there is often a limitation in blood flow ranging from a slight decrease to complete cessation resulting from device introduction, further increasing the potential for thrombosis. A goal of administering anticoagulation is to limit the thrombotic potential during these intervals of decreased blood flow.

## GOALS OF ANTICOAGULATION

Anticoagulation is, of course, not a single medication for a single purpose. Coagulation is a complex process that

has been detailed extensively in the literature, and as such, I will forego further discussion for the purposes of this article. Extraprocedural anticoagulation is in most cases less potent in dosing than during the procedure, as the primary goal before or after the procedure is to prevent platelet aggregation. Although also a significant factor after an interventional procedure, preventing embolization, thrombosis, or any kind of coagulation is the primary focus of procedural anticoagulation.

## TODAY'S OPTIONS

Because of predictable outcomes during a variety of vascular procedures, heparin administration has been the mainstay of procedural anticoagulation for years. Today, however, direct-thrombin and GP IIb/IIIa inhibitors are increasingly being used with encouraging rates of success (ie, bivalirudin, abciximab). Although appropriate heparin dosing can be administered with a remarkable level of security, it requires greater attention to ensure complete and continuous anticoagulation than has been observed with newer agents. Today's direct-thrombin inhibitors, although unable to be reversed the way heparin can, have shorter half-lives and can be eliminated within 60 to 90 minutes. Potential benefits of bivalirudin over heparin include reduced periprocedural thrombosis, more reliable anticoagulation with reduced need for activated clotting time measurement, and less bleeding complications. The randomized coronary intervention trial REPLACE-2 (6,002 patients) demonstrated superiority of bivalirudin over heparin in reducing ischemic events.<sup>1,2</sup>

*(Continued on page 60)*

# Vasopressors

Dopamine versus phenylephrine.

BY JAMES A.M. SMITH, DO

**V**asopressors are a class of drug that induce vasoconstriction and elevate the mean arterial blood pressure. They are different from inotropes, which increase myocardial contractility; however, some drugs have both vasopressor and inotropic effects.

Commonly used in the critical care units and the cath lab, vasopressors are useful when it is critical to elevate the mean arterial blood pressure, such as during septic, hypovolemic, and cardiogenic shock. When it is necessary to elevate blood pressure to perfuse vital organs such as the brain and kidney, vasopressors are particularly helpful.

## MECHANISM

Vasopressors work on the sympathetic nervous system's  $\alpha$ 1-,  $\beta$ 1-, and  $\beta$ 2-adrenergic receptors and on its dopamine receptors. The dopamine receptors are in the renal and mesenteric circulation, the coronary circulation, and the cerebral vascular circulation. When these receptors are stimulated, vasodilation occurs. There is also a type of dopamine receptor that causes vasoconstriction by inducing release of norepinephrine, another pressor.

This comparison of dopamine and phenylephrine offers insights for the use of these important agents. Both are vasopressors, but phenylephrine is a strong stimulant of  $\alpha$ 1-receptors. It causes pure vasoconstriction with little effect on heart rate or cardiac contractility.

As mentioned, dopamine has its own receptors in the mesenteric circulation and elsewhere. The dose response curve for dopamine results in low-dose perfusion to the kidneys and mesenteric vessels while increasing the glomerular filtration rate and urine output. At doses beyond 2 to 10  $\mu$ g/kg per minute, these end organ effects are lost as the vasopressor response increases.

The expected outcome is, simply put, to maintain organ perfusion. It is a given that optimal perfusion pressure for the kidneys is a systolic pressure of at least 90 mm Hg.

To elevate the blood pressure, higher doses are required, but as the dose of dopamine is increased, the mesenteric benefit is lost. It is useful, then, to combine dopamine with another pressor, such as isoproterenol, when the desired effects are renal perfusion and elevation of mean arterial

pressure. This combination minimizes the potential dangers of vasoconstriction by dopamine while avoiding excessive vasodilation by isoproterenol.

## INDICATIONS

In endovascular practice, the time one gets into trouble with blood pressure issues is usually during carotid stenting with protection. The problem is that as the balloon is inflated, it causes a baroreceptor reflex that results in extreme bradycardia, and sometimes very sudden asystole.

As one starts to see bradycardia develop, deflation of the balloon fairly slowly results in recovery of the heart rate while minimizing the potential for embolization. But there are some patients in whom baroreceptor stimulation results in continued hypotension. The problem is that it is often difficult to assess their volume status because of other hemodynamic issues. Many of these patients have had congestive heart failure, and it is difficult at times to determine how much volume they can tolerate. If the patient is euvolemic, that is, they are at dry weight, then the use of vasopressors is very helpful.

Phenylephrine is a pure  $\alpha$ -agonist, and it has no direct effect on either the heart rate or cardiac output; therefore, it produces a strong peripheral vasoconstriction without increasing myocardial oxygen demand. This makes it a very good alternative in patients with severe coronary atherosclerosis.

## DIFFERENCES BETWEEN DOPAMINE AND PHENYLEPHRINE

Simply put, one could say that phenylephrine has a general effect and that dopamine has a local effect, or specific effect, at low doses. The effect of phenylephrine is on  $\alpha$ -adrenergic receptors throughout the body. This results in extreme peripheral vasoconstriction and shunting of blood flow to perfuse vital organs.

## POTENTIAL COMPLICATIONS

With a 1 to 2  $\mu$ g/kg per minute dose of dopamine, a so-called renal dose, increased splanchnic blood flow is achieved. But as dopamine is titrated upward for the benefit

*(Continued on page 60)*

(Continued from page 59)

of blood pressure, the potential for other complications in the peripheral vasculature increases.

Severe peripheral vasoconstriction will compromise arterial flow to a digit or a heel in a patient with advanced peripheral vascular disease, and it can ultimately result in severe ischemic damage and tissue loss.

These potential complications also need consideration in patients with connective tissue disease. For instance, patients with scleroderma and Raynaud's phenomenon can have very severe digital infarctions from sustained vasopressor therapy with dopamine. Therefore, it is advantageous to use a relatively low dose,  $<2 \mu\text{g/kg}$  per minute, of dopamine, but to add a second drug such as isoproterenol to alleviate the problems of peripheral arterial profusion.

Although these conditions may pose complications, they should not necessarily be considered as contraindications for this therapy. When vasopressors are required, it is usually on an urgent basis. Apply your knowledge of the given situation and choose the best therapy at the time. Vasopressors are usually prescribed urgently because they are needed immediately.

An issue regarding phenylephrine is that, as a vasopressor and an  $\alpha$ -adrenergic agonist, it stimulates  $\alpha$  receptors that results in peripheral vasoconstriction, but it may also result in decreased perfusion to other organs, such as the brain and heart. Vasoconstriction in the brain, in the heart, and other vital organs results from receiving phenylephrine in higher doses or as sustained therapy. Phenylephrine is a very useful drug for immediate therapy, and it is an excellent drug for rescue therapy because of its immediate onset of action.

## CONCLUSION

A basic knowledge of these two vasopressors, dopamine and phenylephrine is essential when managing critically ill patients. Although each drug has its own unique potential benefit, the use of combination therapy allows for maximal effects for both splanchnic perfusion and peripheral  $\alpha$ -adrenergic stimulation. Dopaminergic stimulation results in increased mesenteric, brain, and coronary perfusion at low doses; however, this benefit can be lost at higher doses. Doses of dopamine exceeding  $2 \mu\text{g/kg}$  per minute may result in  $\beta_1$ -adrenergic stimulation and may cause dose-limiting dysrhythmias. Maintaining patients on prolonged vasopressor therapy requires close monitoring to avoid detrimental side effects in other target distributions. ■

*James A.M. Smith, DO, is President, Kansas endoVascular Medicine Associates, Wichita, Kansas, and a Fellow in the Society for Vascular Medicine and Biology. Dr. Smith may be reached at (316) 721-1200; james\_smith@via-christi.org.*

(Continued from page 58)

## CONTRAINDICATIONS

Bleeding concerns top the list of potential contraindications to any form of anticoagulation therapy. Administration of these drugs increases the risk of bleeding during the procedure and in the ensuing 24-hour postprocedure period. Of significant concern is any risk of remote intracerebral or retroperitoneal bleeding, which generally have much greater negative impact than do access-site bleeding, hematomas, pseudoaneurysms, etc. Consequently, any patient with known increased bleeding risks should be considered as having a contraindication to anticoagulation, and as such is not likely a good candidate for endovascular intervention. Such patients include those with history of hemorrhagic stroke, recent ischemic stroke, cerebral trauma, and recent major surgery.

Treatment options for patients with recognized contraindications to anticoagulation range from sending the patient to conventional surgery to postponing endovascular intervention for a sufficient period of time to increase the safety margin. The nature of the patient's contraindication, as well as the severity and immediacy of the condition requiring intervention, factor heavily into the decision on proper treatment; if the procedure is elective, it should not be performed in patients demonstrating absolute contraindications to anticoagulation.

## CONCLUSION

Endovascular therapy for peripheral, coronary, and cerebrovascular disease is expanding rapidly. There clearly is a need for predictable and reproducible periprocedural anticoagulation during these interventions. To date, no randomized trials outside the coronary territory and only few registries have compared the newer agents, such as bivalirudin, to heparin. It does appear, however, that procedural anticoagulation by direct thrombin inhibition does provide significant potential benefits over standard heparinization that will likely result in reduced complications and improved outcomes. ■

*Gerald Zemel, MD, is an interventional radiologist at Baptist Cardiac & Vascular Institute, Miami, Florida. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Zemel may be reached at geraldz@baptisthealth.net.*

1. Lincoff AM, Kleiman NS, Kereiakes DJ, et al. REPLACE-2 Investigators. Bivalirudin and provisional glycoprotein IIb/IIIa blockade compared with heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary intervention: REPLACE-2 randomized trial. JAMA. 2003;289:853-863.
2. Lincoff AM, Kleiman NS, Kereiakes DJ, et al. REPLACE-2 Investigators. Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization: REPLACE-2 randomized trial. JAMA. 2004;292:696-703.