Changes in Osmolal Gap and Osmolality in Children with Chronic and End-Stage Renal Failure

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Key Words

Osmolal gap · Osmolality · Chronic renal failure

The osmolality and osmolal gap (OG) of physiological fluids tend to be dominated by small molecules which are present in high concentrations [1]. The OG is an indication of unmeasured solute in the blood; it is defined as the difference between the measured serum osmolality and the calculated serum osmolality [2, 3]. An OG value greater than 10 mosm/kg is considered a critical value, and it is clinically important in two conditions: (a) assessment of serum water content, especially in hyponatremia accompanied by hyperlipemia or hyperproteinemia; (b) evaluation of exogenous low-molecular-weight substances, such as ethanol, methanol and acetone.

Levels of OG and serum osmolality are important in pediatric patients and particularly in patients with chronic renal failure (CRF). In CRF patients under dialysis therapy, especially during hemodialysis (HD), when blood urea levels drop suddenly and significantly, a 'dialysis dysequilibrium syndrome' may develop. Therefore, there is an increased risk for neurological complications (such as cerebral edema) in CRF patients under HD treatment [4, 5]. In several previous studies, OG was found

within the reference range in patients with renal failure [6]. However, the role of OG and serum osmolality in this condition was not established very well. The aim of this study is to determine the serum OG and osmolality in children with various stages of CRF and the effect of dialysis modalities on these parameters. We also investigated the possible relationship among the changes of OG and serum osmolality before and after HD in patients with CRF.

We studied 101 patients (52 boys and 49 girls), with known CRF. Thirty-six patients (age range 5–16 years) underwent HD (HD patients), 29 patients peritoneal dialysis (PD patients) whose age range was 2–14 years, and 25 of them were on continuous ambulatory PD while 4 were treated by continuous cycling PD; 36 nondialyzed (age range 2–16 years) CRF patients (ND patients) were also included. There was a statistically significant difference in age between the PD and HD groups ($p = 0.013$). All HD patients were treated by bicarbonate dialysis 3 times weekly with 0.4–0.7 m² substituted cellulosic membranes. PD was carried out 4–6 times daily in continuous ambulatory PD patients and for 8–10 h/night in continuous cycling PD patients with 1.36% peritoneal dialysis solutions (Dianeal 1.36%, Baxter-Eczacıbası Healthcare, Istanbul, Turkey). There was no medication by mannitol in any groups. Samples of blood were obtained before and

Table 1. Serum biochemical profile (mean $\pm$ SD) and differences between groups in children with renal failure

Parameters	ND group (n = 36)	PD group (n = 29)	HD group (n = 36)		
			before HD	after HD	p (between before and after HD)
Sodium, mEq/l	138.6 $\pm$ 7.0	135.8 $\pm$ 3.9	135.2 $\pm$ 4.3	137.2 $\pm$ 3.9	0.04
Potassium, mEq/l	5.0 $\pm$ 1.2	4.8 $\pm$ 0.9	4.9 $\pm$ 1.4	3.9 $\pm$ 1.4	0.000
BUN, mg/dl	71.7 $\pm$ 38.9	66.6 $\pm$ 26.1	73.6 $\pm$ 26.4	33.7 $\pm$ 11.9	0.000
Creatinine, mg/dl	6.4 $\pm$ 5.3	7.4 $\pm$ 3.3	8.3 $\pm$ 3.2	4.8 $\pm$ 2.0	0.000
Glucose, mg/dl	90.5 $\pm$ 13.0	90.6 $\pm$ 23.1	88.7 $\pm$ 28.0	95.2 $\pm$ 30.0	0.2
Protein, g/dl	6.2 $\pm$ 1.2	5.9 $\pm$ 0.8	5.6 $\pm$ 1.2	5.9 $\pm$ 1.3	0.02
Albumin, g/dl	3.6 $\pm$ 1.0	3.3 $\pm$ 0.6	3.5 $\pm$ 0.9	3.8 $\pm$ 0.9	0.02
Osm _m , mosm/kg	329.3 $\pm$ 31.6 ^a	314.1 $\pm$ 15.2	327.5 $\pm$ 31.6 ^a	311.0 $\pm$ 20.5	0.002
Osm _c , mosm/kg	307.9 $\pm$ 19.1	300.4 $\pm$ 9.1	301.6 $\pm$ 13.2	295.0 $\pm$ 11.1	0.01
OG, mosm/kg	21.4 $\pm$ 20.7	13.7 $\pm$ 14.5	25.7 $\pm$ 26.2 ^b	15.2 $\pm$ 17.6	0.01

BUN = Blood urea nitrogen; Osm_m = measured serum osmolality; Osm_c = calculated serum osmolality.

^a p < 0.05 between before-HD group and PD group, and also between ND and PD groups.

^b p < 0.05 between before-HD group and PD group.

after HD from HD patients and at any time from PD and ND patients. With centrifugation (3,000 rpm, 5 min, 4°C) serum was removed from other components of blood and was stored at -80°C until study.

Serum osmolality was measured by a Knauer Osmometer Automatic (D-14163, Berlin, Germany) and calculations were based on the following formula: osmolality = (2 $\times$ Na⁺) + (glucose/18) + (BUN/2.8) [3]. Serum Na⁺, K⁺, BUN, creatinine, glucose, protein and albumin were determined by standardized procedures. Residual renal function was determined with the calculated creatinine clearance by the Schwartz formula [7] in ND patients, and adequacy of the dialysis method was established by Kt/V_{urea} in HD [8] and in PD patients [9].

One-sample t test, Student's t test and paired t test were used for normally distributed continuous variables. Since the data were not distributed normally, appropriate non-parametric tests were chosen (Mann-Whitney U test and Wilcoxon rank sum test). Bonferroni's correction was applied (p < 0.05/n, where n = number of comparisons) when multiple comparisons were made. All results are expressed as means $\pm$ SD. A p value lower than 0.05 was considered as significant.

Serum biochemical parameters and differences between groups are shown in table 1. The mean urea reduction ratio in the HD group was 58.32 $\pm$ 14.26. The mean OG was statistically significantly higher in patients before HD than after HD. The mean OG of PD was statistically significantly lower than in the patients before HD.

The mean measured osmolalities of PD and after-HD patients were statistically significantly lower than those of the patients before HD and the ND patients. We compared our results with some main reference studies about this subject [3, 10, 11]. However, the OG and measured osmolality levels of our study were not significantly different in the PD group (13.7 $\pm$ 14.5 and 314.1 $\pm$ 15.2 mosm/kg) and in patients after HD (15.2 $\pm$ 17.6 and 311.0 $\pm$ 20.5 mosm/kg) than the reference levels (5.0 $\pm$ 14.0 and 290.0 $\pm$ 5.0 mosm/kg; p > 0.05), but they were found to be significantly higher in ND patients (21.4 $\pm$ 20.7 and 329.3 $\pm$ 31.6 mosm/kg) and in patients before HD (25.7 $\pm$ 26.2 and 327.5 $\pm$ 31.6 mosm/kg) when compared with reference values (p < 0.05).

Hypernatremia caused by reduced water content can increase osmolality but does not cause a rise in OG, since the measured and calculated osmolalities are both high [11]. As OG and osmolality significantly decrease after HD sessions, HD patients have an increased risk of dialysis dysequilibrium syndrome [12]. OG values were normal in PD patients and significantly increased in ND patients and before HD. In addition, measured osmolality was significantly higher in patients before HD than in PD patients. According to our values, there were some osmotically active particles in the blood that changed serum OG and osmolality in CRF patients. We think that these changes were mainly due to elevations in BUN, creatinine and K⁺ concentrations and these particles are cleared more rapidly in HD than PD.

In conclusion, monitoring of the OG and serum osmolality plays an important role to determine the risk of neurological complications in patients with CRF. Because the change of serum sodium levels does not influence it, OG must be calculated in patients who carry the risk of dialysis dysequilibrium syndrome. The surprising outcome in our study was the higher levels of OG and

measured osmolality in patients before HD, but normal levels in PD patients. Therefore, when we have to decide on the dialysis modality, we should consider these results. We conclude that for those with a risk of neurological complications, PD should be the preferred method because a stable serum OG and osmolality have been shown to be achieved.

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