Intrarenal Fenoldopam May Help Protect Kidneys

BY MITCHEL 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 pair of studies.

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 oliguria and diuretic-unresponsive acute kidney injury. Their diuretic unresponsiveness was defined as a failure to double their urine output after a single bolus dose of 80-120 mg furosemide. 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, 43% having sepsis, and 39% with a left ventricular ejection fraction less than 35%.

All patients received intrarenal fenoldopam via a Benephit 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 0.4 mcg/kg per minute, and the actual average dose used 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 patients (11%) died during follow-up, and another four (14%) required dialysis during follow-up. (None of the dialysis patients died.) "This was an unusually low mortality rate," compared with the historic experience with similar patients who did not undergo renal infusion with fenoldopam, said Dr. Tumlin, a nephrologist and professor of medicine at the University of Tennessee in Chattanooga.

The second experience using intrarenal fenoldopam that was 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 to prevent contrast-induced nephropathy and another 40 patients who were treated for acute kidney injury that they developed following coronary artery bypass grafting. The patients had been treated by 38 different physicians at 19 medical centers.

Intrarenal fenoldopam was given to 94% of the registry's patients, at a median dosage 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 at the meeting. The median duration of the fenoldopam infusion was 180 minutes.

Patients who received fenoldopam had 'an unusually low mortality rate.'

DR. TUMLIN

Bilateral renal-artery catheterization was performed successfully in 95% of the registry patients, a procedure that took an average of 2 minutes. Five of the 593 patients in the registry (0.8%) had a complication from renal-artery catheterization: Three had groin complications (the catheter is often inserted through the femoral artery), one had a renal-artery dissection, and one developed hypotension.

Registry outcomes showed that the 0.4-mcg/kg per minute dosage was much more effective than was a 0.2-mcg/kg per minute dosage for preventing contrast-induced nephropathy, and that treatment for at least an hour was more effective than a briefer infusion, said Dr. Rundback, an interventional radiologist and director of the Interventional Institute at Holy Name Hospital, Teaneck, N.J. Dr. Rundback has been a consultant to and a member of the scientific advisory board of FlowMedica.

The predicted incidence of contrast-induced nephropathy was about 27%, yet the rate among 268 patients who were treated with at least 0.4 mcg/kg per minute of fenoldopam for at least 1 hour was less than 1%, Dr. Rundback said. ■

Volume Cuts Renal Artery Bypass Deaths in Low-Risk Patients

BY BRUCE JANCIN

TUCSON, ARIZ. — In-hospital mortality for renal artery bypass in low-surgical-risk patients was more than fourfold greater at low-volume than at high-volume hospitals across the nation during a recent 6-year period.

However, among patients at intermediate or high surgical risk, in-hospital mortality for renal artery bypass (RAB) did not vary significantly based on a hospital's RAB volume, Dr. J. Gregory Modrall reported at the annual meeting of the Southern Association for Vascular Surgery.

This latter finding came as a surprise. The study hypothesis was that a high hospital RAB volume is a proxy for greater surgical team expertise, which was expected to translate into improved outcomes, explained Dr. Modrall of the department of surgery, University of Texas at Dallas.

He and his coinvestigators analyzed the Healthcare Cost and Utilization Project Nationwide Inpatient Sample, the nation's largest all-payer inpatient database, with more than 1,000 participating U.S. hospitals. During the years 2000-2005, they identified 7,413 patients who underwent RAB. The frequency of the operation was 3.2 cases per 100,000 discharges.

Dividing the hospitals into tertiles based on annual RAB volume, the investigators defined low-volume centers as those doing fewer than two per year, medium-volume hospitals as those doing two to five annually, and high-volume hospitals as those doing more than five.

For decades RAB has been a treatment mainstay for renal artery stenosis with presumed renovascular hypertension or ischemic nephropathy. However, according to Dr. Modrall's Nationwide Inpatient Sample analysis, the annual number of RABs performed plummeted by 49% between 2000 and 2005.

The lowest-risk patients had a mortality of 6.4% in low-volume hospitals and 1.5% in high-volume hospitals.

DR. MODRALL

Overall national in-hospital mortality for RAB was 9.6%. There was no significant difference in crude rates based on hospital volume: 9.9% in low-volume, 10.5% in medium-volume, and 8.2% in high-volume centers.

However, it was a different story after adjustment for patient risk profile. In an earlier study, Dr. Modrall and his colleagues identified five independent risk factors for in-hospital mortality with RAB: advanced age, female sex, and a history of chronic renal failure, heart failure, or chronic lung disease.

When the investigators adjusted for risk factor level, patients in the lowest-risk quartile had an in-hospital mortality of 6.4% in low-volume hospitals, 3.7% in medium-volume hospitals, and 1.5% in high-volume hospitals.

In the remaining quartiles of patient risk, however, there was no significant difference in mortality based on hospital volume. For example, patients in the second-highest risk quartile had an in-hospital mortality of 9.9% in low-, 7.8% in medium-, and 11.9% in high-volume hospitals. Among those in the highest-risk quartile, the rates were 15.2%, 20.2%, and 16.3%, respectively.

In a separate multivariate analysis with hospital RAB volume as a continuous variable, there was a 2% decrease in the risk of in-hospital mortality for each additional RAB done per year at a hospital.

"If you have two hospitals operating on precisely the same patient population and one does six cases per year and the other does five, the hospital that does six bypasses per year will have a 2% lower risk of in-hospital mortality," Dr. Modrall said.

These findings have important implications for patient management, the surgeon stressed. "Surgeons who practice in a low-volume hospital may want to consider lower-risk alternatives: transferring the patient to a high-volume referral center with documented expertise in renovascular surgery, or performing renal artery stenting, or even medical management. And certainly if you do contemplate doing renal artery bypass operations, I would strongly urge you to consider the five components of patient risk," he said.

Dr. Bruce A. Perler, a study discussant, observed that Dr. Modrall's "somewhat sobering study" illustrates a key point: "There's no area of vascular surgery where percutaneous angioplasty has had a more profound impact than in renal artery occlusive disease."

It's counterintuitive that high-volume hospitals, which do so much better with low-risk patients, don't also achieve better results with higher-risk patients, noted Dr. Perler, professor of surgery and chief of vascular surgery at Johns Hopkins University, Baltimore.

Dr. Modrall said he thinks patient risk factors are the major determinant of in-hospital mortality. In low-risk patients, surgical expertise as reflected in hospital RAB volume can make a big impact. Not so in heavily risk-laden patients.

"Patients who are high risk have so many risk factors that it really doesn't matter where they have their operation—they're probably going to have relatively poor outcomes," he explained. ■