AJNT

Original Article

Low Incidence of Contrast Induced Nephropathy after Coronary Angiography in Patients with Advanced Chronic Kidney Disease Treated with Prophylactic Continuous Veno-venous Hemofiltration

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Abstract

Introduction: Contrast-induced nephropathy (CIN) is associated with increased risk of in-hospital morbidity and mortality. The purpose of this study was to find out whether continuous venovenous hemofiltration (CVVH) after coronary angiography in chronic kidney disease (CKD) patients is associated with a lower incidence of CIN than that reported in the literature.

Methods: All patients with CKD who underwent coronary angiography in the Chest Disease Hospital, Kuwait, between January 2004 and December 2005 were treated by CVVH after the procedure. Renal function was assessed before and after the procedure.

Results: A total of 98 patients were enrolled in the study, 52 (53.1%) of whom were males. Their mean age was 60.7 years. Before the procedure, the mean serum creatinine level was 4.65 mg/dl and the mean creatinine clearance (Cr Cl) was 18.04 ml/min. Patients underwent CVVH for a mean duration of 21.3 hours, after a mean time-interval of 44.3 min. Their mean serum creatinine was 4.57 mg/dl at discharge (within the first week after the procedure) and 4.78 mg/dl at 15 days after the procedure. Mean Cr Cl was 18.52 ml/min at discharge and 17.62 ml/min at 15 days after the procedure. There was no statistically significant difference between the mean serum creatinine and Cr Cl values before and after the procedure. However, one patient (1.02%) developed CIN and ended on regular hemodialysis. The in-hospital mortality was 0%.

Conclusion: Patients with advanced CKD who undergo coronary angiography may be protected from further deterioration in their renal function after exposure to radiological contrast material if the procedure is immediately followed by CVVH. A randomized controlled clinical trial is needed to verify our encouraging results.

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Introduction

The incidence of contrast induced nephropathy (CIN) is now increasing, owing to the growing use of radiocontrast media (CM) in diagnostic as well as interventional procedures [1]. The most widely accepted definition of CIN is an increase of 25% or more, or an absolute increase of 0.5 mg/dl or more in serum creatinine from base line values at 24-72 hours following exposure to CM [2]. CIN is one of the leading causes of hospital acquired acute renal failure (ARF) and is associated with increased morbidity and mortality [3].

Among all procedures utilizing CM for diagnosis or therapeutic purposes, coronary angiography and percutaneous coronary intervention (PCI) are associated with the highest incidence of CIN [1]. The overall incidence of CIN in the general population is reported to be 0.6-2.3% [4]. However, in several patient subsets the prevalence of CIN is significantly higher [5, 6]. The incidence of CIN in patients with underlying chronic kidney disease (CKD) is extremely high, ranging from 14.8% to 55% [6-8]. The higher the base-line creatinine value, the greater is the risk of CIN [9]. Nevertheless, an increasing number of patients with CKD are being referred for PCI, owing to the greater prevalence of cardiovascular diseases among this group of patients [10]. CIN is a potentially reversible condition, however, currently available strategies, such as hydration and the use of N-acetylcysteine, mannitol, furosemide, dopamine, fenoldopam, or other renoprotective drugs have been variably shown to be effective in patients with normal or mildly impaired renal function [11, 12]. Methods for prevention of CIN in patients with advanced renal failure remain unknown. Additionally, prophylactic hemodialysis, started immediately after the administration of CM to this group of patients didn't show any benefit in CIN prevention [13].

Table 1: Baseline patients' morbidity characteristics (n=98)

Pathology	Notes	Number (%)
Diabetes mellitus		79 (80.6)
Hypertension		82 (83.7)
Previous myocardial infarction		23 (23.7)
Procedure	Diagnostic	19 (19.39)
	PCI*	79 (80.61)
Coronary artery disease	Normal vessels	3 (3.06)
	Single vessel	5 (5.1)
	Two vessels	28 (28.57)
	Three or more vessels	62 (63.26)

*PCI: percutaneous coronary intervention

Table 2: Baseline patients' important measurements that may affect renal outcome after cardiac catheterization (n=98)

	Mean (± SD)	Range
Age (years)	60.7 ±10.99	36-81
Body mass index (kg/m^2)	28.39 ± 4.71	34-55
Baseline serum creatinine (mg/dl)	4.65 ± 0.9	3.4 - 7.1
Baseline creatinine clearance (ml/min)	18.04 ± 4.26	12.23-31.09

Continuous venovenous hemofiltration (CVVH) is an alternative strategy to HD for prevention of CIN in high risk patients [14, 15].

The purpose of this study was to test the efficacy of prophylactic CVVH in the prevention of CIN in patients with advanced CKD.

Methods

A prospective single center study was conducted in Chest Disease Hospital of Kuwait from January 2004 to December 2006. All patients with CKD who were scheduled for PCI were included in the study. Inclusion criteria were age above 25 years, stable serum creatinine concentration above 3.39 mg/dl and creatinine clearance less than 35 ml/min within one month prior to the procedure. Exclusion criteria were presentation with cardiogenic shock, pregnancy, lactation, contraindications to heparinization, intravascular administration of contrast media or exposure to nephrotoxic drugs during the previous two weeks, use of non-steroidal anti-inflammatory drugs during the previous 48 hours, renal transplantation and, patients with end stage renal disease (ESRD) requiring regular dialysis. Angiotensin converting enzyme inhibitors were held on the day of the procedure. Acetylcysteine, mannitol and dopamine, were not used during the procedure. All patients gave a written informed consent.

Patients were started on CVVH as soon as possible after the procedure, and the time interval from contrast exposure to initiation of dialysis was recorded. CVVH was performed through a double lumen intravenous femoral catheter (Quinton, Bothell, WA) placed by the attending nephrologists before the procedure. CVVH for 18-24 hours was started using Prisma continuous fluid management system (Gambro Lakewood Co.) using M100 dialyzer sets (AN69 membrane), with surface area of 0.90 m^2 and with bicarbonate buffered solution for continuous renal replacement therapy (CRRT) from Hospal with the following solute composition in mmol/l: calcium 1.75, magnesium 0.5, sodium 140, chloride 109.5, lactate 3, bicarbonate 32. Blood flow rate was set at 100 ml/min, and the substitution fluid rate was 2 liters/ hour without any additional fluid removal. Anticoagulation was achieved by giving heparin bolus of 500 IU at the start of CVVH then constant heparin infusion to maintain activated partial thromboplastin time between 130-150 seconds.

Blood urea nitrogen (BUN) and serum creatinine were measured before the procedure, at the end of the CVVH session, then daily for the following three days, at hospital discharge, and 15 days after the day of the procedure. Creatinine clearance (Cr Cl) was calculated at the same times using Cockcroft and Gault equation [16]. the incidence of contrast nephropathy, defined as more than 25% increase from baseline serum creatinine values within two weeks after the procedure was calculated. Emergency CRRT was performed if there was oliguria for more than 48 hours despite administration of more than 1 gram of furosemide over 24 hours, or if there was evidence of congestive heart failure, or if serum potassium was above 6 mmol/l. CRRT was discontinued when there was evidence of recovery of renal function with the restoration of urine output of more than 500 ml/day. The need for permanent hemodialysis was defined as persistent Cr Cl less than 5 ml/min. The incidence of CIN, in hospital mortality, and the need for long term dialysis was calculated.

Data were analyzed using SPSS for windows version 13 (SPSS, Inc, Chicago, IL). Continuous variables were expressed as mean ± SD, whereas categorical variables were expressed as frequencies and percentages.

Results

A total of 98 patients were enrolled in the study, 52 (53.1%) of whom were males, and 46 (46.9%) were females. Baseline patients' clinical and measurable indicators that may affect renal outcome after cardiac catheterization are summarized (Tables 1 and 2). Seventy nine patients (80,6%) were diabetic and 82 (83.7%) were hypertensive. Almost a quarter of them (23.7%) had history of previous myocardial infarction and cardiac catheterization showed that 62 patients (63%) had three vessel disease or more. Pre-procedure serum creatinine ranged from 3.42 – 7.14 mg/dl with a mean of 4.65 ± 0.9 mg/dl, pre-procedure Cr Cl ranged from 12.23-31.09 ml/min, with a mean of 18.04 ± 4.26 ml/min.

All patients were subjected to post-procedure CVVH. The mean time interval between the procedure and the start of CVVH was 44.3 ± 18.8 min. The mean duration of the session was 21.3 ± 2.1 hours. None of the studied subjects had femoral catheter related complications, three patients (3.06%) required catheter replacement for clotting. The CVVH course was smooth without intra-procedural complications. The mean serum creatinine after CVVH was 1.62 ± 0.46 mg/dl, 3.51 ± 0.52 mg/dl 48 hours after the procedure, 4.5 ± 0.71 mg/dl 72 hours after the procedure, 4.57 ± 1.0 mg/dl at time of discharge, and 4.78 ± 1.0 mg/dl 15 days after the procedure (Figure 1). There were no statistically significant differences between any of the mean post-procedural serum creatinine values and the mean pre-procedural serum creatinine. Regarding Cr Cl, its mean value was 18.52 ± 4.61 ml/min at the time of discharge and 17.62 ± 4.27 ml/min at 15 days after the procedure (Figure 2). One patient (1.02%) developed CIN that required repeated CVVH sessions during hospitalization and ended up on regular long term hemodialysis. The in-hospital mortality was 0%.

Discussion

Patients with CKD have a predisposition to accelerated atherosclerosis; they thus represent an increasing percentage of the patients undergoing PCI [17]. The clinical outcome of patients in whom CIN develops after PCI is particularly poor, with a reported in hospital mortality rate of more than 20 percent and cumulative one year mortality rate of more than 35 percent [3, 18-21]. Mortality even increases to 45-62 percent if dialysis was required [19, 21]. Given the clinical and prognostic implications, strategies to reduce the incidence of CIN are needed particularly in high risk patients [22]. Several strategies have been evaluated for the prevention of CIN. Among these strategies, only saline hydration [23, 24], the use of low-osmolality contrast agents [25] and treatment with N-acetylcysteine [26-28] or fenoldopam [29, 30] have been shown to provide some protection and to reduce the incidence of CIN. However, the efficacy of these measures is still controversial in patients with severe renal impairment [27]. The pharmacokinetic properties of water soluble iodinated CM are such that they are distributed in the extracellular fluid only, are minimally protein bound, are not metabolized, and are excreted mainly by the glomerular filtration [31]. In normal subjects, elimination of CM takes place rapidly: after two hours approximately 50% of the CM is recovered in urine. In subjects with severe CKD, the same 50% will be eliminated in urine 16-84 hours after injection of the CM [32]. Considering the properties of the iodinated CM, it was hypothesized that it can be removed by dialysis. Our study showed that doing CVVH as soon as possible after contrast injection in patients with CKD reduced the incidence of CIN to 1.02% in this high risk group of patients. This percentage is significantly less than what has been reported in the literatures when other preventive strategies such as saline hydration or N-acetylcysteine were used in patients with CKD. Our results are in accordance with previous studies [33-36].

Hemodialysis (HD) and hemofiltration (HF) have both been studied for the prevention of CIN. To date, there have been few trials evaluating hemodialysis for prevention of CIN [37, 38]. Hemodialysis and CVVH both effectively remove iodinated CM from the blood [39]. Despite this, a recent systemic review of studies

Figure 1: Change in serum creatinine after the procedure

Figure 2: Change in creatinine clearance after the procedure
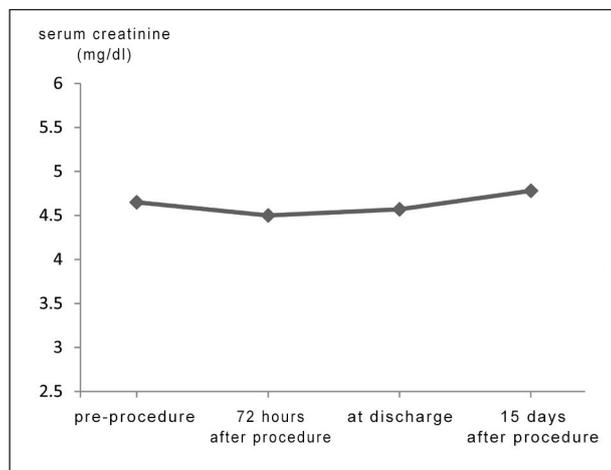
comparing the periprocedural HD with conventional prophylactic measures found that HD did not decrease the risk or the need for acute dialysis following CIN [36]. CVVHF and continuous venovenous hemodiafiltration (CVVHDF) have also been studied for the prevention of CIN after PCI in patients with CKD [36]. In 2003, Marenzi *et al* reported the superiority of CVVH over saline hydration in prevention of CIN after PCI in patients with CKD, where CIN was reported in 5% of the CVVH group versus 50% in the control group [34]. Gabutti *et al* studied the effect of (CVVHDF) performed during and after PCI in patients with CKD and concluded that CVVHDF is not effective in prevention of CIN [40]. Marenzi *et al* compared the use of saline hydration with the use of pre- and post-procedure CVVH or the use of post-procedure CVVH and concluded that pre- and post-procedure CVVH was superior to the other two strategies [35]. On the other hand, Vogt *et al* didn't show any beneficial effect of prophylactic HD for 3 hours after the procedure [13]. Moreover, patients who received HD were more likely to have a decline in renal function and required additional HD treatment. A possible explanation for these results is that HD can induce hypovolemia and consequently may worsen renal ischemic injury, delay recovery of renal functions, and result in a need for prolonged dialysis [41]. On the other hand, CVVH is associated with hemodynamic stability, allows better hydration and regulation of volume status, allows infusion of large volume of bicarbonate containing solution, and allows removal of CM from the circulation with a resultant reduction in the kidneys' exposure to CM [14, 15, 42, 43]. In addition, heparin used during the procedure of CVVH may have a beneficial effect as it may inhibit acute inflammation, attenuate the ischemic reperfusion injury, and reduce the oxidative stress that may be involved in the pathogenesis of CIN [44, 45]. Lastly, considering
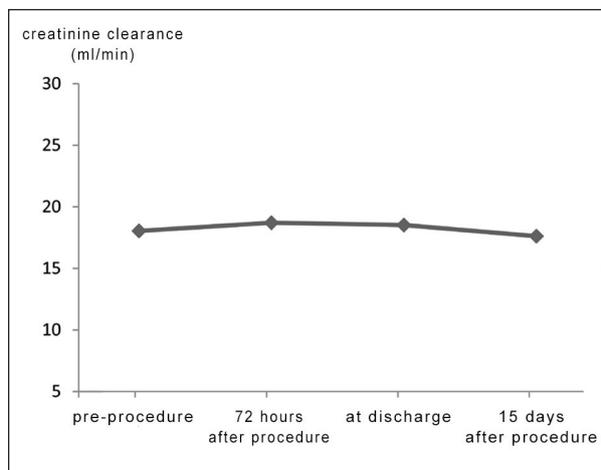
the relatively high cost and the time-consuming nature of CVVH, the limited availability of intensive care unit (ICU) beds and the lengthy immobilization of patients during CVVH, this procedure should be restricted to the high risk patients.

Conclusion

Despite CVVH being expensive, invasive, and time consuming, it may have a beneficial effect in preventing CIN after PCI in high risk patients with advanced CKD. CVVH should be considered as a preventive strategy for CIN after PCI in such patients. A randomized controlled clinical trial is needed to verify our encouraging results.

Limitations of the study

There was no control group, and the effect of CVVH was not compared with the conventional hydration protocols. This study was conducted in a single center and the results may not be generalizable to other centers. CVVH washes out creatinine, and may mask a transient rise in serum creatinin if such a rise was limited to the first 2-3 days after the procedure.

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