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Impact of Preoperative Nesiritide on Renal Function after Mitral Valve Surgery

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ABSTRACT

Nesiritide, a recombinant B-type natriuretic peptide used for the intravenous treatment of acute decompensated congestive heart failure. Concerns have been raised about the long-term use of nesiritide, but data is scarce regarding its use in acute congestive heart failure and during cardiac surgery. We conducted a retrospective data review to address the safety of nesiritide for pretreatment of patients undergoing mitral valve surgery

BACKGROUND

Nesiritide (Natrecor®; Scios, Freemont, CA, USA) is a recombinant B-type natriuretic peptide released by cardiac myocytes that regulates cardio-renal hemostasis. The main pharmacologic property of nesiritide is pulmonary vasodilatation, and it is approved by the US Food and Drug Administration for the intravenous treatment of acute decompensated congestive heart failure (CHF) [Dunavant 2002]. Recently however, some concerns have been raised regarding possible increased mortality [Sackner-Bernstein 2005] as well as impaired renal function [Wang 2004] when nesiritide is used in long-term CHF therapy. It appears that only very scarce data exists on its use in the setting of acute CHF, and even less for patients undergoing cardiac surgery, especially pulmonary hypertensive patients with mitral valve disease. After encouraging results were obtained in a pilot series for preoperative hemodynamic optimization in an intensive-care setting [Salzberg 2005], a subsequent protocol was implemented for routine preoperative nesiritide treatment for selected patients. Institutional review board approval was obtained for this retrospective data review, and informed consent was waived. The objective of this report was to address the safety in terms of outcome and focus on renal function after pretreatment with nesiritide for mitral valve surgery.

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CLINICAL SUMMARY

Data collection was prospectively conducted from May 2003 to July 2005 on patients with pulmonary hypertension undergoing elective mitral valve surgery. Initially patients were enrolled in a pilot trial (n = 14) [Salzberg 2005]. Once we were convinced of the safety and efficacy of this approach in the intensive-care unit setting, we repeated the investigation in a second similar group (n = 28). These patients underwent routine drug infusion on the regular hospital ward before surgery (Table). Mean EuroSCORE for this patient population was 13.43% ± 12.47%. Drugs were administered upon admission to the regular ward, usually the night prior to

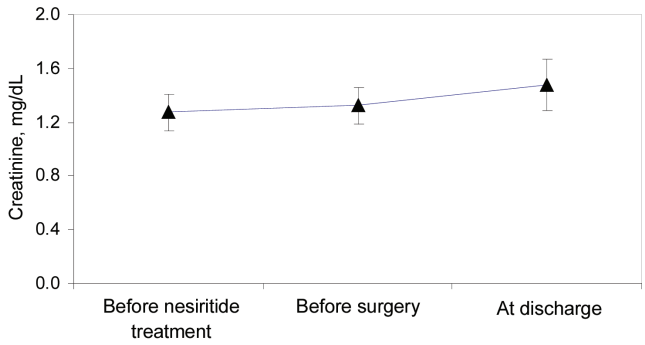

Figure 1. Creatinine levels at 3 different time points.

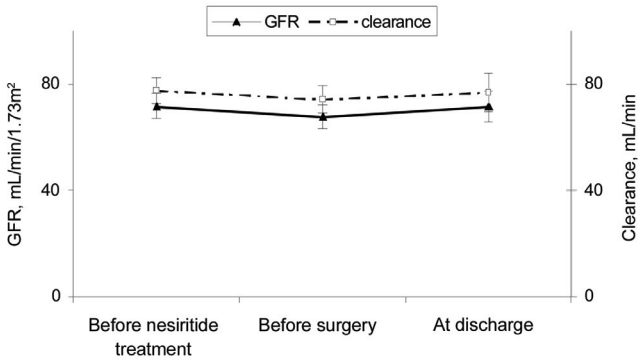

Figure 2. Creatinine clearance and glomerular filtration rate (GFR) at 3 different time points.

Patient Demographics and Outcomes

Patients		n, %
Female/male		23/19
Median age, y		71 (range 23-87)
Reoperation	×1	11 (32)
Atrial fibrillation	×2	5 (16)
Diabetes		7 (22)
Hypertension		11 (32)
Previous myocardial infarction		12 (37)
Chronic obstructive pulmonary disease		8 (25)
EuroSCORE, %		3 (9)
Outcomes		13.4 ± 12.5
Mortality	Cause	
Morbidity	Multiorgan system failure	1 (3)
	Respiratory failure	3 (9)
	Sternal infection	1 (3)
	Renal failure	1 (3)
	Stroke	1 (3)

surgery. After baseline values for systemic blood pressure and heart rate were recorded, the drug was initiated. After a loading dose of 2 µg/kg, nesiritide was started at 0.01 µg/kg per min intravenously as a continuous infusion, as described per the package insert. No changes to dosage were done during the study period. The infusion was discontinued if persistent systemic hypotension occurred. No other drug was administered during the preoperative study period. The use of nesiritide was discontinued when the patient was taken to the operating room. Postoperative nesiritide was administered on patient arrival in the intensive-care unit, at 0.01 µg/kg per minute intravenously on a continuous infusion, identical to the preoperative rate in selected patients. Renal function was assessed at 3 serial time-points (admission, preoperative, and predischarge) with the following variables: plasma creatinine, creatinine clearance, and glomerular filtration rates (GFR). The therapy was well tolerated in all patients. None of the patients suffered from hypotension or arrhythmias, no discontinuation or dose changes were necessary, and no adverse drug-related events occurred. Prior to surgery, the drug was given for a median of 44 hours (range 6-258 hours), with a prolonged duration of therapy (>72 hours) occurring in 10 patients. Operative and in-hospital mortality was 2.4% (n = 1, multiorgan system failure). Postoperatively, 3 patients (7.3%) developed respiratory failure and 1 patient (2.4%) required temporary dialysis for fluid overload after a prolonged cardiopulmonary bypass time. No significant changes in renal function were documented in any patients during the entire study period. Mean creatinine levels were 1.3 ± 0.9 mg/dL before nesiritide treatment, 1.3 ± 0.9 mg/dL before surgery, and 1.5 ± 1.2 mg/dL at discharge and did not change significantly (*P* value not significant) during the study period (Figure 1). A mild, but insignificant (*P* value not significant) decrease was noted in GFR from 71.6 ± 30.8 to 67.7 ± 29.0 mL/min per 1.73m^2 after nesiritide infusion. These depressed values returned to the prenesiritide levels before discharge, 71.5 ± 38.4 mL/min per 1.73m2 at discharge for GFR (Figure 2).

DISCUSSION

In patients with pulmonary hypertension undergoing mitral valve surgery, we have shown that preoperative nesiritide is safe and effective. We have obtained excellent short-term outcomes after surgery (especially as indicated by EuroSCORE); moreover, it appears that despite cardiopulmonary bypass, no significant changes in renal function occur. Even though the number of patients was limited in this trial, we believe that preoperative nesiritide may be beneficial and does not negatively impact renal function in this patient population.

Concerns raised by recent reports of negative effect on renal function and increased mortality [Dunavant 2002] in chronic CHF patients must be put in the context of physiopathology of the underlying condition. Our population was composed of patients with organic mitral valve disease and secondary acute renal insufficiency, as opposed to CHF patients whose peripheral organs are exposed to a state of chronic low output. However, more in line with our findings, a recent drug utilization study [Cheng 2005] confirms our findings that nesiritide does not negatively impact renal function. Our results are encouraging, but must be taken with caution owing to our limited numbers and the absence of a control group. Our experience does, however, lead to the conclusion that preoperative nesiritide use is safe for patients with pulmonary hypertension undergoing mitral valve surgery. We believe that nesiritide may play some part in obtaining excellent short-term surgical outcomes by optimizing ventricular loading conditions in addition to having a potential beneficial paracrine effect. Additional randomized prospective studies of nesiritide on larger patient populations should be performed to better characterize efficacy and safety of this novel therapeutic approach.

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