Tips from Other Journals

Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

What Is the Best Vasopressor for the Treatment of Shock?

Background: Consensus guidelines recommend that dopamine or norepinephrine be the first-choice vasopressor for patients in shock. Dopamine may increase splanchnic and renal perfusion more than norepinephrine, but observational studies have reported that it is also associated with a greater risk of death. The true benefits of these agents compared with each other are unknown. De Backer and colleagues conducted a multicenter, randomized, double-blind trial to determine if using norepinephrine instead of dopamine could reduce the death rate among patients in shock.

The Study: The authors enrolled 1,679 adult patients in shock (i.e., signs of tissue hypoperfusion despite hydration, with a mean arterial pressure less than 70 mm Hg or systolic blood pressure remaining below 100 mm Hg) who received dopamine or norepinephrine. If hypotension persisted with the maximal drug dosage (20 mcg per kg per minute for dopamine or 0.19 mcg per kg per minute for norepinephrine), open-label norepinephrine was added.

Patients were excluded for serious arrhythmias (e.g., rapid atrial fibrillation [more than 160 beats per minute]) or if they had already received a vasopressor for more than four hours during the current episode of shock. The primary end point was the rate of death at 28 days. Secondary end points included the rates of death in the intensive care unit and in the hospital, and the duration of stay in the intensive care unit.

Results: Septic shock (62.2 percent) was the most common etiology, followed by cardiogenic shock (16.7 percent) and hypovolemic shock (15.7 percent). Baseline characteristics were similar between groups, as were initial mean arterial pressure and the mean time to achieve a mean arterial pressure of 65 mm Hg.

Overall mortality rates were similar; however, subgroup analysis found that dopamine was associated with a higher risk of death in patients with cardiogenic shock. Arrhythmias were nearly twice as common in the dopamine group compared with the norepinephrine group (24.1 versus 12.4 percent), with atrial fibrillation being the most common arrhythmia with either agent. There was nearly a fourfold greater discontinuation rate with dopamine because of severe arrhythmias, compared with norepinephrine (6.1 versus 1.6 percent).

Conclusion: The authors conclude that although there is no overall difference in the rate of death between patients treated with dopamine or norepinephrine, dopamine is associated with more arrhythmias and increased mortality among patients with cardiogenic shock.

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Source: De Backer D, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med.* March 4, 2010;362(9):779-789.

Aspirin After Peptic Ulcer Bleeding: Is It Worth the Risk?

Background: Peptic ulcer bleeding is usually treated endoscopically, then followed by proton pump inhibitor therapy, and the discontinuation of aspirin or other antiplatelet agents until the ulcer heals. The resulting risk of cardiovascular or cerebrovascular events and death is believed to be offset by reducing the risk of recurrent bleeding, but the true risk-benefit ratio is unknown. Sung and colleagues conducted a randomized, placebo-controlled trial to examine the effect of continuing aspirin therapy in patients being treated for peptic ulcer bleeding. ▶

The Study: The authors recruited 156 patients with acute peptic ulcer bleeding who were already on low-dose aspirin (325 mg per day or less) for prophylaxis or treatment of cardiovascular disease. Within 24 hours of bleeding onset, all patients received endoscopic treatment with epinephrine and thermal coagulation, followed by pantoprazole (Protonix; 80-mg bolus intravenously, then 8 mg per hour intravenously for 72 hours, then 40 mg per day orally for the remainder of the study). After endoscopic hemostasis was achieved, patients were randomized to receive 80 mg per day of aspirin or placebo for eight weeks and were monitored for episodes of recurrent peptic ulcer bleeding and cardiovascular or cerebrovascular events.

Patients were excluded if they were using aspirin for primary prophylaxis; had gastric outlet obstruction or ulcer perforation; were taking corticosteroids, nonsteroidal anti-inflammatory drugs, or other anticoagulants; or if hemostasis could not be achieved.

Results: Although the 30-day incidence of recurrent ulcer bleeding was 10.3 percent in the aspirin group and 5.4 percent in the placebo group, the risk comparison was not statistically significant (hazard ratio [HR] = 1.9; confidence interval, 0.6 to 6.0). Total number of units of blood transfused and duration of hospital stay were similar between the two groups. However, the aspirin group had a significantly lower 30-day mortality rate than the placebo group (1.3 versus 9.0 percent; HR = 0.2), with similar estimates of eight-week mortality (HR = 0.2). Mortality caused by cardiovascular, cerebrovascular, or gastrointestinal complications was also lower in the aspirin group (HR = 0.2).

Conclusion: The authors conclude that continuing low-dose aspirin therapy after peptic ulcer bleeding may increase the risk of rebleeding, but it is also associated with a 12 percent reduction in all-cause mortality in comparison with placebo. The protective effect of aspirin (in combination with pantoprazole) seems to outweigh its potential gastrointestinal toxicity in these patients. The authors of this study tentatively suggest that aspirin be stopped for three to five days after the index bleed and resumed after stabilization, because most observed deaths from gastrointestinal bleeding occurred within the first few days after index bleeding. However, confirmatory studies examining the optimal time to restart antiplatelet therapy are needed.

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Source: Sung JJ, et al. Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. *Ann Intern Med.* January 5, 2010;152(1):1-9. ■