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Original Article

The Effect of Metabolic Acidosis on Nutritional Status And Adequacy of Dialysis in Pediatric Patients On Regular Haemodialysis

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ABSTRACT

Background: Metabolic acidosis is a well known feature of end-stage renal disease (ESRD) leading to protein breakdown, decreased cardiac inotropism and increased severity of bone disease.

Objective: This work was designed to study the consequences of metabolic acidosis on nutritional status and adequacy of dialysis in pediatric regular haemodialysis (HD) patients.

Methods: Arterial blood samples were drawn immediately before HD from 30 patients with ESRD on regular HD therapy to determine pH, $PaCO_2$, HCO_3, serum albumin, serum creatinine, blood urea nitrogen (BUN), C-reactive protein (CRP) and complete blood count (CBC), Post-dialysis arterial blood samples were drawn 3 minutes after session from all patients, to determine pH, $PaCO_2$, HCO_3, serum creatinine and BUN. The normalized protein catabolic rate (nPCR) was calculated and correlated with serum albumin, bicarbonate level and CRP. Kt/V and urea reduction ratio (URR) were calculated and correlated with degree of biocarbonate correction.

Results: Children with ESRD on regular HD therapy had elevated pre-dialysis BUN and serum creatinine levels in comparison with post-dialysis results. Pre-dialysis serum albumin was 3.43 ± 0.56 g/dl. Dietary protein intake was 1.32 ± 0.53 g/kg/day, PNA was 42.28 ± 10.3 g/dl, nPNA was 1.77 ± 0.53 g/kg/dl. All patients had metabolic acidosis in the pre-dialysis period which was corrected after dialysis. pH was 7.31 ± 0.057 and 7.45 ± 0.04 respectively. Dialysis raised the level of HCO_3 and $PaCO_2$ with mean ± SD of HCO_3 19.4 ± 2.53 and 26.7 ± 2.17 mmol/L and of $PaCO_2$ was 35.9 ± 3.36 and 41.76 ± 1.83 Hg respectively. The patients were adequately dialysed as the mean ± SD of Kt/V and URR were 1.25 ± 0.25 and 64.13 ± 7.29 respectively. 80% of patients had -ve CRP and 20% of them had elevated CRP. The quantity of dialysis measured by Kt/V and URR showed no statistically significant correlation with either the pre- or the post-dialysis HCO_3, ($p > 0.05$). There was no correlation between pre-dialysis HCO_3 and nPNA, pre-dialysis creatinine and albumin. There was -ve correlation between pre-dialysis HCO_3 and protein intake ($p < 0.05$). CRP correlated negatively with both serum creatinine and pre-dialysis serum albumin ($p < 0.05$) but no correlation with both nPNA and protein intake ($p > 0.05$) could be found.

Conclusions: Pre-dialysis metabolic acidosis is still a common finding in HD patients, but it can be corrected by increasing the quantity of dialysis. Metabolic acidosis has a significantly deleterious effect on nutritional status of patients with CRF. Both serum albumin and creatinine concentrations are influenced by inflammation. nPNA does not reflect the real dietary protein intake of the patients.

INTRODUCTION

Metabolic acidosis is a well recognized complication of progressive ESRD. It is a consequence of the inability to excrete non volatile acids in the face of the expected loss of renal bicarbonate synthesis[1].

One of the main goals of HD is the treatment of acidosis by a diffusive entry of

bicarbonate from dialysate to the blood and the clearance of retained anions that form non volatile acids[2].

Metabolic acidosis in patients with chronic uremia impairs nitrogen utilization, suppresses albumin synthesis and promotes skeletal muscle catabolism resulting in decreased serum creatinine level[3-5].

Both serum albumin and creatinine concentrations are considered to reflect nutritional status (nPCR). Also, both albumin and creatinine concentrations have been found to correlate with inflammation (CRP) in HD patients when analyzed either cross sectionally or longitudinally is found to be a reflection of either malnutrition, inflammation or a combination of both processes[6].

For these reasons both albumin and creatinine concentrations can be associated with CRP, serum bicarbonate as well as dietary protein intake[7].

AIM OF THE WORK

Our study aimed to correlate the quantity of dialysis as measured by URR and Kt/V, with the degree of correction of acidosis as guided by serum bicarbonate before and after dialysis, and investigate the relationships of serum albumin and creatinine levels with CRP, nPNA and serum bicarbonate level.

PATIENTS AND METHODS

This study was conducted on thirty patients with ESRD, on regular HD therapy, selected from the Pediatric Dialysis Unit of Abu-El-Rish Hospital, Cairo University. The studied patients included 12 male and 18 female patients and their age ranged between 2 to 16 years. All patients were treated by HD three times weekly with polysulfone membrane (the duration of dialysis procedure was 3 hours; blood flow rate ranged from 90-280 ml/min according to body weight, dialysate flow rate was 500 ml/min and did not changed). Inclusion criteria included children on regular HD treatment, for not less than 4 months, using bicarbonate dialysate and free from apparent acute illness. Exclusion criteria were patients less than one year of age and more than 16 years, diabetics on alkali therapy, and patients on regular dialysis for less than 4 months.

The studied patients were divided into 2 groups according to the level of HCO_3 (the degree of metabolic acidosis):

Group 1: patients with predialysis HCO_3 < 19 mmol/L; it included 14 patients.

Group 2: patients with predialysis HCO_3 ≥ 19 mmol/L; it included 16 patients.

All patients were subjected to full medical history, full clinical examination and assessment of nutritional status by estimation of dietary protein, (nPNA).

PNA = 20.1 + 7.5 UNA (g/kg/day).

nPNA = PNA/body weight (g/kg/day).

and body mass index (BMI) = $\frac{wt\ (kg)}{Ht^2\ (m)}$

weight/age percentile

Height/age and BMI/age. Assessment of dialysis adequacy; by calculation of:

1. Kt/V = -L n (R-0.008 xt) + (4-3.5R) UF/W

Ln = natural logarithm, R = post-dialysis BUN/pre-dialysis BUN.

t = dialysis session length in hours

UF = ultra filtration volumes in liters.

W = patients post-dialysis weight in kilogram.

2. URR which = 100 $(1-C_t/C_o)$

C_t = post-dialysis BUN, C_o = pre-dialysis BUN.

Laboratory investigations:

Blood samples were drawn from the arterial side of the arteriovenous fistula of all patients during the first dialysis session of the week prior to dialysis. The blood samples were divided into three parts, heparinized blood sample were used for measuring blood gases and electrolytes which included PH, PCO_2 and HCO_3 were performed on automated blood gases analyser (CIBA-CORNING 850). Second part was put with EDTA for CBC and 3rd part was put in empty tube for CRP, serum creatinine, albumin and BUN. Post-dialysis samples were drawn 3 min after session and divided into two tubes; one heparinized for blood gases and 2nd tube left empty for serum creatinine and BUN.

Statistical analysis

The collected data were tabulated and subjected to computer assisted analysis using Microsoft Excel version 5.0 for chart preparation and the statistical package for social science (SPSS) version 10. The following methods were employed:

- Frequency and percentage distributions.
- Mean and standard deviation.
- Comparison of means using the independent sample T test; testing differences between means for statistical significance.
- Correlations between numerical data using Pearson correlation; correlation coefficients (r values) were obtained and tested for significance using the T test.
- Correlations between non numerical data using spearman correlation; correlation coefficients (r values) were obtained and tested for significance using the T test.
- In general, p values less than 0.05 are considered significant, less than 0.01 highly significant and those below 0.001 very highly significant.

RESULTS

Thirty patients (12 males and 18 females) were enrolled in the study. Most of the patients were below 3rd percentile for weight and height (50%). As regards the BMI for age percentile, 36.7% of these patients were below the 3rd percentile and 36.6% of them were in the 10th – 90th percentile (Table 1).

The mean values ± SD of the pre- and post-dialysis BUN were 68.23 ± 15.33 and 24.43 ± 6.96 mg/dl respectively. Those of serum creatinine were 5.62 ± 2.44 and 2.22 ± 0.86 mg/dl respectively and pre-dialysis albumin was 3.43 ± 0.56 g/dl (Table 2).

All patients had metabolic acidosis in the predialysis period that was corrected after dialysis and the mean value ± SD of the predialysis HCO_3 was 19.4 ± 2.53 mmol/L and post-dialysis was 26.7 ± 2.17 mmol/L (Table 3).

The mean value ± SD of protein intake was 1.32 ± 0.53 g/kg/day and the mean value ± SD of nPNA of these patients was 1.77 ± 0.53 g/kg/day (Table 4).

Most of the patients were adequately dialyzed as the mean values ± SD of Kt/V and URR were 1.25 ± 0.25 and 64.13 ± 7.29 respectively (Table 5).

There was no correlation between both pre- and post-dialysis HCO_3 and the parameters of dialysis adequacy ($p > 0.05$) (Table 6).

There was no correlation between the

predialysis HCO_3 and each of nPNA, pre-dialysis serum creatinine and predialysis serum albumin. On the other hand, predialysis HCO_3 correlated negatively with the protein intake ($p < 0.05$) (Table 7).

The studied subjects were divided into 2 groups according to the predialysis HCO_3; group 1 (patients with higher degree of acidosis) showed significantly lower values as regards Kt/V, URR, pre-dialysis creatinine and albumin level ($p < 0.05$) (Table 8).

CRP correlated negatively with both serum creatinine and the predialysis serum albumin concentrations ($p < 0.05$) and there was no correlation between it and both nPNA and protein intake ($p > 0.05$) (Table 9).

Table 1: Weight, height and BMI for age percentile distribution of the studied patients.

	Percentile range	Frequency	Percent
Weight	$< 3^{rd}$ 3^{rd} - $< 10^{th}$ $10^{th} - 90^{th}$	15 6 9	50 20 30
Height	$< 3^{rd}$ 3^{rd} - $< 10^{th}$ $10^{th} - 90^{th}$ $> 90^{th}$	15 4 10 1	50 13.3 33.3 3.3
BMI	$< 3^{rd}$ 3^{rd} - $< 10^{th}$ $10^{th} - 90^{th}$ $> 90^{th}$	11 6 11 2	36.7 20 36.7 6.6

Table 2: Blood chemistry of the studied patients.

	Mean	± SD
BUN (mg/dL)		
Pre-dialysis	68.33	15.33
Post-dialysis	24.43	6.96
Creatinine (mg/dL)		
Pre-dialysis	5.62	2.44
Post-dialysis	2.22	0.86
Pre-dialysis albumin (g/dL)	3.43	0.56

Table 3: Acid base status of the studied patients.

	Mean	± SD
pH		
Pre-dialysis	7.31	0.057
Post-dialysis	7.45	0.04
HCO_3 (mmol/L)		
Pre-dialysis	19.4	2.53
Post-dialysis	26.7	2.17
$PaCO_2$ (mmHg)		
Pre-dialysis	35.9	3.36
Post-dialysis	41.76	1.83

Table 4: Dietary protein intake catabolism of the studied patients.

	Mean	± SD
Protein intake (g/kg/day)	1.32	0.53
PNA (g/dL)	42.28	10.3
nPNA (g/kg/d)	1.77	0.53

Table 5: Dialysis parameters of the studied patients.

	Mean	± SD
Kt/V	1.25	0.25
URR	64.13	7.29

Table 6: Correlation between the pre- and post-dialysis serum bicarbonate and parameters of dialysis adequacy.

Variable	Pre-dialysis HCO_3 (mmol/L)		Post-dialysis HCO_3 (mmol/L)	
	r	p	r	p
Kt/V	0.212	> 0.05	0.204	> 0.05
URR	0.237	> 0.05	0.301	> 0.05

p > 0.05 = not significant

Table 7: Correlation between pre-dialysis serum bicarbonate and the nutritional parameters.

Variable	Pre-dialysis HCO_3 (mmol/L)	
	r	p
nPNA (g/kg/day)	0.301	> 0.05
Protein intake (g/kg/day)	- 0.610*	< 0.05*
Pre-dialysis serum creatinine (mg/dL)	0.354	> 0.05
Pre-dialysis serum albumin (mg/dL)	0.240	> 0.05

p > 0.05 = not significant p < 0.05* significant

Table 8: Comparison between the dialysis adequacy and nutritional status in the studied groups.

	Group 1 (pre HCO_3 < 19 mmol/L) No. = 14		Group 2 (pre HCO_3 ≥ 19 mmol/L) No. = 16		T	p
	Mean	± SD	Mean	± SD		
Kt/V	1.13	0.17	1.36	0.266	2.70*	< 0.05*
URR	61.01	5.66	66.87	7.62	2.35*	< 0.05*
nPNA (g/kg/day)	1.81	0.48	1.73	0.58	0.382	> 0.05
Protein intake (g/kg/day)	1.61	0.53	1.07	0.40	3.14	> 0.05
Pre-creatinine (mg/dL)	4.5	1.09	6.61	2.87	2.58*	< 0.05*
Pre-albumin (mg/dL)	3.2	0.53	3.63	0.52	2.18*	< 0.05*

p > 0.05 = not significant p < 0.05 significant

Table 9: Correlation between inflammation and the nutritional parameters.

Variable	Pre-dialysis CRP	
	r	P
NPNA (g/kg/day)	- 0.06	> 0.05
Protein intake (g/kg/day)	0.075	> 0.05
Pre-dialysis serum creatinine (mg/dL)	- 0.638*	< 0.05*
Pre-dialysis serum albumin (g/dL)	- 0.676*	< 0.05*

p > 0.05 not significant p < 0.05* significant

DISCUSSION

Metabolic acidosis is a well known feature of ESRD, leading to protein breakdown, decreased cardiac inotropism and increased severity of bone disease[2].

The cross sectional data in this group of chronic HD patients showed that pre-dialysis metabolic acidosis is still a common finding, even in patients who use bicarbonate dialysate and receive adequate dialysis, assessed by an average Kt/V and URR of 1.25 ± 0.25 and 64.13 ± 7.29 respectively.

Metabolic acidosis has been shown to have a role in suppression of albumin synthesis and promotion of skeletal muscle catabolism resulting in decreased of both serum albumin and creatinine levels[3].

Our study showed that the quantity of dialysis measured by Kt/V and URR has no statistically significant correlation with either the pre-dialysis HCO_3 concentration ($r = 0.021$ and 0.237 respectively; $p > 0.05$), nor the post-dialysis HCO_3 concentration ($r = 0.204$ and 0.301 respectively; $p > 0.05$). However comparison between patients with moderately severe metabolic acidosis (group 1: $HCO_3 < 19$ mmol/L) and those with mild acidosis (group 2: $HCO_3 \geq 19$ mmol/L) showed that each of Kt/V and URR were significantly lower in the first group than in the latter group ($t = 2.70$ and 2.35 respectively, $p < 0.05$); suggesting that in patients who use bicarbonate dialysate, correction of acidosis resulting from improves by increasing the quantity of dialysis. This is in agreement with the findings of [8,9].

Our results revealed a statistically significant inverse correlation between the pre-dialysis HCO_3 and the dietary protein intake ($r = 0.610$, $p < 0.05$). However, there was no statistically significant correlation between the pre-dialysis HCO_3 and nPNA (nPCR), ($r = 0.301$, $p > 0.05$). Also there was no significant difference in nPNA between patients with HCO_3 less than 19 (group 1) and those with mildly decreased $HCO_3 > 19$ mmol/L (group 2) ($t = 0.382$, $p > 0.05$); reflecting that the low pre-dialysis HCO_3 might be mainly the result of increased protein intake.

Goa et al.[2] and Mauriolo did not find a correlation between the pre-dialysis serum HCO_3 level and nPCR and they reported that the pre-dialysis serum bicarbonate level represents the combined effect of a variety of factors, including dietary protein intake, residual renal function, adequacy of dialysis and ultrafiltration, and each individual case might be related to different sorts and degrees of potential causes for acid load and generation. In addition, patients with moderate metabolic acidosis have higher pre-dialysis BUN, serum uric acid, and phosphorus concentrations than patients without metabolic acidosis which supports the role of metabolic acidosis in inducing endogenous protein breakdown.

Concerning the relation between pre-dialysis HCO_3 and nPNA, our findings are inconsistent with those of Uribarri et al.[10] and Chaveau et al.[11] who found a good correlation between pre-dialysis serum bicarbonate and nPCR in chronic HD population.

A possible explanation of these inconsistent results would be that these studies did not estimate the dietary protein intake of their patients and calculated the nPCR only. At a steady state nRCR is

assumed to be approximately equal to dietary protein intake and is used as an objective tool to quantify protein intake and patients compliance with the dietary prescription in HD patients[12]. However, while nPCR may provide an index of protein catabolism, it does not differentiate between protein derived from dietary sources or catabolism of endogenous proteins[13]. Also, nPCR may overestimate nitrogen intake, especially in the non steady state situation that may accompany acute illness[14]. In addition, if our study had been limited to patients with severe pre-dialysis acidosis, perhaps a significant correlation might have been discovered.

In this study, pre-dialysis HCO_3 correlated inversely with both the pre-dialysis serum creatinine and albumin levels. However, this relation did not reach the statistically significant level ($r = 0.354$ and 0.240 respectively; $p > 0.05$). comparison between patients of group 1 ($HCO_3 < 19$ mmol/L) and those of group 2 ($HCO_3 \geq 19$ mmol/L) showed that each of pre-dialysis creatinine, and pre-dialysis albumin concentrations were significantly lower in the patients with moderately severe metabolic acidosis than in those with mild metabolic acidosis ($t = 2.58$ and 2.18 respectively; $p < 0.05$). These findings in addition to the negative nitrogen balance observed in our patients (dietary protein intake: 1.32 ± 0.53 g/kg/day and nPNA: 1.77 ± 0.53 g/kg/day) and the large percent of patients who are below the 10^{th} percentile of weight for age (70%), height for age (63.3%) and BMI for age (56.7%) despite adequate dietary protein intake lends support to the important role of metabolic acidosis in inducing endogenous protein breakdown. Our findings are similar to the results of the previous studies[15-17].

Movillie et al. studied 12 HD patients before and after 3 months of correction of acidosis and showed a significant increase of serum albumin level, where as nPCR decreased[4].

CRP has been evaluated in ESRD patients and is reported to be elevated compared with healthy populations. This increase has been linked to multiple factors, including effects of HD procedure, biocompatibility of the dialysis membrane, as well as multiple hospitalizations because of infections and/or other causes[18].

Inflammation (as assessed by CRP) correlates inversely with both serum creatinine and albumin levels ($r = 0.638$ and 0.676 respectively; $p < 0.05$). Also, our results showed a direct relationship between nPNA and CRP ($r = 0.06$; $p > 0.05$). CRP also correlated inversely with dietary protein intake ($r = 0.075$; $p > 0.05$); however, these relationships did not reach the statistically significant level. These results are similar to those of Goodman and Biolo et al.[19,20].

Therefore, the inflammatory response may induce protein energy malnutrition by decreased intake, in addition to increased catabolism. This is an important finding when one considers that serum albumin and serum creatinine are all proposed to be acute phase reactants and acute illness can trigger an abrupt decrease in their concentration independent of change in nutrient intake[2].

In conclusion, pre-dialysis metabolic acidosis is still a common finding in HD

patients, even in those who use bicarbonate dialysate and receive adequate dialysis. Increasing the quantity of HD as measured by URR and Kt/V positively helps the correction of acidosis.

Metabolic acidosis results in both decreased albumin synthetic rate and enhanced muscle protein catabolism and this could be anticipated to be associated with hypoalbuminemia and reduced creatinine levels.

Both serum albumin and creatinine concentrations are influenced by inflammation. Therefore, when short term clinical outcomes are considered, markers of both nutrition and inflammation should be evaluated. In the presence of metabolic acidosis or inflammation, nPNA does not reflect the real dietary protein intake of the patients probably as a result of increased catabolism of endogenous proteins.

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