Pediatr Nephrol (1998) 12:589–591
© IPNA 1998

Pediatric Nephrology

Original article

Ammonia clearance by peritoneal dialysis and continuous arteriovenous hemodiafiltration

Kar Yin Wong[1], **Sik Nin Wong**[2], **Shu Yan Lam**[2], **Sidney Tam**[3], **and Nai Shun Tsoi**[1]

[1] Department of Pediatrics, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong
[2] Department of Pediatrics, Tuen Mun Hospital, Hong Kong
[3] Department of Clinical Biochemistry, Queen Mary Hospital, Hong Kong

Received September 2, 1997; received in revised form Feburary 26, 1998; accepted March 2, 1998

Abstract. We report the use of continuous arteriovenous hemodiafiltration (CAVHD) in a neonate with severe hyperammonemia due to a urea cycle disorder. We compared the ammonia clearance (C_{NH_3}) for peritoneal dialysis (PD) and CAVHD. C_{NH_3} for CAVHD was 7.45 ml/min per m^2 at a dialysate flow of 300 ml/h and was 10.55 ml/min per m^2 at a dialysate flow rate of 600 ml/h. The mean PD clearance was 2.15 ml/min per m^2. Our data suggest that CAVHD is superior to PD for the removal of plasma ammonia. We conclude that CAVHD should be considered a reasonable alternative in the treatment of neonatal hyperammonemia in urea cycle disorders when medical treatment fails.

Key words: Continuous arteriovenous hemodiafiltration – Hyperammonemia – Peritoneal dialysis – Urea cycle disorder

Introduction

Urea cycle disorders are rare disorders characterized by various enzymatic defects in the catabolism of protein. The ammonia so produced is highly toxic to neural tissue, and delay in removal of ammonia results in high morbidity and mortality. Treatment modalities aiming at rapid ammonia removal are usually needed. Exchange transfusion (ET), peritoneal dialysis (PD), hemofiltration [continuous arteriovenous hemofiltration/continuous venovenous hemofiltration (CAVH/CVVH)], and hemodialysis (HD) have all been employed [1–3]. HD is considered the most-effective treatment [2, 4], but practical difficulties may be encountered, especially in neonates. We failed to lower the ammonia level in our patient with medical treatment, PD, and ET. Continuous arteriovenous hemodiafiltration (CAVHD) was then instituted, with a rapid drop in plasma ammonia. The clearance rate of ammonia (C_{NH_3}) was compared for the two methods of dialysis.

Correspondence to: K.Y. Wong

Case report

The patient was the first child of a healthy non-consanguineous couple delivered at full-term by cesarean section. His birth weight was 3 kg and physical examination was normal. He was well until day 4 of life, when he was found to be unresponsive and cyanotic. Immediate resuscitation was performed. Electrocardiography showed ventricular tachycardia, and arterial blood gas showed severe metabolic acidosis (pH 6.8). Cardioversion and amiodarone were given to revert the arrhythmia, and he was subsequently transferred to a cardiac center. No structural heart disease was found. Metabolic screening revealed hyperkalemia, metabolic acidosis, and deranged renal function (serum creatinine 220 μmol/l). Plasma ammonia level was 750 μmol/l (normal 10–140 μmol/l).

A Tenckhoff catheter was inserted percutaneously, and PD was started to treat hyperammonemia and renal failure. Dianeal dialysate solution 4.25% (Baxter, Fla., USA)[1] was run at 25 ml/kg per hour. The infusion, dwell, and collection times were 10, 20, and 30 min, respectively. The ammonia level continued to rise, with a peak of 1,970 μmol/l 24 h after the commencement of PD. Higher dialysate volumes were not tolerated by the patient because of increased ventilator requirement. He was then transferred to our hospital for further management.

A double-volume ET with fresh whole blood (170 ml/kg body weight) was performed after admission, but the reduction of ammonia was not satisfactory, with an immediate post-ET ammonia level of 1,230 μmol/l. Arginine infusion was started. He was fasted and intravenous glucose was supplied. In view of the poor C_{NH_3}, CAVHD was started while PD continued. French 5 umbilical arterial and venous catheters were used for the procedure, with an Amicon Minifilter (Amicon, Danvers, USA). Regional anticoagulation was used with heparin and protamine. Dialysis was accomplished with 1.5% Dianeal dialysate solution (Baxter)[2] running at rates of 300–900 ml/h using an infusion pump (Lifecare 5000, Abbott, USA). Substitution fluid with Hartman's solution was administered via a peripheral intravenous line. Plasma ammonia was successfully reduced to below 300 μmol/l within 36 h of the commencement of CAVHD. Ammonia concentration was measured with an end-point colorimetric assay by Kodak Ekta-

[1] Composition of 4.25% Dianeal solution: sodium 125–150 mmol/l; potassium 0–4.5 mmol/l; calcium 0–2.5 mmol/l; magnesium 0.25–1.5 mmol/l; acetate/lactate 30–60 mmol/l; calcium 90–120 mmol/l; glucose 4.25 g/dl, pH 5.0–6.5
[2] Composition of 1.5% Dianeal solution: same as 4.25% Dianeal solution except glucose concentration 1.5 g/dl)

chem 500 Dry Chemistry Analyzer (Johnson and Johnson Clinical Diagnostics, Rochester, N.Y., USA), and C_{NH_3} was estimated for PD and CAVHD.

No complications were encountered related to the procedure, except for clotting of the hemofilter 36 h after commencement of CAVHD. However, the patient's neurological and hemodynamic condition did not improve. The prognosis was grave and conservative treatment was adopted after counselling his parents. He finally died on day 13 of life of multi-organ failure. Plasma amino acid assay revealed an absence of citrulline, with significantly elevated glutamine and alanine, and increased urinary orotic acid. The findings were compatible with ornithine transcarbamylase deficiency.

Methods

Freshly collected heparinized (lithium or sodium heparin) blood or dialysate samples were kept in air-tight vials with minimal head space. They were delivered to the laboratory promptly on an ice-bath. The cellular components were separated quickly by centrifugation, immediately followed by ammonia measurement on the Ektachem Analyzer. The between-run and within-run coefficients of variation were 9.1% and 6.6%, respectively at 55 µmol/l, and 7.0% and 5.9%, respectively at 136 µmol/l. C_{NH_3} was calculated by dividing the multiplication product of filtrate ammonia concentration ($[NH_3]fil$) and volume of filtrate (Vf) by plasma ammonia concentration ($[NH_3]p$) over time:

$$C_{NH_3} = \frac{[NH3]fil \times Vf}{[NH3]p \times time}$$

Table 1. Ammonia clearance (C_{NH_3}) by peritoneal dialysis (PD)

Cycle	Plasma NH_3 (µmol/l)	NH_3 in PD fluid (µmol/l)	Spent dialysate volume (ml)	C_{NH_3} (ml/min)
1	1,930	483	136	0.567
2	1,580	627	55	0.364
3	1,230	544	66	0.486

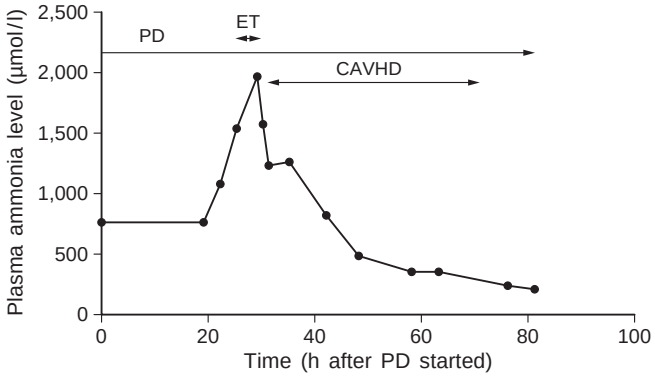

Fig. 1. Plasma ammonia level with the various therapeutic modalities. *PD*, Peritoneal dialysis; *ET*, exchange transfusion; *CAVHD*, continuous arteriovenous hemodiafiltration

Peritoneal dialysis. Three cycles of PD were used for calculation before institution of CAVHD. Blood for ammonia was taken at mid-cycle, and hourly dialysate output was collected simultaneously. The ammonia concentration of the filtrate for each cycle was then analyzed. The results are shown in Table 1. Mean C_{NH_3} by PD of the three cycles was 0.47 ml/min (2.15 ml/min per m^2, estimated surface area 0.22 m^2).

Continuous arteriovenous hemodiafiltration. C_{NH_3} was estimated over four 30-min cycles, approximately 10 h after the PD samples were obtained. Blood samples from the arterial (pre-filter) limb of the CAVHD circuit were obtained at mid-cycles for ammonia level. Spent dialysate volume was collected over the same period with graduated burette, and ammonia concentration was analyzed. Dialysate flow rate was adjusted to 300 ml/h, 600 ml/h, and 900 ml/h in sequential cycles, using 1.5% Dianeal dialysate solution (running as a countercurrent flow). The results are shown in Table 2. Mean C_{NH_3} at dialysate flow rate of 300 ml/h was 7.45 ml/min per m^2, while that for 600 ml/h was 10.55 ml/min per m^2. There was no more increase in C_{NH_3} (10.36 ml/min per m^2) as the dialysate flow rate was increased to 900 ml/h. Blood flow rate of the CAVHD circuit was not measured, but an estimation could be ob-

Table 2. C_{NH_3} by continuous arteriovenous hemodiafiltration (CAVHD)

Cycle	Dialysate flow rate (ml/h)	Plasma NH_3 (µmol/l)	NH_3 in filtrate (µmol/l)	Spent dialysate volume[a] (ml)	C_{NH_3} (ml/min)	Net ultra filtration rate[b] (ml/h)
1	300	479	128	150	1.336	0
2	300	424	137	180	1.939	+60
3	600	468	93	350	2.318	+100
4	900	221	35	433	2.286	–34

[a] Volume of spent dialysate collected over 30 min
[b] '+' refers to loss from patient

Table 3. Estimation of blood flow rate of CAVHD by creatinine clearance

Cycle	Pre-filter creatinine (µmol/l)	Post-filter creatinine (µmol/l)	Filtrate creatinine (µmol/l)	Hourly spent dialysate volume (ml)	Hourly net ultrafiltration output (ml)	Estimated blood flow (ml/min)
5	300	252	72	314	+14	6.63
6	303	241	33	653	+41	3.14
7	261	228	25	812	+37	5.99

tained by calculating simultaneous pre- and post-filter serum creatinine levels, the filtrate creatinine, and the volume of spent filtrate over the three separate CAVHD cycles (Table 3). It was 3.14–6.63 ml/min, and was expected to vary during the process of dialysis. The plasma ammonia level with various treatment modalities is shown in Fig. 1.

Discussion

Our results illustrate that CAVHD is superior to PD in ammonia clearance when performed for neonatal hyperammonemia as a result of urea cycle disorders. The efficacy is at least two to five times that of PD at a low dialysate flow rate. C_{NH_3} for CAVH has been reported to range from 5 ml/min per m^2 [3] to 19.4 ml/min per m^2 [6], but that of CAVHD has not been reported. C_{NH_3} appeared to be related to dialysate flow rate in CAVHD to some extent, although the net ultrafiltration volumes of the four cycles were different. However, filtration alone could not explain C_{NH_3} at the fourth cycle, when the net ultrafiltration was negative (Table 2).

HD is the most-effective method for the removal of ammonia, being at least ten times more effective than PD [1, 2, 4]. However, the more-sophisticated circuit and the higher extracorporeal circulatory volume required have limited its use to bigger children in specialized centers, although the successful use of this technique in infants less than 5 kg has been reported [6]. CAVH and CVVH, with or without dialysis, have been shown to be effective and safe in many studies [5, 7–10]. The circuit that we used has an extracorporeal volume of 12 ml. This was shown to be safe in our patient, who did not experience any change in hemodynamic state throughout the procedure, as did 61%–71% of HD patients [6]. Umbilical 5-Fr catheters were adequate to achieve a good blood flow and ultrafiltration rate.

CAVHD and CVVHD have been used more frequently in the past decade as an alternative renal replacement therapy for small children [7, 9]. The removal of small molecules is feasible with CAVH/CVVH, but hemofiltration alone is inferior to CAVHD for acute renal failure [5, 7]. Adding dialysate will improve solute removal [7–9], and data are emerging about the clearance rates of individual substances by this method for pediatric patients.

C_{NH_3} of PD was estimated by Siegel and Brown [1] to be 10.1 ml/min per m^2, which was higher than that in our patient. This may partially be explained by differences in hemodynamic characteristics and pathophysiological variables in our patient. Moreover, the PD cycle characteristics were different, as further increase in cycle volume in our patient was limited by his respiratory difficulty. Comparison of the direct clearance rate of various metabolites can be made, as in our patient, to decide which modality of treatment is best, in addition to observation of the clinical response. We believe that HD is the best method for ammonia removal if medical treatment fails, and more studies are required to demonstrate the definitive benefits and role of CAVHD. In conclusion, CAVHD should be considered an acceptable alternative if HD is not available and other forms of treatment are either impossible or ineffective.

Acknowledgements. Part of this study was presented as an abstract at the 6th European Congress of Pediatric, Surgical, and Neonatal Intensive Care held in Greece in 1993.

References

1. Siegel NJ, Brown RS (1973) Peritoneal clearance of ammonia and creatinine in a neonate. J Pediatr 82:1044–1046
2. Wiegand C, Thompson T, Bock GH, Mathis RK, Kjellstrand CM, Mauer SM (1980) The management of life-threatening hyperammonemia: a comparison of several therapeutic modalities. J Pediatr 96:142–144
3. Sperl W, Geiger R, Maurer H, Guggenbichler JP (1990) Continuous arteriovenous haemofiltration in hyperammonaemia of newborn babies. Lancet 336:1192–1193
4. Rutledge SL, Havens PL, Haymond MW, McLean RH, Kan JS, Brusilow SW (1990) Neonatal hemodialysis: effective therapy for the encephalopathy of inborn errors of metabolism. J Pediatr 116:125–128
5. Ring E, Zobel G, Stockler S (1990) Clearance of toxic metabolites during therapy for inborn errors of metabolism. J Pediatr 117:349–350
6. Sadowski RH, Harman WE, Jabs K (1994) Acute hemodialysis of infants weighing less than five kilograms. Kidney Int 45:903–906
7. Bishof NA, Welch TR, Strife CF, Ryckman FC (1990) Continuous hemodiafiltration in children. Pediatrics 85:819–823
8. Assadi FK (1988) Treatment of acute renal failure in an infant by continuous arteriovenous hemodialysis. Pediatr Nephrol 2:320–322
9. Bunchman TE, Donckerwolcke RA (1994) Continuous arterial-venous diahemofiltration and continuous veno-venous diafiltration in infants and children. Pediatr Nephrol 8:96–102
10. Sperl W, Geiger R, Maurer M, Murr C, Schmoigl C, Gersdorf ES, Sailer M (1992) Continuous arteriovenous haemofiltration in a neonate with hyperammonaemic coma due to citrullinaemia. J Inherit Metab Dis 15:158–159