Combined amino acid and glucose dialysate in children on automated peritoneal dialysis

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Chronic renal failure (CRF) presenting in childhood may have a long-standing adverse effect in nutrition and growth. This is because growth in childhood is predominantly dependent on nutrition, and decreased spontaneous oral intake was demonstrated in several studies in children with CRF. Energy intake correlates negatively with glomerular filtration rate (GFR), and the intake deteriorates with the severity of CRF. Children undergoing peritoneal dialysis (PD) were observed to suffer from wasting, and/or protein energy malnutrition. Early introduction of enteral feeding may result in normal growth, if it maintains an adequate energy intake. Recently, the use of amino acid (AA) containing dialysis fluids was considered for its nutritional benefits in malnourished dialyzed children. Some studies have reported a significant improvement in some nutritional parameters, while others have shown no significant improvement in the same parameters. It was demonstrated that AA dialysis is an efficient form of peritoneal dialysis in patients on automated peritoneal dialysis (APD), and should be considered for children with poor nutritional status for whom enteral nutrition supplementation has been unsuccessful. Peritoneal dialysis solutions containing a mixture of AA and glucose in a proper ratio can serve as a source of protein and calories. The objective of this prospective study was to find out if the use of AA dialysate will improve nutritional markers and growth in children receiving APD. We also investigated whether AA dialysate had any adverse side effects.

All children on APD who are followed-up at the King Abdul-Aziz University Hospital (KAUH) between September 2008 and September 2009 were recruited for the study. Syndromatic and children on growth hormone were excluded from the study. Seven children (5 girls and 2 boys) fulfilled the criteria, and their parents gave their consent for their inclusion in the study. Their mean age was 11.33 ± 3.7, and the mean duration on PD before the study was 15 ± 0.8 months. None of the children had secondary pubertal signs. During the study period, children received hourly APD cycles of 1100-1400 ml/M² for 10 hours, utilizing a mixture of manufactured AA dialysate (1.1%), and dextrose solution (1.5 or 2.5%) with a 1:1 ratio. Children were studied for a 12-month duration. The following were monitored at a 3-month interval: height standard deviation score (HtSDS); body mass index (BMI); serum albumin; pre-albumin; renal function tests; bone profile; acid-base disturbances; and serum AA levels (alanine, arginine, asparagine, aspartic acid, citrulline, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, ornithine, phenylalanine, serine, tryptophan, taurine, threonine, and tyrosine). The measurement of AA in the serum was carried out during the day when the children were not receiving APD. Dialysis efficiency was measured by the clearance of urea nitrogen (Kt) divided by urea distribution volume (v). The Kt/V was measured before and at the end of the study.

All studied children were prescribed high calorie diet (70-100 kcal/kg/day), which was given orally as they refused enteral feeding (nasogastric or gastrostomy). Their adherence to high calorie diet was doubtful. The peritoneal WBC was checked monthly as part of the study protocol. This study was approved by the research ethical committee at KAUH, and it was conducted according to the principles of Helsinki Declaration.

The analysis of variance (ANOVA) test was used for statistical analysis. A p < 0.05 was considered significant. The KIGS software (Pfizer International Growth database) was used to calculate HtSDS and BMI. The results were expressed as mean ± standard deviation.

There was no difference in the peritoneal equilibration test (PET) before, and after finishing the study. Similarly the ultra-filtrate (UF) did not change before, during, or after the study. The mean Kt/V before the study was 2.04 ± 0.33, and it was 1.7 ± 0.78 (p=0.32) after the study. There was no improvement in HtSDS, and there was no significant difference between the start and follow-up visits (p=0.996) (Figure 1). Most of the children were malnourished at the start of the study, as their BMI was less than 20, except for one child with a BMI of 25.5. The median BMI at the start was 15 (range: 13.6-25.5). There was no improvement in the BMI (p=0.996), and there was no significant difference between the start and follow-up visits (p=0.95). There was no improvement in the serum albumin (normal range; 33-48 g/L), that is: mean at the start was 31.9 ± 3.6; at 3 months was 28.3 ± 5.9; at 6 months was 27.4 ± 7.6; at 9 months was 29.9 ± 5.9; at 12 months was 29.9 ± 5.9; at 15 months was 29.9 ± 5.9; at 18 months was 29.9 ± 5.9; and at 21 months was 29.9 ± 5.9.

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Individual height standard deviation scores (HtSDS) of studied patients while receiving amino acid (AA) dialysate at the start of the study at 3, 6, 9, and 12 months (m). The thick line represents the mean HtSDS.

± 8.9; and at 12 months was 30.8 ± 6.5 (p=0.74). There was no improvement in the serum pre-albumin (normal range: 0.16-0.35 g/L): mean at the start - 0.36 ± 0.1; at 3 months was 0.26 ± 0.16; at 6 months was 0.32 ± 0.05; at 9 months was 0.30 ± 0.9; and at 12 months was 0.35 ± 0.35 (p=0.74). There was no significant change in the serum level of 14 amino acids over the 12 month duration of the study, such as: alanine, arginine, asparagine, glutamic acid, glutamine, glycine, histidine, lysine, methionine, ornithine, serine, taurine, threonine, and tyrosine. While there was a decrease in the serum level of tryptophan and phenylalanine, there were inconsistent changes in the serum level of aspartic acid, citrulline, isoleucine, leucine, and phenylalanine. The mean serum bicarbonate (HCO3) at the start of the study was 25.8 ± 3.1 on no pharmacologic treatment. However, all the studied children needed oral sodium bicarbonate (NaHCO3) to compensate for the metabolic acidosis during the study duration, and it was not required after stopping the AA dialysate. Their need for NaHCO3 started 4 weeks after starting the AA dialysis solution, and they required 2-3 mmol/kg/day of NaHCO3 in order to keep HCO3 >20 mmol/L. We have also observed a significant increase in the urea level (p=0.026). We have observed a rise in the white blood cell count (WBCs) in the peritoneal dialysis fluid (PDF) >100 cells/ml in 5 children (71%). We also have to stop the AA dialysate in 4 children. Only 3 children completed the study, as the fifth child had a high PDF cell count of 311 cell/ml with 75% monocytes, who improved spontaneously after a few weeks. The sixth child had an increase in WBC twice to 86 (70% monocytes [Mon] and 11% neutrophils [N]), and 55 (78% Mon and 15% N) but not more, and completed the study without the need to hold, change, or discontinue the dialysis. The last child had a PDF WBC of 0-2 throughout the study. The rise of peritoneal WBCs was not associated with the clinical picture of peritonitis, or elevation of acute phase reactant, such as C-reactive protein or peripheral WBC count. All the cultures were negative for both bacteria and fungus.

The sixth child had experienced a blockage of the PD catheter after 2 months of starting the study, and needed catheter replacement, however, she completed the 12 months study. We have observed no improvement in any of the nutritional markers after using AA dialysate for 12 months in malnourished children, who were receiving APD. However, we observed satisfactory fluid and waste removal, as there was no change in the UF or the KT/V before, during, and after the study. This is similar to a previous report that compared with glucose dialysate, AA dialysates provide reduced but satisfactory fluid and waste removal. Our results of no nutritional benefits after a 12 month use of AA dialysate in APD children is similar to Canepa et al in children receiving continuous ambulatory peritoneal dialysis. Alternatively, others reported an increase in blood urea nitrogen (BUN), total body nitrogen, and appetite in children on APD using a once daily long dwell of AA dialysate. Similar to our results, they reported no significant changes in total plasma albumin and AA levels.

In agreement to a previous report, we observed a significant increase in the blood urea level. However, no change was observed in the BUN when the AA dialysate was infused simultaneously with glucose in APD patients, and this support the hypothesis that AA when infused simultaneously with glucose is utilized...
for protein synthesis, and not catabolized for energy production. The moderate increase of BUN in our study may be explained by the improper utilization of the infused AA as an energy source, despite being co-infused with dextrose. The considerable severity of malnutrition in our patients could contribute to that. This also can explain the need of our entire cohort for NaHCO3 when they were receiving AA dialysate. It was recommended to use dialysis solutions with a buffer concentration of 40 mmol/L to maintain acid-base homeostasis.

Similar to a previous report, we did not observe a change in serum albumin or pre-albumin level. While others reported an increase in serum albumin with the use of AA dialysate, and a significant improvement was observed in somatic protein status, such as lean body mass (LBM) and handgrip strength. We observed no changes in the most of the measured AA levels, and an inconsistent change in 5 AA levels (4 of which are essential AA). A previous study reported no changes, an improvement, or decreased AA levels. This variation could be explained by timing of the blood sample for AA, as the peak absorption of AA occurs one-hour post-infusion. We did not observe any changes in the dialysate small solute clearance, or on the ultrafiltration rate. This is similar to previous studies, which showed an efficient and safe dialysis when using a 1.1% AA solution. It was hypothesized that an AA dialysate offers a significant reduction in carbohydrate load (approximately 40-50%), lower exposure to, and absorption of glucose degradation products, reduced oxidative stress, and improved volume control when compared with a glucose based solution. This study was confirmed in a group of children that the use of a 1.1% amino acid dialysate allows the advantages of avoiding higher peritoneal membrane glucose exposure, while maintaining effective small solute clearance and ultrafiltration.

We have observed an unexplained asymptomatic rises in peritoneal WBC counts in 5 of the studied patients, which led to the catheter removal in 2 of them. It resolved in the other 2 children after stopping the AA solution, and resolved spontaneously on the last child. Cloudy peritoneal dialysate caused by cellular increase of N, eosinophils, or M were reported before as a result of intraperitoneal visceral inflammation, endotoxin contaminated PD fluid, allergic reaction, drug associated, or as a result of intraperitoneal irritation by blood, or air induced by placement of a new catheter. Infectious causes remain the most common cause of increased peritoneal WBC, which was excluded in our studied patients. The limitation of our study was the small number of the studied children, absence of control, and the inability of the most patients to finish the study because of the observed increase in the peritoneal WBC.

In conclusion, in this study, the use of high dose amino acid dialysate in a group of children who refused enteral feeding provided effective small solute clearance and ultrafiltration, thus lowering glucose exposure to the peritoneal membrane. However, we did not observe any improvement on nutritional status, or growth parameters in over 12 month study duration of this study. In addition, it was noted that this dose of AA dialysate was associated with a rise in peritoneal WBC count, the cause of which is unclear. High dose AA dialysate should be used with caution in children, and a trial of stopping AA dialysate is indicated in case of observed high peritoneal WBC before removing PD catheters.

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