Drug Monitor

Rosiglitazone and Broken Bones

Women with type 2 diabetes who receive long-term treatment with rosiglitazone have approximately double the risk of bone fractures than women treated with metformin or glyburide, say researchers for the A Diabetes Outcome Progression Trial (ADOPT).

In ADOPT, 2,511 men and 1,840 women with type 2 diabetes were assigned randomly to receive treatment with one of the three drugs. Only 89 men (3.5%) reported a fracture, and no difference in the fracture rate was found between the treatment groups. By contrast, 111 women (6%) had fractures and, of these, 60 (54%) were taking rosiglitazone—compared with 30 (27%) who were taking metformin and 21 (19%) who were taking glyburide. Both premenopausal and postmenopausal women taking rosiglitazone suffered fractures, although the majority of fractures were seen in the postmenopausal women. Among women who reported a fracture, 18% of those taking rosiglitazone had more than one, as did 17% of those taking metformin and 14% of those taking glyburide.

Although the fractures were predominantly of the limbs, the risk did not seem related to increased falls or accidents: 12% in the rosiglitazone, 17% in the metformin, and 24% in the glyburide groups reported an accidental limb injury or fall within 30 days before the fracture.

The differences between the drugs' effects did not appear until after a year of therapy, which "highlights the value of large, long-term clinical trials," the researchers say. They also point out that, recently, pioglitazone treatment was observed to result in increased fracture risk. Therefore, it's important that patients' bone health be assessed according to standards of care.

The mechanism by which thiazolidinediones increase fracture risk is unclear, note the researchers, although one recent study of rosiglitazone in postmenopausal women without diabetes indicated both an acceleration of bone resorption and a reduction in new bone formation.

Source: *Diabetes Care.* 2008;31(5):845–851.

Degraded Drugs

Drugs commonly carried in ambulances across the country are vulnerable to potentially dangerous degradation, warn researchers from St. John's Hospital and Missouri State University, both in Springfield.

Over the course of one month, they found a statistically significant decrease in concentration of eight of 23 drugs commonly used by paramedics. All of the drugs were exposed to 12-hour cycles of thermal extremes (–6°C and 54°C, both of which were documented as actual temperature points on ambulances) and assayed each week, using high performance, liquid chromatography, for the concentration remaining.

Lidocaine, diltiazem, dopamine, nitroglycerin, ipratropium, succinylcholine, haloperidol, and naloxone all had ending concentrations of less than 90%, with strong correlation to thermal exposure time. The drugs of greatest concern are those with fairly narrow dosing ranges, the researchers say. Although they acknowledge the temperature ranges the drugs were subjected to were extreme, they attest that the ranges are very possible if medications are kept refrigerated before and after being carried on the ambulance.

Source: *Am J Emerg Med.* 2008;26(5):566–573. doi:10.1016/j.ajem.2007.09.004.

Can Ularitide Improve Renal Function in Heart Failure?

Decompensated heart failure (DHF) can result in decreased blood flow to the kidneys, and pharmacologic treatment for DHF can reduce renal function further. Therefore, investigators of SIRIUS II—a phase II, double-blind, randomized, controlled trial to determine the efficacy of ularitide (a synthetic version of the renal natriuretic peptide urodilatin)—studied the drug's ability to preserve short-term renal function in 221 patients with DHF.

Patients received standard therapy plus a single, 24-hour infusion of placebo or ularitide (at dosages of 7.5, 15, or 30 ng/kg/min) and were monitored for two days. Ularitide 15 ng/kg/min reduced serum blood urea nitrogen levels, rapidly elevated cardiac output (CO), reduced right atrial pressure (RAP), and maintained mean arterial pressure (MAP).

Although the elevation in CO and reduction in RAP were most pronounced in the group that received the ularitide 30 ng/kg/min infusion, that dosage also lowered blood pressure more markedly and reduced MAP to below 70 mm Hg more frequently. According to the researchers, these effects may counteract those of RAP reduction and CO elevation and negatively affect renal function, which may make the lower ularitide dosage the better option.

No patient required dialysis throughout follow-up, and only one patient had a serious adverse renal effect—which probably was unrelated to ularitide. The researchers say assessment of long-term renal function needs to be completed. ●

Source: *Am Heart J.* 2008;155(6):1012.e1–1012.e8. doi:10.1016/j.ahj.2008.02.011.