Drug Monitor

SSRIs and Bleeding Risk

As the number of prescriptions for selective serotonin reuptake inhibitors (SSRIs) has increased over the past decade, so have reports suggesting a link between the drugs and an elevated bleeding risk. This situation may be exacerbated by the concomitant use of such medications as nonsteroidal anti-inflammatory drugs, aspirin, angiotensin receptor blockers, and clopidogrel.

Given the lack of reliable epidemiologic data demonstrating the incidence of bleeding events in patients treated with SSRIs, a researcher from Johns Hopkins University, Baltimore, MD searched medical literature for evidence of this link. He found over 120 MEDLINE-cited, peer-reviewed research articles and over 50,000 web pages devoted to SSRI-related bleeding events. These sources show that, despite generally favorable safety profiles, all SSRIs exhibit antiplatelet properties and have been implicated in bleeding episodes. There is a strong consensus that blockade of serotonin reuptake affects primary hemostasis, namely platelet activity.

Nevertheless, most of the reports show a predominantly superficial location of bleeding events. Episodes usually are not profound, rarely require transfusions, and generally are resolved when SSRI treatment is discontinued. Severe internal bleeding, including life threatening conditions such as cerebral hemorrhage, is rare.

The author concludes that clinicians should weigh the benefits and potential risks of SSRIs for each patient. Patients with even mild hereditary platelet defects and those being treated with antiplatelet drugs may be more vulnerable to SSRI-induced hemorrhages. Prospective studies, says the author, are "urgently needed" to define the risk in patients taking concomitant long-term SSRI and antiplatelet therapies.

Source: *Am J Med.* 2006;119:113–116.

Can IM Pralidoxime Safely Be Converted to an IV Form?

When administering the nerve agent antidote pralidoxime to seriously ill patients, the intravenous form is preferable to the intramuscular because it enables patients to achieve therapeutic blood concentrations more rapidly. The intravenous form, however, is in short supply in some areas, such as Franklin County, OH, where researchers from Ohio State University and the Central Ohio Trauma System, both in Columbus, were concerned to find only 36 g of IV pralidoxime—less than 4 g per hospital—available for the population of 1.1 million people. (By contrast, the stockpile of IM pralidoxime consisted of 4,398 g, primarily available in nonhospital settings.) In response, they tested a method for converting the drug from an intramuscular to an intravenous formulation for potential use in the event of mass casualties due to nerve agent exposure.

To make this conversion, they used a modified version of the Henretig technique. Five autoinjectors, each containing 2 mL of a 300 mg/mL solution of pralidoxime were injected into sterile, empty 30-mL vials. The vials were vented to prevent pressure buildup. The resulting 3-g (10-mL) pralidoxime contents of each vented vial were used to prepare two concentrations diluted for intravenous administration. One 250-mL, 0.9% sodium chloride injection USP intravenous bag at 8 mg/mL contained 2 g pralidoxime and one 100-mL, 0.9% sodium chloride injection USP bag at 10 mg/mL contained 1 g pralidoxime. Sterility and stability studies revealed that the solution was stable under a variety of environmental conditions at temperatures ranging from –20°C to 50°C for up to 28 days.

The investigators point out that the CDC has established a voluntary program called CHEMPACK in which large quantities of the nerve agent antidotes atropine, pralidoxime (both intramuscular and intravenous), and diazepam will be stockpiled for immediate access, should the need arise. Since the program is voluntary, however, not all hospitals and communities will participate. Those without CHEMPACK stores or IV pralidoxime may benefit from using the conversion process these researchers described. ●

Source: *Ann Emerg Med.* 2006;47:272–277.