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LEAD ARTICLE

Acid-Base Balance in Peritoneal Dialysis Patients: A Stewart-Fencl Analysis

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Background. Evaluation of acid-base disorders using the Stewart-Fencl principle is based on assessment of independent factors: strong ion difference (SID) and the total concentration of non-volatile weak acids (Atot). This approach allows for a more detailed evaluation of the cause of acid-base imbalance than the conventional bicarbonate-centered approach based on the Henderson-Hasselbalch principle, which is a necessary yet insufficient condition to describe the state of the system. The aim of our study was to assess acid-base disorders in peritoneal dialysis (PD) patients using both of these principles. *Methods*. A total of 17 patients with chronic renal failure (10 men), aged 60.7 (22–84) years, treated by PD for 25.7 (1–147) months were examined. A control group included 17 healthy volunteers (HV) (8 males), with a mean age of 42.7 (22–77) years and normal renal function. Patients were treated with a solution containing bicarbonate (25 mmol/L) and lactate (15 mmol/L) as buffers; eleven of them used, during the nighttime dwell, a solution with icodextrin buffered by lactate at a concentration of 40 mmol/L. The following equations were employed for calculations of acid-base parameters according to the Stewart-Fencl principle. The first is SID = $[Na^+] + [K^+] + 2[Ca^{2+}] + 2[Mg^{2+}] - [Cl^-] - [UA^-]$, where SID is the strong ion difference and $[UA^-]$ is the concentration of undetermined anions. For practical calculation of SID, the second equation, SID = $[HCO_3^-] + [Alb^-] + [Pi^-]$, was used, where $[Alb^-]$ and $[Pi^-]$ are the charges carried by albumin and phosphates. The third is Atot, the total concentration of weak non-volatile acids, albumin [Alb] and phosphates [Pi]. *Results*. The capillary blood pH in PD group was 7.41 (7.27–7.48), $[HCO_3^-]$ levels 23.7 (17.6–29.5) mmol/L, SID 36.3 (29.5–41.3) mmol/L, sodium-chloride difference 39.0 (31.0–44.0) mmol/L, [Pi] 1.60 (0.83–2.54) mmol/L, and [Alb] 39.7 (28.8–43.4) g/L (median, min-max). Bicarbonate in blood correlated positively with SID (Rho = 0.823; $p < 0.001$), with the sodium-chloride difference (Rho = 0.649; $p < 0.01$) and pH (Rho = 0.754; $p < 0.001$), and negatively with residual renal function (Rho = –0.517; $p < 0.05$). Moreover, the sodium-chloride difference was also found to correlate with SID (Rho = 0.653; $p < 0.01$). While the groups of PD and HV patients did not differ in median bicarbonate levels, significantly lower median value of SID were observed in PD patients, 36.3 vs. 39.3 mmol/L ($p < 0.01$); additionally, PD patients were shown to have significantly lower mean value of serum sodium levels, 138 vs. 141 mmol/L ($p < 0.01$), and serum chlorides levels, 100 vs. 104 mmol/L ($p < 0.001$). Despite the higher $[UA^-]$ levels in PD patients, 9.1 vs. 5.4 mmol/L ($p < 0.001$), this parameter was not found to correlate with bicarbonate levels. *Conclusions*. The results suggest that the decreased bicarbonate in PD patients results from a combination of decreased sodium-chloride difference and mildly increased unmeasured anions.

Keywords acid-base balance, bicarbonate, icodextrin, lactate, peritoneal dialysis, Stewart principle

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The internal milieu of the patient with chronic renal failure is characterized by the presence of metabolic acidosis. Correction of metabolic acidosis is one of the main objectives

of dialysis treatment. In peritoneal dialysis (PD), correction of metabolic acidosis is obtained by the addition of bicarbonate (HCO_3^-) or, possibly, its metabolic precursor lactate (acetate in the past) into the peritoneal dialysis fluid. Clinical use of PD fluids buffered with bicarbonate, either alone or in a mixture with lactate, has become widespread mostly because these solutions showed a higher degree of biocompatibility in pre-clinical and some clinical trials.[1–5]

Recent studies have shown that metabolic acidosis may persist in a non-negligible proportion of patients treated by PD (8–60%) while metabolic alkalosis may be present in other patients (17–27%).[6–11] Though in hemodialysis (HD) patients, both high and low serum bicarbonate levels are associated with an increased risk for mortality and hospitalization,[12] mild acidosis appears to be associated with a better outcome in PD patients.[13,14]

The cause of metabolic acidosis in chronic renal failure has been thought to be an inability to excrete non-volatile acids in the face of reduced renal bicarbonate synthesis (i.e., acidosis with an increased anion gap, AG).[15–17] However, recent studies have suggested that other mechanisms may be also involved in its etiopathogenesis.[18]

While these other mechanisms cannot be taken into account by the traditional, bicarbonate-centered approach to assessing the status and disorders of acid-based balance (ABB) derived from the Henderson-Hasselbalch equation, they can be taken into consideration by an alternative approach to ABB assessment formulated by Stewart in the 1980s and further refined into a form that could be employed in clinical practice by Fencl and Figge.[19–23] Stewart-Fencl theory allows assessing metabolic changes in ABB using not only the plasma bicarbonate levels but also the so-called independent variables . These are subsequently responsible for changes in the serum levels of bicarbonates and, hence, also pH. These independent variables include the strong ion difference (SID) and total levels of weak non-volatile acids (Atot). Just as in the classical Henderson-Hasselbalch concept, assessment of the respiratory component is based on partial carbon dioxide pressure (pCO_2). Derived from Stewart-Fencl theory but also from the equation characterizing extracellular fluid electroneutrality, the following equations could be derived[20]:

$$[HCO_3^-] = SID - [Alb^-] - [Pi^-],$$

where SID value is defined by the following equation[19]:

$$SID = [Na^+] + [K^+] + 2[Ca^{2+}] + 2[Mg^{2+}] - [Cl^-] - [UA^-],$$

where the UA^- is total electrical charge carried by undetermined anions (anions not commonly determined, such as ketoacids, sulfates, lactate, exogenous substances, etc.). Given the usual levels of the above ions, the most important parameters for a change in SID are the value of sodium-chloride difference and, potentially, also UA^-. Changes in the sodium-chloride difference may occur even when the serum levels of sodium and chloride are within the physiological range, as this is fairly broad. Elevated chloride levels and in some cases decreased sodium levels have been implicated as the main cause of the decrease in SID and development of metabolic acidosis in patients with chronic kidney disease in pre-dialysis.[18] While a decrease in plasma levels of sodium and chlorides has been reported in PD patients treated with an icodextrin-based PD repeatedly,[24–26] the effect of these alterations on the internal milieu of PD patients has not been investigated to date.

The value of Atot is the sum of concentrations of nonvolatile weak acids: albumin [Alb] and inorganic phosphates [Pi]. Abnormal plasma levels of albumin and phosphates are common both in HD and PD patients, with hypoalbuminemia and hyperphosphatemia being more common with PD and HD, respectively.[27–31] The effects of hypoalbuminemia and hyperphosphatemia on ABB status in chronic kidney disease patients have to date been investigated only to a limited extent.[18]

It follows from the above that the Henderson-Hasselbalch equation is a necessary yet insufficient condition to describe the state of the system.

A decrease in $[HCO_3^-]$ may be due not only to changes in pCO_2 (detectable using the Henderson-Hasselbalch equation) but also to a decrease in SID or an increase in Atot, or to a combination of both (that is undetectable by the Henderson-Hasselbalch equation). Therefore, we conducted a study designed to assess the status and causes of ABB disorder in PD patients using a more comprehensive Stewart-Fencl principle and its newer improvement.[22,23]

PATIENTS AND METHODS

For the purpose of the study, a total of 17 patients (10 men) with chronic renal failure and a mean age of 60.7 (22–84) years, treated by PD in our unit, were investigated. The mean duration of PD treatment was 25.7 (1–147) months. Thirteen patients were treated by CAPD and two by APD (who were switched to CAPD using the same volume and solution composition two days prior to the examination). Two patients experiencing partial repair of their residual renal function after the initiation of PD were treated by a

single exchange of the icodextrin-based PD solution for overnight dwell (Extraneal®, Baxter, Castelbar, Ireland; base lactate 40 mmol/L). Icodextrin for overnight dwell was also used by eight CAPD patients. The overnight exchange lasted from 10 p.m. to 8 a.m. The basic prescription included a glucose solution buffered with 25 mmol/L bicarbonate and 15 mmol/L lactate (Physioneal®, Baxter, Castelbar, Ireland). The PD prescription including the prescription of icodextrin-based solution was individualized depending on the results of the latest peritoneal equilibration test[32] and clinical needs of each patient. The mean residual urine volume was 848 (0–2000) mL/24 hours. The underlying disease resulting in renal failure was diabetic nephropathy in 6 cases, glomerulonephritis in 6, polycystic kidney disease in 2 cases, and tubulointerstitial nephritis, bilateral nephrectomy, and hypertensive nephrosclerosis in one case each. A control group was made up of 17 healthy volunteers (8 males), with a mean age of 42.7 (22–77) years, with normal renal function.

Patients and healthy volunteers were in stable condition, showed no clinical and laboratory signs of current infection, and had no history of an infectious complication, including peritonitis, within three months prior to entering the study. None of the patients was using an oral sodium bicarbonate supplement, 4 patients (23.5%) were using sevelamer (mean dose, 2000 mg/day), and 13 patients (76.5%) were using calcium carbonate (mean 2.4 g/day). 58.8% of patients were on furosemide at a mean dose of 145.5 mg/day, and 58.8% of patients were treated with ACE inhibitors and/or AT1 blockers. Dialysis dose was calculated using PD Adequest® software (version 2.0, Baxter Healthcare Corporation, Deerfield, Illinois, USA). Residual renal function (RRF) was estimated from residual glomerular filtration rate calculated from 24-hour urine collection as the average of residual renal creatinine and urea clearances.[33] In addition to standard biochemical investigations (ions, urea, creatinine, albumin) (Olympus AU 640, Chemelex, Barcelona, Spain), plasma levels of lactate were determined on the same analyzer. Albumin was measured by the bromcresol green method. ABB parameters and ionized calcium were determined by capillary blood analysis using a blood gas analyzer (ABL 700 Radiometer, Bronshoj, Denmark), which calculated bicarbonate concentration from measured pCO_2 and pH values. Capillary blood samples were transported to the laboratory, with the time from collection to analysis not exceeding 20 minutes.

The study was conducted in compliance with the Declaration of Helsinki and approved by the local ethics committee, and all patients signed their informed consent prior to entering the study.

ABB parameters were calculated from the results obtained using the Stewart-Fencl principle.

The following equations were employed for practical calculations[20,22,23,34]:

$$SID = [HCO_3^-] + [Alb^-] + [Pi^-] \quad (1)$$

where

$$[Alb^-] = -10 \times [Alb] \times (0.1204 \times pH - 0.625)$$

and

$$[Pi^-] = [Pi] \times (0.309 \times pH - 0.469)$$

$[Alb^-]$ and $[Pi^-]$ represent charges carried by the above anions.

$$[UA^-] = [Na^+] + [K^+] + 2[Ca^{2+}] + 2[Mg^{2+}] - [Cl^-] - SID \quad (2)$$

Further, using our data, AG was calculated as part of the tradition ABB concept, with the following formula:

$$AG = [Na^+] + [K^+] - [Cl^-] - [HCO_3^-]. \quad (3)$$

Given the need to correct the value of AG on a change in serum albumin levels, the corrected AG was calculated (AGc)[20]:

$$AGc = AG + 0.25 \times (\text{Alb norm.} - \text{Alb measured}).$$

Also calculated was AG corrected to albumin, phosphate, and lactate levels[22]:

$$AGc = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-]) - (0.2 \times [\text{Albumin}]) + (1.5 \times [\text{Pi}]) - [\text{Lactate}] \quad (4)$$

Next, the AG minus [Alb-] difference was also calculated.

Comparison of individual groups of patients and HV was performed using the unpaired t-test. Correlations among individual variables were determined by Spearman's rank order correlation test. Multivariate analysis was not undertaken because of the relatively small number of patients examined.

RESULTS

Results of the biochemical parameters and calculated ABB parameters of PD patients and HV are shown in Table 1. pH was decreased below the lower limit of the norm in

Table 1
Biochemical characteristics of the study group and control group

	PD patients, median (min-max)	HV, median (min-max)
pH[§]	7.41 (7.27–7.48)*	7.45 (7.39–7.48)
HCO_3^- (mmol/L)[§]	23.7 (17.6–29.5)	24.3 (20.0–26.6)
pCO_2 (kPa)[§]	5.1 (4.6–5.7)	4.9 (3.9–5.7)
Base excess (mmol/L)[§]	–0.2 (–8.3–5.9)	0.1 (–2.5–2.4)
Anion gap (mmol/L)	20.2 (16.0–24.9)[†]	18.2 (11.3–21.4)
Anion gap corrected for albumin phosphates and lactate (mmol/L)	12.48 (9.48–17.77)[‡]	8.43 (1.74–13.27)
Anion gap corrected for albumin (mmol/L)	20.68 (18.43–25.80)[‡]	16.33 (9.88–20.78)
Difference between anion gap and charge carried by albumin (mmol/L)	8.78 (7.12–14.50)[‡]	4.22 (–1.98–8.71)
Lactate (mmol/L)	1.43 (0.99–2.46)	1.06 (0.76–2.81)
Strong ion difference (mmol/L)	36.26 (29.49–41.32)[†]	39.29 (35.31–42.46)
Sodium–chloride difference (mmol/L)	39.0 (31.0–44.0)	37.0 (31.0–40.0)
Undetermined anions (mmol/L)	9.10 (6.02–14.01)[‡]	5.41 (–0.56–9.54)
Sodium (mmol/L)	138 (134–143)[†]	141 (139–145)
Chlorides (mmol/L)	100 (93–112)[‡]	103 (101–109)
Potassium (mmol/L)	4.2 (3.3–4.8)	4.1 (3.6–4.6)
Calcium total (mmol/L)	2.22 (1.72–2.64)	2.30 (2.17–2.49)
Ionized calcium (mmol/L)[§]	0.98 (0.49–1.35)[‡]	1.19 (1.00–1.34)
Magnesium (mmol/L)	0.86 (0.62–1.09)	0.89 (0.78–1.05)
Albumin (g/L)	39.7 (28.8–43.4)[‡]	49.0 (45.4–53.5)
Inorganic phosphates (mmol/L)	1.60 (0.83–2.54)[‡]	1.12 (0.92–1.43)
Creatinine (μmol/L)	612 (358–1200)[‡]	87 (65–105)
Urea (mmol/L)	15.5 (8.6–34.6)[‡]	4.7 (3.3–6.3)
Residual renal function (mL/min)	5.62 (0–10.25)	—
Kt/V urea	1.93 (1.33–3.64)	—
Total weekly creatinine clearance (L/1.73 m^2)	87.95 (36.08–142.85)	—
Dialysate-to-plasma creatinine ratio; hour 4 of the peritoneal equilibration test	0.78 (0.60–0.85)	—
Mass transfer area coefficient (mL/min)	13.44 (8.54–17.75)	—

Difference between groups: *$p < 0.05$, [†]$p < 0.01$, [‡]$p < 0.001$.
[§]Capillary blood.

only three patients (17.6%), and it was increased above the upper limit in the same number of patients. Six patients (35.3%) had bicarbonate levels below 22 mmol/L, with serum bicarbonate levels in capillary blood being higher than 26 mmol/L and 28 mmol/L in only two (11.8%) and one patient (5.9%), respectively. An increase in pCO_2 was not documented in our group; by contrast, pCO_2 was found to be below the lower limit of the norm in four cases (23.5%). The median albumin levels were within the norm; however, almost one in four patients (four cases) was within the hypoalbuminemic range. While the median of phosphatemia was only slightly elevated above the normal, mild hyperphosphatemia was present in nearly the half (eight) of patients. The median levels of sodium and chlorides were within the norm, with hyperchloremia and hypochloremia present in only one (5.9%) and four patients (23.5%), respectively.

When searching for an association between the levels of bicarbonate versus other variables, we observed very close direct correlations with SID (see Figure 1), sodium-chloride difference (see Figure 2), and the residual renal function (Rho = –0.517; $p < 0.05$). There was no correlation between serum bicarbonate and both sodium and chlorides levels. Sodium-chloride difference was also found to correlate with SID (Rho = 0.653; $p < 0.01$) and inversely with serum chloride levels (Rho = –0.792; $p < 0.001$); no correlation with natremia was shown. $[UA^-]$ did not correlate with SID or $[HCO_3^-]$. A significant correlation was demonstrated between $[UA^-]$ and the differences between AG minus albumin anions (Alb^-) (see Figure 3) and between $[UA^-]$ and AG corrected for albumin, phosphate, and lactate (Rho = 0.733; $p < 0.001$). Despite their supraphysiological value in dialysis solution, the plasma levels of lactate were not increased above normal, and did not correlate with either $[UA^-]$ or serum bicarbonate levels.

No correlation was shown to exist between albumin, phosphate, and bicarbonate levels, or between bicarbonate and the charges carried by ($[Alb^-]$ and $[Pi^-]$).

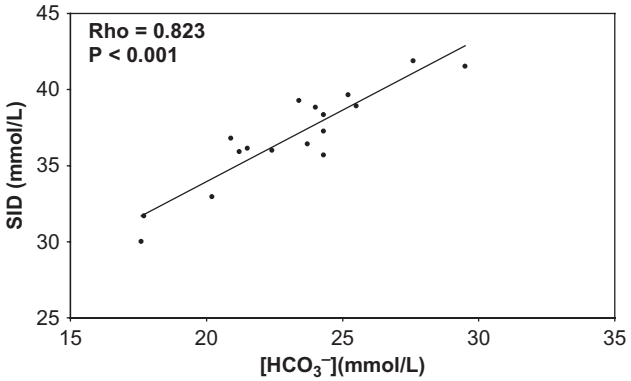

Figure 1. Correlation between bicarbonate in blood and strong ion difference. Spearman's rank order correlation test. Abbreviations: SID = strong ion difference, $[HCO_3^-]$ = bicarbonate in blood.

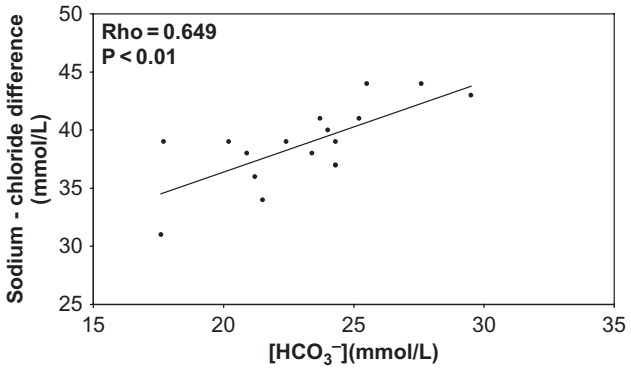

Figure 2. Correlation between bicarbonate in blood and sodium-chloride difference. Spearman's rank order correlation test. Abbreviation: $[HCO_3^-]$ = bicarbonate in blood.

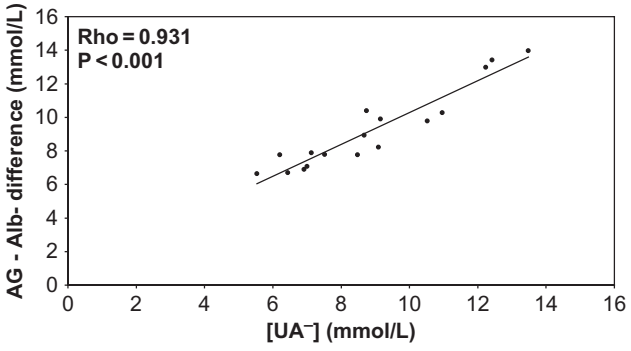

Figure 3. Correlation between undetermined anions and difference between anion gap and charge carried by albumin. Spearman's rank order correlation test. Abbreviations: AG-Alb^- difference = difference between anion gap and charge carried by albumin, $[UA^-]$ = undetermined anions.

Table 2
Additional significant correlations of investigated parameters

N = 17	Rho	*p*
$[HCO_3^-] \times$ [SID]	0.823	<0.001
$[HCO_3^-] \times [Na^+–Cl^-]$ difference	0.649	<0.01
[SID] $\times [Na^+–Cl^-]$ difference	0.653	<0.01
$[UA^-] \times$ AG – Alb^- difference	0.931	<0.001
pH × [SID]	0.646	<0.01
pH $\times [Na^+–Cl^-]$ difference	0.466	0.0580*
$[HCO_3^-] \times$ RRF	–0.517	<0.05

*This correlation was close to reaching statistical significance.

Abbreviations: SID = strong ion difference, $[Na^+–Cl^-]$ difference = sodium–chloride difference, $[UA^-]$ = undetermined anions, AG = anion gap, AG – Alb^- difference = difference between anion gap and charge carried by albumin, RRF = residual renal function.

A correlation between RRF and sodium-chloride difference did not reach statistical significance (Rho = –0.412; $p = 0.0976$). No statistically significant correlation was shown between ultrafiltration during overnight dwell time and bicarbonate levels or sodium-chloride difference. We were unable to demonstrate a significant relation between Kt/V, total weekly creatinine clearance, MTAC or creatinine D/P, and bicarbonate levels.

Compared with patients treated only with glucose solutions, icodextrin-treated patients showed significantly lower serum sodium level (median 137 mmol/L vs. 141 mmol/L, $p < 0.01$), while the difference in chloremia did not reach statistical significance. As these two subgroups did not differ in any other parameters, they were subsequently considered as a single one. Additional correlations of the investigated parameters are summarized in Table 2.

DISCUSSION

Our data show that more than one-third (35%) of PD patients had decreased serum $[HCO_3^-]$, although blood pH was decreased in only 17.6% of patients, apparently because of adequate compensation of the decrease in $[HCO_3^-]$. This compensatory mechanism is believed to be preserved in end-stage renal disease patients.[35,36] Our findings regarding acidosis correction are essentially consistent with results of other large studies. Some have reported completely corrected acidosis in a larger proportion of patients; however, as bicarbonate was determined in venous plasma in these studies, its levels are likely to be slightly overestimated given the absence of local lactate production.[6–8,37]

The finding that there was no significant difference in bicarbonate values between healthy volunteers and PD patients might be explained by the presence of several cases of alkalosis in PD patients.

When interpreting our results using the Henderson-Hasselbalch concept, the metabolic acidosis in our PD patients is controlled by respiration. Traditional assessment of ABB also seeks to determine whether or not metabolic acidosis is associated with an increase in AG. When assessing AG (non-corrected or corrected), our patients showed a slight increase over the upper limit of the norm and that was significantly higher in PD patients compared with HV. The traditional Henderson-Hasselbalch concept does not consider an effect of $[Na^+]$ and $[Cl^-]$ on ABB in these cases, as the plasma levels of these ions were in most cases within normal (with hyperchloremia documented in only one case, whereas several patients showed a slight decrease in $[Cl^-]$ below the lower limit of the norm). If analyzing our data according to Stewart-Fencl theory, the decrease in $[HCO_3^-]$ and its compensation by a decrease in pCO_2 are interpreted in the same manner, and the recognition of metabolic acidosis is not at variance with the Henderson-Hasselbalch concept. However, differences do emerge in the assessment of other factors affecting serum bicarbonate level. First, it should be noted that UA^- in our PD patients was within the normal range; however, the significantly higher levels compared with HV suggest mild retention of undetermined ions in patients. This finding is consistent with the finding of higher AG levels, as mentioned above.

In the HV group, a negative UA^- value was even seen in a single case. Clearly, a negative UA^- value is highly unlikely, even impossible, physiologically or in terms of maintaining electro neutrality. However, it should be remembered that, when calculating this parameter, a total of eight values determined separately in the laboratory are eventually incorporated into the equation, so the total of individual measurement errors may result in a negative value, even in the presence of a very low UA^- value.

The levels of lactate, which could potentially affect UA^-, were not elevated, possibly because lactate, crossing from peritoneal dialysis fluid to extracellular fluid, is very rapidly metabolized to bicarbonate.[6,38]

When analyzing our results using the Stewart-Fencl principle, our patients were also found to have SID at the lower limit of the norm, and a significant correlation between serum bicarbonate and SID was found.

As (in quantitative terms) SID is largely affected by sodium-chloride difference, it is not surprising that this parameter correlates closely with serum bicarbonate. The median value of the sodium-chloride differences did not differ between the PD and HV groups; however, it should be also remembered the two groups did not differ in bicarbonate levels either, very likely because of the relatively broad physiological range of sodium and chloride levels (approx. 10 mmol/L).

The sodium-chloride difference in both dialysis solutions used was within the physiological range.

The level of serum bicarbonate did not appear to depend on Atot components (plasma albumin and phosphates). Our PD patients were characterized by borderline hypoalbuminemia and borderline hyperphosphatemia as compared with HV.

From the point of view of clinical practice, it is necessary to analyze the relationship between AG and $[UA^-]$. It follows from the equation expressing extracellular fluid electro neutrality that:

$$AG \quad [Alb^-] = [UA^-] + [Pi^-] - 2([Ca^{2+}] + [Mg^{2+}]).$$

It is self-evident from the above equation that there is a direct relation between $AG - [Alb^-]$ and $[UA^-]$, as the parameter $[Pi^-] - 2([Ca^{2+}] + [Mg^{2+}])$ is relatively small in relation to $[UA^-]$. This theoretical premise is confirmed by the significant correlation between $AG - [Alb^-]$ and $[UA^-]$ demonstrated in our study. It follows from the analysis that $AG - [Alb^-]$ may be slightly elevated even in the presence of normal $[UA^-]$ in cases where $[Pi^-]$ is higher than $2([Ca^{2+}] + [Mg^{2+}])$ (i.e., the presence of significant hyperphosphatemia). AG corrected to albumin, phosphate, and lactate levels draws its value closer to UA^- value, resulting in a close correlation between the two parameters. The AG corrected in this manner then becomes a parameter suggesting the level of UA^-.

The significantly increased UA^- levels seen in PD patients, as compared with HV, support the idea of UA^- retention in our patients.

As a result, $[UA^-]$ are likely to be removed by PD to a sufficient extent, with the implication being that our PD patients receive adequate dialysis. Kt/V values were not within the limits recommended by KDOQI guidelines[39] in all our patients. However, these were individuals showing signs of anabolism when Kt/V may be falsely reduced. Another major issue is the interpretation of the decrease in sodium-chloride difference and, hence, decrease in SID.

Theoretically, several possible causes must be considered. Some studies suggest higher $[HCO_3^-]$ losses by residual nephrons,[8,15,40] while others do not support this hypothesis.[6,7] In our patients, $[HCO_3^-]$ losses by residual diuresis were not investigated; however, significant correlation between RRF and $[HCO_3^-]$ was demonstrated. Higher $[HCO_3^-]$ losses cannot play any role in anuric patients though. Another possible cause of sodium-chloride difference decrease might be inadequate dietary salt intake as sodium chloride exerts an acidifying effect.

The possibility of dilution (due to inadequately high water intake) cannot be excluded either.

The additive effects of some other factors (e.g., change in sodium and chloride distribution in individual fluid compartments) cannot be ruled out. Further research in this area is necessary.

The decrease in natremia and/or chloremia in icodextrin-treated patients has been repeatedly reported. It is most likely due to osmolar loading related to the increased plasma oligosaccharide levels, and the resulting osmotic dilutive effect.[25] It is not surprising then that the sodium-chloride difference did not differ between icodextrin-treated patients and those treated with a glucose solution, as did no other biochemical markers of interest. Other factors affecting ABB in PD patients not taken account of by Henderson-Hasselbalch or Stewart-Fencl principle include, in particular, protein catabolic rate, transport characteristics of the peritoneal membrane, and the type of phosphate binders. Unlike some earlier studies,[41–43] we did not demonstrate a correlation between protein catabolic rate and serum bicarbonate. Peritoneal transport characteristics no doubt affect transperitoneal base transport.[44,45] However, the relationship between peritoneal permeability and systemic acid base parameters is rather ambiguous,[6,7,9,45,46] and our study failed to document it. Regarding phosphate binders, which are used by the overwhelming majority of dialysis patients, some—but not all—studies in PD patients reported a correlation between calcium carbonate prescribing and serum bicarbonate,[47] and demonstrated the acidifying effect of sevelamer.[7,48] In our study, sevelamer was used by 23.5% of patients, calcium carbonate by 76.5%. Given the size of our sample, no detailed analysis of the effect of phosphate binder on ABB was undertaken.

In conclusion, the obtained results suggest that the decreased bicarbonate level in PD patients results from the combination of decreased sodium-chloride difference and mildly increased unmeasured anions.

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