

Original

Evaluation of Efficacy and Safety of Continuous Hemodiafiltration in cases of Acute Renal Failure.

N. Nand, R.K. Yadav, K. Bharti, M. Sharma

Postgraduate, Department of Medicine, Nephrology and Biochemistry
Pt. B.D. Sharma University of Health Science, Rohtak, Haryana, India

Abstract: 30 consecutive critically ill patients of ARF were randomly divided into two groups of 15 cases each. Group A patients received continuous arteriovenous hemodiafiltration (CAVHDF) whereas group B cases were subjected to continuous venovenous hemodiafiltration (CVVHDF). The inclusion criterion was hemodynamic instability or cases unfit for intermittent hemodialysis. Despite the sepsis and hemodynamic fragility, haemodiafiltration was effective in achieving biochemical control. At the initiation of therapy, mean blood urea was 232.4 ± 71.5 and 239.6 ± 75.47 mg/dl in group A and B respectively. But after 42.9 hr of CAVHDF and 40.3 hr of CVVHDF, urea had fallen to mean value of 107.13 ± 66.17 and 112.73 ± 77.36 mg/dl respectively. All the patients had gradual and steady improvement in bicarbonate concentration toward normal. Urea clearance was 21.97 ± 1.56 and 22.73 ± 0.81 ml/min in the two groups. Ultrafiltration rate was 128.5 ± 9.51 ml/hr and 136 ± 10 ml/hr in group A group B respectively. Both modalities of treatment were well tolerated. Requirement of vasopressive agents did not change significantly. None of the patients developed hypotension secondary to the procedure. Symptomatic relief and improvement in parameters were observed in all cases. Complication rate was less; survival was 33.7%; thus haemodiafiltration is probably the best available treatment to treat critically ill and hemodynamically unstable patient of ARF having multiorgan dysfunction.

Key words: hemofiltration, hemodiafiltration, acute renal failure.

INTRODUCTION

Improvement in survival of acute renal failure (ARF) remains one of the foremost challenges in critical care medicine¹; despite advances in dialysis therapy, the mortality rate in critically ill patient with ARF continue to be high. Intermittent hemodialysis has been widely used and remains the standard renal replacement therapy for ARF in critically ill patient with oliguria and multiorgan dysfunction, the intermittent nature of this treatment is associated with a number of disadvantages, therefore in an attempt to overcome these disadvantages, a variety of continuous renal replacement therapies (CRRT) have been proposed; however, there are very few prospective studies, which have shown that CRRT have a significant impact on outcome of acute renal failure. Therefore in order to assess the efficacy and outcome of continuous haemodiafiltration (HDF) on critically ill patients, this prospective study was undertaken. In this study, we are reporting our.

Experience of the use of CAVHDF and CVVHDF in critically ill cases of ARF, requiring renal supportive therapy.

MATERIAL AND METHODS

Thirty (30) consecutive critically ill patients of ARF were randomly divided into two groups of fifteen cases each. Group A patients received continuous venovenous hemodiafiltration (CVVHDF) whereas group B cases were subjected to continuous hemodiafiltration, the inclusion criterion was based on one or more of the following:

- (i) The patients of ARF who were critically ill (APACHE III score >80) and hemodynamically unstable (SBP <90 mm Hg),
- (ii) The patients of ARF who were on invasive ventilator support.
- (iii) Persistent volume overload despite daily hemodialysis.

For CAVHDF, vascular access was accomplished by insertion of wide bore femoral arterial and femoral venous catheters whereas for CVVHDF, vascular access was established by a double lumen venous catheter in femoral vein.

All patients were critically ill and were managed in the intensive

care unit. A 1.1-M² hollow fibre haemodiafilter (cellulose acetate) was connected to the arterial and venous access in pumpless circuit during CAVHDF and with pump during CVVHDF. Standard peritoneal dialysis fluid (sodium chloride 0.556 g%; sodium acetate 0.476 g%; calcium chloride 0.022 g%; magnesium chloride 0.0152 g%; sodium metabisulphate, 0.015 g%, anhydrous dextrose 1.1 g%) was run counter current to blood flow at a controlled rate of 1-1.5 liters/hour to provide diffusive clearance. The ultra filtrate was collected in a graded collection bag. Every hour, the ultra filtrate was replaced with alternating bicarbonate based or calcium based replacement solution. Depending upon patient's stability, a net negative balance or 100-200 ml/hour was attempted. Rate of ultra filtration was modulated by adjusting the height of the collection apparatus in relation to the right atrium. An initial loading dose of heparin (50 IU/kg) was given systemically five minutes prior to hemodiafiltration (HDF). Heparin was then infused into the arterial line at a dose (usually 10 IU/hour) sufficient to double the partial thromboplastin time (PTT).

Besides basal investigations; like blood urea, electrolytes, urea, arterial blood gas analysis, bleeding and clotting time were carried out every 4 hourly. Serum and dialysate creatinine, PTI/PTTK and complete hemogram were repeated every day. Vital signs, ultra filtration rate, urine output and net negative balance were monitored every hour.

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation and the discrete variables as percentage. Student's paired and unpaired t-test were employed to find out the significance of difference between the means. The chi square test with appropriate modification (Fisher's exact test) was used to examine the significance of difference between the proportions.

RESULT

Demographic Data

Mean age of patients in the two groups was 39.9 ± 14.46 and 43.3 ± 12.72 years respectively. Septicemia was responsible for nearly half the cases of ARF (46.7) followed by trauma and/or postoperative

Correspondence: Professor Nitya Nand, 3/7J Medecal Enclave, Rohtak 124001, Telephone: 01262-213878

E-mail: m.nitya@mailcity.com

complication (13.3%) and hepatic-renal syndrome (13.3%). An APACHE III score was calculated on all patients at the commencement of HDF. The mean APACHE III score was 101.1 in both groups. Failure of two or more organs was present in nearly all patients (90%). Even patients (37%) were on mechanical ventilation and eighteen patients (60%) were receiving positive inotropic or vasopressor support at the time of introduction of HDF. Baseline investigation profile in two groups is shown in table 1. It is clear that all the patients in the two groups were well matched in terms of various biochemical and hematological parameters.

Table-1: Demographic Data In Two Groups

Parameters	Group A	Group B
Male/Female	7/8	9/6
Systolic B.P	101.06±18.10	103.2±23.33
Diastolic B.P (mm of Hg)	55.86±8.95	60.26±13.32
Hg (g %)	8.15±1.28	7.9±1.66
Oliguria	15	15
Ascites	12	11
Septicemia	7	7
Hepato-organ	13	14
Blood urea (mg %)	232±71.5	239±75.47
Serum creatinine (mg %)	4.68±1.78	6.89±3.82
Hyperkalemia (>6.0 meq/L)	5	5
APACHE-III	101.06±11.67	101.13±23.33

Biochemical parameters

Despite the presence of sepsis and hemodynamic fragility, haemodiafiltration was extremely effective in achieving biochemical. At the intimation of therapy, mean blood urea was 232±71.5 mg/dl and 239±75.47 mg/dl in group A and B respectively. But after 42.9 hours of CAVHDF and 40.3 hours of CVVHDF, blood urea had fallen to mean value of 107.13±66.17 and 112.73±77.36 mg/dl, respectively. Similar, the serum creatinine value fell from a mean of 4.68±1.78 to 3.41±2.0 mg/dl in group A and 6.89±3.82 to 5.38±3.63 mg/dl in group B. In 70% of cases, we were able to maintain blood urea at 60-80 mg/dl and creatinine level at 2.2-4.3 mg/dl during or after the procedure. All the patients (in both groups) had gradual and steady improvement in bicarbonate concentration towards normal value and it was maintained throughout the duration of treatment. Seventeen patients (57%) had normalization of acidosis within 24 hours of HDF. Serum potassium levels were maintained within range of 2.6-4.7 meq/l with 24 hours of initiation of HDF. Estimates of urea and creatinine clearance, obtained by random measurement throughout the duration of HDF, revealed a urea clearance of 21.97±1.56 ml/min during CAVHDF and 22.73±0.81 ml/min during CVVHDF. Similarly, creatinine clearance was 23.21±1.23 ml/min and 23.16±1.05 ml/min, respectively (table 2). Ultra filtration rate ranged from 0-500 ml/hr in both groups with mean value of 128.5±9.51 ml/hr in group A and BMS 136±10 ml/hr in group B.

Table-2: Basal biochemical and hemodynamic parameters after 24 hours of hemodiafiltration

	0 hour	24 hour	P value
Urea (mg/dl)			
Group A	232.4±71.50	131.9±65.12	<0.001
Group B	239.6±75.47	134.5±66.12	<0.001
Creatinine (mg/dl)			
Group A	4.68±1.78	3.94±1.95	<0.05
Group B	6.89±0.97	5.76±3.6	<0.05
Potassium (meq/l)			
Group A	5.05±1.01	3.94±1.95	0.001
Group B	4.98±0.97	3.60±1.00	0.001
Bicarbonate (mEq)			
Group A	10.66±4.51	16.2±3.52	<0.01
Group B	12.27±7.03	17.9±4.47	<0.01
Mean Arterial Pressure (mm Hg)			
Group A	71.06±20.02	78.33±18.46	>0.05
Group B	73.13±22.04	81.66±19.27	>0.05

Hemodynamic Tolerance

Both modalities of HDF were hemodynamically well tolerated despite the fact that 18 the 30 patients were on vasopressor support at the initiation of therapy. Requirement for dopamine, dobutamine or nor adrenaline did not change significantly when it was measured at zero, one four, and 24 hours of HDF. The mean arterial pressure (MAP) was 71.07 and 73.13 mmHg at start of HDF in group A and B, respectively, it increased to 78.33 and 81.66 mm of Hg after 24 hours of HDF. Despite significant fluid removal. None of the patients developed hypotension secondary to the procedure. In fact there was improvement in hemodynamic parameters.

Outcome

Symptomatic relief and improvement in clinical parameters i.e. nausea, vomiting, altered sensorium observed; half the patients was (58%) recovered their renal functions and their urine output improved. Thirteen patients (42%) did not recover renal functions and died of their original illness. Out of eleven patients who were on mechanical ventilator support, 5 patients were successfully weaned off. Kt/v in CAVHDF was 1.02±0.48 and in CVVHDF it was 1.09±0.56. Value was more of Kt/v in both groups were than one, thus, confirming its adequacy.

Complications

Clotting of filter were the common complication observed. During CAVHDF, six patients (40%) had clotting of hemofilter while during CVVHDF; three patients (20%) had clotting. The mean life of filter before clotting was 30 hours in this study. Other complications were related to anticoagulation. Four patients (13%) had bleeding manifestation during treatment. All these 4 patients were having coagulopathies before inclusion in the study and were in very high-risk group for the development of hemorrhagic complication. A total of 17 patients (58%) recovered their renal functions of which 11 patients were discharged from the hospital. The survival rate was 33.7 with a mortality rate of 63.3%.

DISCUSSION

Severe acute renal failure is a major component of the multiorgan failure syndrome and is now most commonly seen within the ICU. Its development in critically ill patients portends a poor prognosis and significantly complicates management. Continuous renal replacement therapies are now widely accepted in management of these critically ill patients with ARF.⁴⁻⁶ In present study, we evaluated the efficacy and outcome of continuous haemodiafiltration, a mode of CRRT, successfully in 30 critically ill patients without any significant complication of the procedure. These patients received continuous dialysis therapy because conventional hemodialysis would have failed to offer control of azotemia and fluid & electrolyte balance to use of the newer HDF bases techniques that is. Whether they have a clinically significant efficacy and positive impact on critically ill patients with ARF.

The current study reveals a number of important data. Firstly, HDF was found to be extremely efficient procedure in clearance of small molecular weight (urea, potassium), as well as middle molecular weight (creatinine) solutes and in achieving control of uremia even in patients with hemodynamic instability. This fact is borne out by our experience, as we achieved significant fall ($p < 0.001$) in these biochemical parameters i.e. urea, creatinine, and potassium (Table 2). Most of the patients (70%) achieved consistent and steady state of urea and creatinine level during HDF. This superior metabolic control with HDF also corroborates with other investigators.⁸⁻⁹

The clearance of urea and creatinine, when potentiated on 24 hours basis were 31.6 liters with CAVHDF and 32.7 liters with CVVHDF.

These values compare favorably with the clearance of 30-40 liters in 4 hours conventional hemodialysis which is usually performed on an alternate day basis.¹⁰ HDF also normalized serum potassium, sodium and bicarbonate concentration within 24 hours of initiation of procedure. Other studies have also concluded that HDF is physiologically superior to intermittent haemodialysis (IHD) in correction of azotemia and deranged electrolyte levels.⁷⁻⁸

The most important fact this study has established is hemodynamic stability achieved during fluid withdrawal in HDF. Hemodynamic stability during HDF is presumed to be due to slow and gradual removal of urea and water which allow time to optimize intravascular and left ventricular filling, leading to improvement in cardiac output.^{2-5,10} Both modalities of HDF achieved a significant fluid removal even in critically ill patients without having significant deleterious episodes of hypotension in contrast to hemodialysis where incidence of hypotension is 20-30%^{10,11}. In the present study, most of the patients were vasopressor dependent, therefore, ultra filtration rate was kept below 200 ml/hr so as to avoid hypotension. This ultra filtration rate was low contrary to other investigation, who achieved it in range of 500-1000ml/hr.^{10,11} One possible explanation for this difference may be that most of patients in our study were vasopressor dependent, proving lower blood flow rates leading to low ultra filtration rate. During the period of study the rate and quantity of fluid removal was individualized, depending to hemodialysis, this technique in the graduated bag and fluid removal and solute clearance could be controlled and modified at any time of the day and night, allowing adaptation to the rapidly changing hemodynamic situation of critically ill patients. The second and most important advantage was maintenance of hemodynamic stability during fluid withdrawal.

The most important surrogate marker of dialytic efficiency and safety is the "adequacy of dialysis". According to NCDS¹² dialysis is said to be adequate if value of Kt/v achieved is one or more. In the present study, we calculated Kt/v by using simplified Barth method¹³, which takes into consideration pre, mid and post dialysis blood urea levels. Value of Kt/v in CAVHDF was 1.02 and in CVVHDF it was 1.09. Values of Kt/v in both groups were more than one, thus confirming its adequacy in the management of critically ill patients with ARF. To the best of our knowledge, no other randomized clinical in available where adequacy of CAVHDF and CVVHDF has been compared in cases of ARF.

The most encouraging finding in our study were the high percentage of renal function recovery and survival in critically ill patients with ARF. Of the 30 patients with ARF, 58% recovered their renal function.

A total of 11 patients (36.7) survived and discharged from hospital. The mortality rate of 63.36% is lower than the reported rates for patients with similar APACHE III score. Chen et al¹⁴ in complicated ARF, found a mortality rate of 86% with in APACHE III score >90. In the present study, mean APACHE III score was 10 in both groups. The issue of whether CRRT can lead to improved survival in critically ill patients cannot be addressed by the current study as no control group received alternative forms of RRT as it was considered unethical to subject unstable patients of IHD.¹⁵

Our study suggests that HDF provides better biochemical control of uremia than previously utilized treatment modalities. Haemofiltration is also probably the best available treatment to treat overloaded cases of ARF without compromising their hemodynamic stability. It is relatively simple, safe and is well tolerated. The treatment of choice in critically ill patients with ARF.

REFERENCES

1. **Draimi W.** Prophylactic use of continuous renal replacement therapies with normal renal function. *Am J Kid* 1996; 28 (5 suppl 3): S114-20.
2. **Lameire N, Biesen VV, Vanholder R, Colariti F.** The place of intermittent hemodialysis in the treatment of acute renal failure in the ICU Patients. *Kidney Int* 1998;53 (Suppl66): S110-9.
3. **Canaud B, Bragg-Gresham JL, Marshall MR, Desmeules S, Gillespie BW, Depner T.** Mortality risk for patients receiving hemodiafiltration versus hemodialysis: European result from the DOPPS. *Kidney Int* 200; 69:2087-93.
4. **Geronemus R, Schneider N.** Continuous arteriovenous haemodialysis a new modality for treatment of acute renal failure *Trans Asia* 1984; 30: 610-3.
5. **Ronco.** Continuous renal replacement therapies for the treatment of acute renal failure in intensive care patients. *Clin Nephrol* 1994; 4: 187-98.
6. **Canaud BMS, Morena M, Leray-Moragues H, Chalabi L, Cristol JP.** Overview of clinical in hemodiafiltration: with do we need now? *Hemodial int* 2006; 10 (suppl): S5-S12.
7. **Uchino S, Bellomo R, Ronco C.** Intermittent versus continuous renal replacement therapy in the ICU: Impact of electrolyte and acid-base balance. *Intens Care Med* 2001;27:1037-43.
8. **Von Bommel EFH, Bouwy ND, So KL, Vincent HH, Zielse R, Bruinig HA, et al.** High-risk surgical acute failure treated by continuous arteriovenous hemodiafiltration: Metabolic control and outcome in sixty patients. *Nephron* 1995; 70: 185-92.
9. **Belomo R, Rono C.** Acute renal failure in the intensive care unit: Adequacy of dialysis and the case for continuous therapies. *Nephrol Dial Transplant*, 1996;11:424-8.
10. **Pattison MF, Lee SM, Ogden DA.** Continuous arteriovenous hemodiafiltration: An aggressive approach to the management of acute renal failure. *Am J Kid Dis* 1998;XII(1):43-7.
11. **Bellomo R, Ernest D, Love J, Parkin G, Boyce N.** Continuous arteriovenous haemodiafiltration: Optimal therapy for acute renal failure in an intensive care setting? *Aust NZ. Med* 1990;20:237-42.
12. **Gotch FA, Sargent JA.** A mechanistic analysis of the National Cooperative Dialysis study (NCDS). *Kid Int* 1985;28: 526-34.
13. **Barth RH.** Direct calculation of kt/v: A simplified approach to monitoring of hemodialysis. *Nephron* 1988; 50:191-5.
14. **Chen Y, Chen Yinb C, Hsu H, Yang C, Fang J.** APACHE III scoring system in critically ill patients with acute renal failure requiring dialysis. *Dial Transplant* 2002;31(4):222-9.
15. **Fiore GB, Ronco C.** Internal hemodiafiltration (iHDF): a possible option to expand hemodiafiltration therapy. *Int J Artif Organs* 2004; 27:420-23.

LITERATURE REVIEW

Clinical and laboratory findings and therapeutic responses in children with nephrotic syndrome.

A.A.S.L Safaei, S Maleknejad ; *Indian journal of Nephrology*;2010; Volume : 20; Issue : 2; 68-71

Nephrotic syndrome (NS) is a clinical entity characterized by massive loss of urinary protein leading to hypoproteinemia and edema. This prospective cross sectional study was performed on 44 children with idiopathic nephrotic syndrome (INS). The objectives were to study the clinical and biochemical parameters at the time of diagnosis of nephrotic syndrome and to study the histopathological distribution of different subtypes of INS and drug response pattern. There were 29 (66%) males and 15 females (34%). The mean age of NS was 4.87±3.24 years. Facial edema was found in 42 (95%), microscopic hematuria in 10 (23%), gross hematuria in 2 (4.5%), and hypertension in 5 (11.2%) of patients. In 17 children who underwent biopsy, focal segmental glomerulosclerosis was the most common pathologic finding (41%). Other subtypes included minimal change in three (18%), membranoproliferative glomerulonephritis in 1(5.8%), diffuse proliferative glomerulonephritis in 2 (11.6%), membranous glomerulonephritis in 1 (5.8%), and diffuse mesangial proliferation in 3 (17.5%) of cases. At the time of hospital admission, peritonitis were present in five (11.4%), pneumonia and upper respiratory infection (sinusitis) in eight (18%), cellulitis in two (4.5%). Among 44 children with NS, 29 (66%) were steroid sensitive cases, nine (20.5%) were steroid resistant and six (13.5%) were steroid dependent. Among patients with steroid sensitive NS, 37% were without relapsers, 38.8% frequent relapsers and 26.4% were infrequent relapsers. These results suggest that there are differences between season of incidence, response to treatment with corticosteroid and pathologic findings in our study and other studies in Iran and other countries.