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Original article

Prevention of Contrast Induced Nephropathy by 16-hours Post-contrast Continuous Veno-venous Hemodiafilteration

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Abstract

Contrast induced nephropathy (CIN) is the most common cause of iatrogenic in-hospital kidney dysfunction with high morbidity and mortality. In our 5-year prospective study, we evaluated the role of 16-hour post-procedural continuous veno-venous hemodiafilteration in a 132 patient with high risk Mehran integer index for CIN who had to be subjected to coronary arteriography including primary one. All patients had eGFR < 40 ml/minute and 23 (17.4%) of whom were < 20%. The results showed stable kidney disease post-contrast with no significant local or systemic complications in both males and females. In-conclusion; we advocate its use to protect high-risk patients from CIN.

Keywords: ***contrast, nephropathy, CVVHDF, hemodiafilteration, PCI, treatment.***

Introduction

Contrast induced nephropathy (CIN) is the development of acute kidney injury (AKI) following the administration of radiographic contrast media in the absence of other identifiable causes. AKI is defined, in the 2012 KDIGO document, as increment of serum creatinine (SCr) by > 25% or 0.3 mg/dl (26.5 umol/L) within 48hours or an increase in SCr to > 1.5 times baseline within 7 days post-contrast administration.[1] It is the most common form of iatrogenic in-hospital kidney dysfunction with an estimated prevalence of 12 % in patients undergoing percutaneous coronary intervention (PCI) and has an annual morbidity and mortality at 52% and 30%, respectively.[2] Several methods were advocated to protect against CIN viz. saline hydration, N-acetyl cysteine, vasodilators, Captopril, Ascorbic acid, Theophylline and Atorvastatin. However, only the first 2 had shown practical benefit which was only limited to those with mild renal impairment.[1] The risk of CIN is progressively higher in patients with advanced renal disease, diabetes mellitus, age > 75 years and intra-arterial contrast-use.[3] In our area; diabetic glomerulosclerosis is the most prevalent kidney disease and since both are associated with accelerated atherosclerosis; protection of those with moderate-severe renal failure, from the intra-arterial CIN, indicates more aggressive approaches with direct blood purification systems.[4] Iodinated contrast agents are readily dialyzable with > 80% removal from the plasma within 4-5 hours of hemodialysis.[5] However, 3 studies failed to show benefit of such approach.[6-8] On the other hands, in 2003, Marenzi et al reported a beneficial role of continuous peri-procedural veno-venous hemofilteration (4-8 hours prior to PCI and 18-24 hours after it) compared to isotonic saline hydration in prevention of CIN as well as improvement of in-hospital and long-term prognosis.[2] In our study; we evaluated, prospectively, the protective role of post-procedural continuous veno-venous hemodiafilteration (CVVHDF) in limiting CIN, in high risk renal patients who had to undergo PCI.

Patients and methods

The study was conducted between 1st January 2013 and 31st December 2018. Patients with advanced kidney disease, and multiple co-morbid conditions, who had to be subjected to coronary arteriography for ischemic heart disease or pre-kidney transplantation with positive Thallium stress-testing were treated with CVVHDF immediately after the PCI. Patients were excluded if they had persistent hypotension (systolic blood pressure < 80 mm Hg), hypoxia, sepsis, severe peripheral arterial disease (ankle-brachial index < 0.6), reno-vascular disease as well as renal transplant and dialysis patients. Moreover, those who had received recently NSAIDs (not low-dose Aspirin), excessive diuretics, ACEI and ARB, Aminoglycosides, Calcineurin-inhibitors were also excluded.

Study design:
CVVHDF was performed, by dialysis team, in the coronary care unit immediately after the PCI via a double-lumen femoral hemodialysis catheter (Quinton, Bothell, WA, USA). The duration of CVVHDF was 16 hours in those with CrCl < 15 ml/minute/1.73 m2. In those with CrCl < 40 ml/minute/1.73 m2 yet > 15; the duration was limited to12 hours only. All patients had: (a) an intra-arterial coronary study using a (b) single infusion of (c) iodixanol (Visipaque) which is an iso-osmolar non-ionic contrast agent.

Clinical assessment was done by both coronary care and dialysis physicians. Laboratory testing was done every 8 hours for the first 48 hours then after 1 week and 2 weeks unless clinically indicated. CrCl was calculated at the same time using Cockcroft and Gault equation.[9]

Procedure:
CVVHDF was carried out using Gambro Prismaflex dialysis machine and M100 dialyzer sets (AN69 membrane) with surface area of 0.90 m2. The blood flow was 150-200 ml/minute, dialysate flow was 1500 ml/hour and the replacement fluid was 1500 ml/hour. The replacement fluid (Hemosol) was a 5 liter disposable bag from Baxter comp. It consisted of 2 parts mixed immediately before use. The first bag was 250 ml and contained Ca Cl (5.145 g), Mag Cl (2.033 g), Lactic acid (5.4 g). The second bag was 4750 ml and contained Na Cl (6.45 g) and Na HCO3 (3.09 g). To avoid the risk of bleeding from arterial puncture of PCI; heparin is avoided in the first 4-6 hours. Periodic flushing of the filter is done using normal saline at a rate of 100 ml every 30 minute). Low-dose heparin (250-500 unit/hour) can be used in the remaining time if there is no associated risk of bleeding.

Statistical analysis:
The SPSS statistical package version 21 was used for data entry and processing. The p-value of < 0.05 was used as the cut-off level for significance. To start, data were assessed for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Since age, body weight, latent period prior to CVVHDF, Duration of CVVHDF, serum creatinine and eGFR were not normally distributed, they were expressed as a median (min-max) and Wilcoxon Signed rank test was used to assess the difference between the different groups.

Results

Table 1. Demographical data on the high-risk patients subjected to post-PCI CVVHDF

Character	Male (n=69)	Female (n=63)	Total (n=132)	*p*-value *
Age	57 (43-67)	55 (41-68)	56 (41-68)	NS
Weight	87 (60-98)	88 (67-98)	87 (60-98)	NS
Pre-eGFR (ml/min.):				
< 40-20	58	52	132	NS
< 20.	12	11	23	NS
C-morbid conditions:				
Age > 60 years:	27	20	47	NS
Diabetes mellitus:	44	39	83	NS
Hypertension:	52	47	99	NS
CHF (LVEF: < 20%):	13	15	28	NS
Primary PCI:	27	32	59	NS
Nephrotic syndrome:	36	39	75	NS
Cirrhosis:	0	1	1	
High uric acid:	49	52	101	NS
Hypercholesterolemia:	60	58	118	NS
Multiple myeloma:	1	0		
Post-procedural catheter insertion time:	30 (20-35)	30 (20-34)	30 (20-35)	
Duration of CVVHDF:	16 (14-17)	16 (15-18)	16 (14-18)	
Serum creatinine:				
Pre-PCI:	352 (241-536)	365 (190-562)	354 (190-562)	NS
2 days post-PCI:	340 (220-510)	340 (180-550)	340 (180-550)	NS
14 days post-PCI:	351 (240-540)	360 (190-570)	360 (190-570)	NS
eGFR:				
Pre-PCI:	24 (17-38)	21 (14-38)	22 (14-38)	NS
2 days post-PCI:	24 (17-41)	22 (14-38)	23 (14-41)	NS
14 days post-PCI:	23 (17-38)	21 (14-35)	22 (14-38)	NS
Complications:				
Deep venous thrombosis:	1	2	3	
Catheter clotting:	2	3	5	

Abbreviations: PCI: percutaneous coronary intervention, CVVHDF: continuous venovenous hemodiafilteration, e-GFR: estimated glomerular filtration rate.
* Statistical analysis was done using non-parametric methods (Mann-Whitney and Wilcoxon signed ranks tests) and data are presented as Median (minimal-maximal values)

A total of 132 patients were included in the study during the past 5 years. The demographical data on the patients are summarized in table 1. Males were 69 (52%) while females were 63 (48%). There was no significant difference between females and males with regards distribution, age, body weight, pre-eGFR, co-morbid conditions and complications. There median time interval between the procedure and start of CVVHDF was 30 (20-35) minutes and was not different between males and females. Moreover, mean duration of CVVHDF was 16 (14-18) hours and was not different between both sexes. The study group had significant co-morbid conditions and risk factors for CIN. All patients had eGFR < 40 ml/minute and 23 (17.4%) of whom were < 20%. Moreover, 47 (36.6%) were elderly (age > 60 years) and with diabetes mellitus 83 (62.9%), hypertension 99 (75%), congestive heart failure, recent myocardial infarction 59 (44.7%) and hyperuricemia 101 (76.5%). The local and systemic complications of the procedure were few

and none of the patients had cardiac side effects or had required dialytic support.

Impact of CVVHDF on CIN:

Peri-procedural changes in serum creatinine and eGFR are summarized in table 1. There was no significant difference in these 2 parameters before PCI, 2 days and 14 days later.

Discussion

In our study we tried to provide a practical method for protection of high-risk renal patients from CIN. It included (a) post-procedural (b) hemodiafilteration (c) without significant heparinization (d) for just 16 hours only and (e) in an intermediate care unit. According to Mehran model for predicting risk factors for CIN, our patients had an integer score > 16 indicating a risk of CIN: > 57.3% and a need for dialysis of > 12.6%.[10] Hence, it was unethical to have a control group subjected to contrast without attempts to protect them. Our patients tolerated the procedure without systemic side-effects and had stable kidney in function weeks after it. In our study, we have used CVVHDF which incorporate the use of high-flux dialyzers to attain maximal blood purifications of contrast media and high-safety profile in those with significant cardiac instability.[11] The start of CVVHDF was within 30 minutes post-PCI which permitted inclusion of those with primary PCI. Moreover, the duration of the sessions was nearly 16 hours which was relatively short leading to less local and systemic complications.[12] The choice of just 16 hours was based on 2 previous observations. The first one is that the injection of such water-soluble contrast media is followed by their rapid distribution into the extracellular body compartments. The progressive decrease in their serum level is caused by renal elimination or blood purification method which leads to a rediffusion of the contrast medium out of the tissue and back into the intravascular space after intravenous injection.[13] The second one is that 50% of the injected contrast-dose is recovered in the urine after 16 hours in patients with advanced kidney disease indicating amble clearance even of extravascular space.[14] Previous studies have failed to show significant protection of hemodialysis from CIN.[6-8] We believe that their use of low-flux filters while contrast media are middle molecule limited proper blood purification.[15] Moreover, the 4-hour hemodialysis did not permit removal of the refluxing contrast from the extravascular space. In our study, the post-contrast CVVHDF permitted the care of such unstable patients and even those who needed primary PCI.[14] Our study indicated that 30 minutes-delay is a permissible time and duration of save exposure to contrast even in high risk renal patients. Such delay provides adequate imaging and intervention without the risk of dye dilution with periprocedural CVVHDF.[2] Moreover, this observation indicates that direct tubular toxicity is the main culprit in CIN. In our study, we limited the use of heparin to avoid post-PCI bleeding. Hence, our success in protection against CID indicates its role in protection from ischemic reperfusion injury.[16] In conclusion; post-contrast CVVHDF for just 16 hours, in high risk patients with advanced kidney disease, is an effective and safe method of prevention of CIN.

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