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Original Article

Effect of bicarbonate based dialysate versus acetate based dialysate on parathormone blood level in haemodialysis treated chronic renal failure patients

Mohamed A Zaater*, Mona A Amin*, Mahmoud K Zaater** and Mohamed Shaarawy***

Internal Medicine*, Clinical biochemistry Departments**, Cairo University and Atomic Energy Authority**, Egypt

Abstract

Renal osteodystrophy may result from multiple factors. Hyperparathyroidism, hypocalcaemia, hyperphosphataemia, altered vitamin D metabolism and metabolic acidosis are the most common factors. The clinical impact of acidosis on intact parathyroid hormone (iPTH) level and calcium-phosphate metabolism is still a matter of debate.

In the present study we compared the effect of bicarbonate haemodialysis versus acetate haemodialysis on iPTH blood level. Forty chronic renal failure (CRF) patients on acetate based regular haemodialysis treatment and 10 normal control subjects were studied. All patients and control were subjected to laboratory investigations including predialysis blood urea, serum creatinine, calcium [Ca], phosphorus [PO4], alkaline phosphatase [ALP], bicarbonate and iPTH before the start of the study. Then patients were randomly assigned to one of two groups: group I continued haemodialysis with acetate based dialysate for 6 months, group II shifted to bicarbonate based haemodialysis. After 6 months, the previously done investigations were repeated.

The results revealed that group II patients who shifted to bicarbonate haemodialysis had significant increase in serum bicarbonate levels from 18.02 $\pm$ 0.37 mmol/L to 20.3$\pm$0.71 mmol/L ($P<0.05$) and decrease in their serum levels iPTH from 393.6$\pm$113 pg./ml to 307.6$\pm$90.1 pg./ml ($P<0.05$) and serum level of PO4 from 1.48$\pm$0.16 mmol/L to 1.44$\pm$0.11 mmol/L ($P<0.05$). On the other hand, group I patients who continued on acetate haemodialysis had no changes as regard serum bicarbonate, iPTH or PO4 levels. We can conclude that bicarbonate haemodialysis is better than acetate haemodialysis due to better correction of uraemic acidosis and improvement of secondary hyperparathyraidism.

Correspondence and offprint requests to: Mohamed A Zaater, Internal Medicine, Cairo University, Egypt.

Key words: Chronic renal failure; Haemodialysis; iPTH; calcium; phosphorus; bicarbinate

Introduction and aim of the work

Despite advances in management of chronic renal failure (CRF) patients, renal osteodystrophy in haemodialysis (HD) treated CRF patients is still a major health problem. Renal osteodystrophy may result from multiple factors. Hyperparathyroidism, hypocalcaemia, hyperphosphataemia, altered vitamin D metabolism and metabolic acidosis are the most common contributing factors [1]. The clinical impact of acidosis on iPTH level and calcium phosphate metabolism is still a matter of debate [2]. Regular haemodialysis using acetate based dialysate failed to correct predialysis plasma bicarbonate to more than 16-17 Meq./L. With the introduction of bicarbonate based dialysate, predialysis plasma bicarbonate could be increased to 19-20 Meq./L but metabolic acidosis is still not completely corrected [3].

The aim of this work was to compare the effect of bicarbonate based dialysate for regular haemodialysis treatment of chronic renal failure patients versus acetate based dialysate on calcium-phosphate metabolism, iPTH level in plasma and progression of secondary hyper parathyroidism.

Material and methods

The study included 40 chronic renal failure patients on regular haemodialysis (HD) thrice weekly four hours each, with acetate based dialysate for at least 2-3 years prior to the study. Exclusion criteria included patients who had diabetes, neoplasia, liver disease, cachexia or had been previously parathyroidectomized. Ten age and sex matched healthy subjects were included as a normal control.

For all patients and controls the following investigations were done at the start of the study. (1) Full clinical evaluation. (2) Predialysis laboratory assessment for: blood urea, serum creatinine, serum calcium (Ca), serum phosphorus (PO4), serum alkaline phosphatase (ALP), serum bicarbonate and serum intact parathyroid hormone level (iPTH). Serum intact parathyroid hormone level was determined by chemileumiscence immunoassay using autoanlyzer DPC, USA.

Hemodialysis was performed with volumetrically controlled machines. Polysulphon dialyzers with 1.2 square meter surface area were used for all patients.

Patients were randomly assigned into either one of two groups: Group I: included 20 patients continued haemodialysis using acetate based dialysate. Their age ranged from 19 to 65 years. This group consisted of 12 males (60%) and 8 females (40%). Group II: included 20 patients shifted to bicarbonate based dialysate (using bicarbonate concentration delivery of 32 Meq/L) with age ranging between 26 and 68 years. This group consisted of 14 males (70%) and 6 females (30%).

Six months after the beginning of the study, all patients in the two groups were subjected to all the previous predialysis investigations including blood urea, serum creatinine, serum Ca, serum Po4, serum ALP, serum bicarbonate and serum iPTH level.

Results

The study included 40 patients with chronic renal failure (C.R.F) on regular haemodialysis using acetate based dialysate and 10 age and sex matched healthy subjects serving as a normal controls.

Base line investigations revealed that there was a significant elevation of serum creatinine, blood urea ,phosphate ,alkaline phosphatase, iPTH ,in patients compared to controls ($P<0.001$) and there was a significant lower levels of bicarbonates and calcium in pateints compared to controls ($P < 0.001$).

Patients groups were randomly divided into two groups: *Group I:* continued on acetate based dialysate for 6 months & *Group II:* shifted to bicarbonate based dialysate for 6 months.Before the start of the study ,there were no statistical significant difference between both groups of patients as regard blood urea,serum creatinine, phosphate ,alkaline phosphatase, iPTH, bicarbonates and calcium ($p>0.05$) " table 1, fig. 1 and 2".

Table 1. Laboratory data (Mean ± S.D) of group I (acetate haemodialysis) versus group II (bicarbonate haemodialysis) before the beginning of the study

	Group I		*Group II*		*P value*
	Mean	S.D.	Mean	S.D.	
Blood urea (mg/dL)	160.1	± 20.7	151.1	± 20.07	>0.05
Serum creatinine (mg/dL)	9.34	± 0.69	9.26	± 0.70	>0.05
Serum Ca (mmol/L)	2.10	± 0.13	2.11	± 0.13	>0.05
Serum Po_4 (mmol/L)	1.49	± 0.12	1.48	± 0.16	>0.05
Serum ALP(U/L)	339.1	±76.7	335.4	± 0.13	>0.05
Serum Na (mmol/L)	136	± 2.45	136.9	± 2.85	>0.05
Serum K (mmol/L)	5.78	± 0.59	5.36	± 0.85	>0.05
Serum bicarbonate (mmol/L)	17.97	± 0.62	18.02	± 0.73	>0.05
Serum iPTH (pg/mL)	399.2	± 117.1	393.6	± 113	>0.05

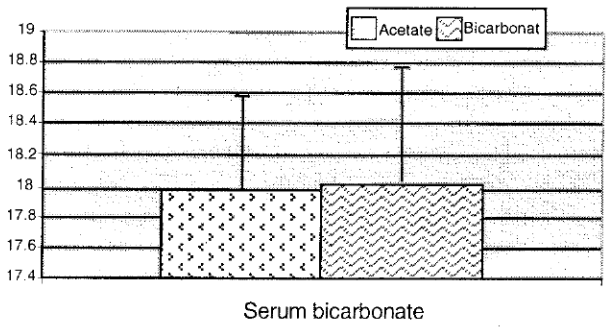

Fig 1. Comparison between mean value and S.D of serum bicarbonate in both groups before the study

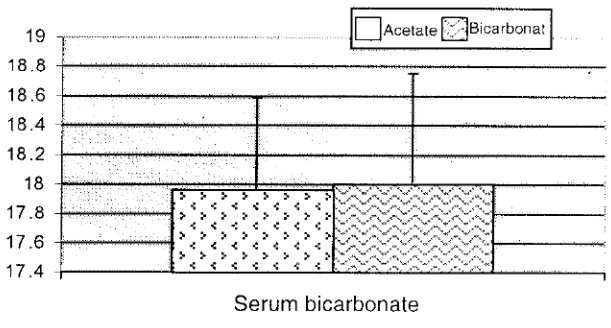

Fig 2. Comparison between mean value and S.D of serum (iPTH) in both groups before the study

6 months following acetate based dialysis in group I, there was no statistical significant change regarding the serum creatinine, blood urea, phosphate ,alkaline phosphatase , iPTH , bicarbonates and calcium (P>0.05) . Table 2, while in group II patients there was no statistical significant change in the level of serum creatinine ,blood urea , alkaline phosphatase, and calcium (P>0.05), but the mean value of serum bicarbonate levels was statisticaly significant higher than the starting levels (P<0.001) and the mean of serum phosphate levels was significantly lower than the starting level (P<0.05). The mean level of iPTH was also significantly lower in group II after 6 months than the starting level (P<0.001) (table 3).

Table 3, laboratory data (Mean±S.D) of group II (bicarbonate haemodialysis) before the beginning of the study and after 6 months.

Table 2. Laboratory data (Mean ± S.D) of group I (acetate haemodialysis) before the beginning of the study and after 6 months

	Before		*After 6 months*		*P value*
	Mean	S.D.	Mean	S.D.	
Blood urea (mg/dL)	160.1	± 20.7	158	± 8.34	>0.05
Serum creatinine(mg/dL)	9.34	± 0.69	9.24	± 0.89	>0.05
Serum Ca (mmol/L)	2.10	± 0.13	2.11	± 0.13	>0.05
Serum Po_4 (mmol/L)	1.49	± 0.12	1.48	± 0.12	>0.05
Serum ALP(U/L)	339.1	±76.7	342.3	± 76.1	>0.05
Serum Na (mmol/L)	136	± 2.45	135.9	± 3.54	>0.05
Serum K (mmol/L)	5.78	± 0.59	5.88	± 0.67	>0.05
Serum bicarbonate(mmol/L)	17.97	± 0.62	17.90	± 0.56	>0.05
Serum iPTH (pg/mL)	399.2	± 117.1	400.4	± 116.8	>0.05

Table 3. Laboratory data (Mean ± S.D) of group II (bicarbonate haemodialysis) before the beginning of the study and after 6 months

	Before		*After 6 months*		*P value*
	Mean	S.D.	Mean	S.D.	
Blood urea (mg/dL)	151.1	± 20.07	158	± 18.5	>.05
Serum creatinine (mg/dL)	9.26	± 0.70	9.18	± 0.81	>.05
Serum Ca (mmol/L)	2.11	± 0.13	2.12	± 0.15	>.05
Serum Po_4 (mmol/L)	1.48	± 0.16	1.44	± 0.11	<.05*
Serum ALP(U/L)	335.4	±68.9	329.6	± 81.3	>.05
Serum Na (mmol/L)	136.9	± 2.85	136.1	± 3.28	>.05
Serum K (mmol/L)	5.36	± 0.85	5.56	± 0.70	>.05
Serum bicarbonate (mmol/L)	18.02	± 0.73	20.3	± 0.71	<.001*
Serum iPTH (pg/mL)	393.6	± 113	307.6	± 90.1	<.001 *

After 6 months of the study there was no significant statistical difference between both groups of patients as regard the serum creatinine, blood urea, alkaline phosphatase, and calcium (P>0.05) "table (4) " .
Table 4, laboratory data (Mean±S.D) of group I (acetate haemodialysis) versus group II (bicarbonate haemodialysis) after 6 months.

But there was significanty lower levels of serum phosphate , and iPTH levels in group II compared to group I (P>0.05) "fig 3 and 4" and higher levels of bicarbonates in group II than in group I patients (P<0.05) (fig. 5).

Table 4. Laboratory data (Mean ± S.D) of group I (acetate haemodialysis) versus group II (bicarbonate haemodialysis) after 6 month

	Group (I)		*Group (II)*		*P value*
	Mean	S.D.	Mean	S.D.	
Blood urea (mg/dL)	158	± 8.34	158	± 18.5	>0.05
Serum creatinine (mg/dL)	9.24	± 0.89	9.18	± 0.81	>0.05
Serum Ca (mmol/L)	2.11	± 0.13	2.12	± 0.15	>0.05
Serum Po_4 (mmol/L)	1.48	± 0.12	1.44	± 0.11	<0.05*
Serum ALP(U/L)	342.3	±76.1	329.6	± 81.3	>0.05
Serum Na (mmol/L)	135.9	± 3.54	136.1	± 3.28	>0.05
Serum K (mmol/L)	5.88	± 0.67	5.56	± 0.70	>0.05
Serum bicarbonate(mmol/L)	17.9	± 0.56	20.3	± 0.71	<0.001*
Serum iPTH (pg/mL)	400.4	± 116.8	307.6	± 90.1	<0.001*

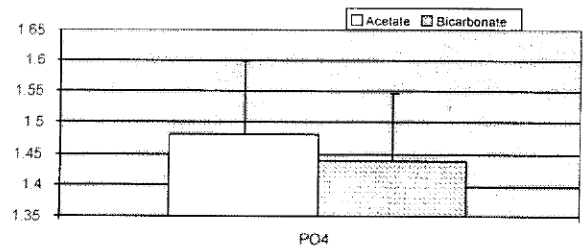

Fig. 3. Comparison between mean value ± S.D of serum (Po4) in both groups after 6 months of the study

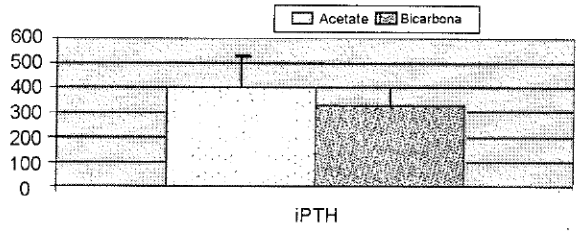

Fig. 4. Comparison between mean value and ± S.D of serum (iPTH) in both groups after months of the study

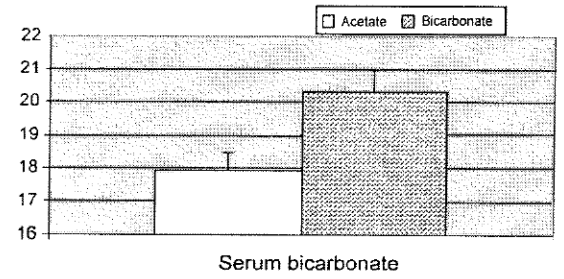

Fig. 5. Comparison between mean value ± S.D of serum (bicarbonate) in both groups after 6 months of the study

Discussion

Acidosis has been implicated in the genesis of renal osteodystrophy [4]. Also it promotes bone demineralization and negative calcium balance in chronic renal failure patients [5]. Uncontrolled uraemic acidosis together with hyperphosphataemia, hypocalcaemia, and altered vitamin D metabolism may result in secondary hyperparathyroidism and metastatic calcification [6]. One of the goals of haemodialysis therapy in chronic renal failure patients is correction of metabolic acidosis resulting from the inability to excrete hydrogen ions. The degree of acidosis present in haemodialysis patients can vary widely in severity depending on the length of each dialysis treatment, protein intake, frequency of dialysis treatment and type of buffer present in the dialysate [7].

The present study was performed to compare the effect of acetate buffered dialysate versus bicarbonate buffered dialysate on improving uraemic acidosis and suppressing the high iPTH blood level in chronic renal failure patients on regular haemodialysis. This study included forty patients with CRF on regular haemodialysis by acetate based dialysate, three times weekly, four hours each, for at least two to three years prior to the start of the study and ten age and sex matched healthy subjects were included as a normal controls. Patients were randomly assigned to either acetate based haemodialysis treatment (group I) or bicarbonate based haemodialysis treatment (group II). The two patients groups included in the study were not different regarding age, sex, dialysis duration, serum levels of bicarbonate, calcium, phosphorus, alkaline phosphatase and intact parathyroid hormone.

Investigations after 6 months from the start of the study were repeated. Patients dialysed by bicarbonate based dialysate were found to have significant higher serum bicarbonate level compared to the group dialyzed by acetate based dialysate ($P<0.05$). Our study is in agreement with that of Kokot et al., [8] who studied the effect of acidosis and hyperleptinaemia on nutritional state of C.R.F patients and they found that patients haemodialyzed by acetate based dialysate had severe metabolic acidosis, their serum bicarbonate was 17.7 mmol/L, but patients haemodialyzed by bicarbonate based dialysate their serum bicarbonate increased up to 20 mmol/L. Also Walff et al., [9] found that acidosis was more adequately corrected with bicarbonate based dialysate. Man NK and his collagues [10] studied the effect of bicarbonate based dialysate on chronic haemodialysis patients and they found that correction of metabolic acidosis was more in bicarbonate dialysis compared to acetate dialysis. Otte et al., [11] compared acetate buffered dialysate and bicarbonate buffered dialysate for haemodialysis patients and they observed that bicarbonate dialysis increase predialysis serum bicarbonate level more than acetate dialysis with improvement of metabolic acidosis.

In the present study, improvement of metabolic acidosis in the studied patients group dialyzed by bicarbonate based dialysate was associated with significant decrease of iPTH blood level compared to patients group dialyzed by acetate based dialysate. Mean value of iPTH in bicarbonate dialysis patients was 307.6 ± 90.1 pg/mL and of acetate dialyzed patients was 400.4 ± 116.8 pg/mL ($P< 0.05$). Unfortunately, few published studies addressed this topic. In 2001, Movilli et al., [12] demonstrated that correction of uraemic acidosis significantly decrease iPTH blood level, (before the study mean value was 399 ± 475 pg/mL and at end of the study mean value was 305 ± 353 pg/mL) ($P< 0.001$). Also Lu et al., [13] found that correction of metabolic acidosis by oral bicarbonate was associated with reduction of iPTH concentration in uraemic patients on regular haemodialysis. In those two studies correction of metabolic acidosis was achieved by oral bicarbonate for about 3 months which may expose the patients to volume overload, increase of blood pressure and its possible complications, but in the present study we achieved improvement of metabolic acidosis by using bicarbonate

buffered dialysate. In spite of the high cost of bicarbonate dialysis, patients treated with this modality were not exposed to volume overload or increase of blood pressure between dialysis sessions as it may occur with oral bicarbonate therapy.

Kaut JA et al., [7] found in cross sectional studies in uraemic patients negative correlation between serum bicarbonate levels and iPTH blood levels.

Correction of metabolic acidosis in haemodialysis patients suppresses iPTH secretion by increasing the sensitivity of the parathyroid gland to ionized calcium. This could be explained as cloned calcium receptor possesses four acidic amino acid residues which are the possible binding sites for extracellular calcium. Acidosis might induce conformational alterations in these binding sites, thus reducing their sensitivity to circulating calcium concentrations. Improvement of metabolic acidosis prevents these alterations in calcium receptors and restore its sensitivity to calcium ions [14]. The correction of metabolic acidosis is associated with decrease level of ionized calcium which on the contrary should stimulate iPTH secretion, but the decrease iPTH levels support the hypothesis of the direct effect of acidosis on the parathyroid calcium receptors.

In the present study in the subgroup dialyzed by bicarbonate based dialysate, the correction of metabolic acidosis and decrease of iPTH were not associated with significant change of serum calcium level but were associated with significant decrease in the serum phosphorus level. The explanation for the decrease of serum phosphorus in patients dialyzed by bicarbonate based dialysate is the increase clearance of phosphate in bicarbonate dialysis than in acetate dialysis [15]. Otte et al., [11] are in agreement with the present study as they studied the difference between acetate and bicarbonate dialysis and found that no significant difference in the serum Ca level with patients dialyzed by bicarbonate compared to patients dialyzed by acetate.

Also, in the present study, patients dialyzed by bicarbonate buffered dialysate, the improvement of metabolic acidosis and reduction of iPTH level was not associated with significant decrease in serum alkaline phosphatase. These findings are in agreement with Movilli et al., [12] who found recently that correction of acidosis suppress high iPTH blood level without any significant change in serum calcium, phosphorus, and alkaline phosphatase.

Conclusion

From the present study it is concluded that regular haemodialysis treatment for chronic renal failure using bicarbonate based dialysate is more superior than haemodialysis using acetate based dialysate regarding prevention of renal osteodystrophy. Heaemodialysis with bicarbonate based dialysate correct the metabolic acidosis, hyperphosphataemia, and the increased iPTH level more effeciently than haemodialysis using acetate based dialysate. It is recommend to dialyze chronic renal failure patients with bicarbonate based dialysate at least for those with hyperphosphataemia which is difficult to control or those with advanced renal osteodystrophy.

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