Intrarenal Fenoldopam May Protect Kidneys

BY MICHIEL L. ZOLER

Hollywood, Fla. — Targeted renal therapy with the vasodilating drug fenoldopam was effective for treating acute kidney injury and for preventing contrast-induced nephropathy in results from a large, randomized trial.

By infusing the drug directly into patients’ renal arteries with a specially designed catheter, targeted therapy allows the use of a substantial dose of fenoldopam mesylate while avoiding systemic adverse effects such as hypotension, Dr. James A. Tumlin said at ISET 2009, an international symposium on endovascular therapy.

He reported treating a series of 28 patients with the drug, and made incandescent use of acute kidney injury. Their average serum creatinine level at entry into the study was about 1.7 mg/dL. Many of the patients had one or more comorbidities, with 57% having respiratory distress, 46% on mechanical ventilation, 39% having sepsis, and 39% with a left ventricular ejection fraction less than 35%.

All patients received intrarenal fenoldopam via a Benepath peripheral vascular catheter, made by FlowMedica Inc. The catheter is designed to infuse both renal arteries with a single device, and was approved by the Food and Drug Administration in late 2008 for targeted renal therapy in patients at risk for developing acute kidney injury. Dr. Tumlin is a consultant to and has received grant support from FlowMedica.

Their goal dosage was a fenoldopam infusion of 0.6-4 mcg/kg per minute, and the median maintenance dose was 0.39 mcg/kg per minute, with a maximum dose given to any patient of 0.8 mcg/kg per minute. The target duration of treatment was 48 hours, and the actual average duration was 42 hours, with a maximum of 72 hours.

Renal recovery, defined as a fall in serum creatinine, occurred in 17 patients (61%) by the fourth day after treatment, and in 27 (96%) of patients by a week after treatment. Three of the 11 patients (31%) died during follow-up, and another four patients (14%) required dialysis during follow-up. (This was an unusually low mortality rate) compared with the 12% mortality rate from a previous trial of patients treated with a similar drug in placebo-controlled studies.

“Anesthesia and Major Surgery

Bronchospastic Diseases

Setting of congestive heart failure, and sick sinus syndrome (unless a permanent pacemaker is in place), or severe

BYSTOLIC should be used with caution in patients with moderate hepatic impairment (Child-Pugh Class B or C), and in patients who are hypotensive or anaphylactic.

Nebivolol exposure increases with inhibition of CYP2D6 (see Interactions).

Thyrotoxicosis

Anesthesia and Major Surgery

Azathioprine, myelosuppressive agents, and inhibitory mononuclear cell-mediated immunity. These adverse events were in most cases observed at a similar frequency in placebo-treated patients in the controlled studies.

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In a two-year study of nebivolol in mice, a statistically significant increase in the incidence of testicular Leydig cell hyperplasia and adenomas was observed at 0.06 mg/kg/day and higher, which was consistent with an indirect LH-mediated effect of nebivolol in mice and not evidence of a tumorigenic effect was observed in a 24-month study in Wistar rats.

Peripheral Edema

Nebivolol is contraindicated in patients with severe bradycardia, heart block greater than second degree, sick sinus syndrome, and in patients with marked intracranial pressure.

The second experience using intrarenal fenoldopam presented at the meeting included data from 593 patients who were enrolled in a targeted renal therapy registry. The series included 340 patients who were treated with fenoldopam and another 190 patients who were receiving fenoldopam and were treated with other drugs or therapies. The registry included patients who were treated for acute kidney injury that they developed following coronary artery bypass grafting.

Intrarenal fenoldopam was given to 94% of the registry’s patients, at a median dose of 0.4 mcg/kg per minute, with a range of 0.05-0.8 mcg/kg per minute. The remaining patients received another drug, such as sodium bicarbonate, reported Dr. John H. Rundback in a separate talk. The median duration of the fenoldopam infusion was 48 hours.

The registry outcomes showed that the 0.05-0.8 mcg/kg per minute dose was much more effective than a 0.2-0.8 mcg/kg per minute dose for preventing contrast-induced nephropathy, and that for treatment that at an hour was more effective than a briefier, said Dr. Rundback, an interventional radiologist and director of Cardiac Catherization and Interventional Cardiology at Sri Holy Family Hospital in Chattanooga, N.J. Dr. Rundback has been a consultant to and a member of the scientific advisory board of FlowMedica.