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Correction of metabolic acidosis in continuous ambulatory peritoneal dialysis patients with borderline dialysis adequacy: effect on nutritional status, systemic inflammatory response, and patient morbidity

Key Messages

1. In peritoneal dialysis patients with mild acidosis and Kt/V below 2.1, oral sodium bicarbonate is probably effective in improving nutritional status and reducing the duration of hospitalisation.
2. Oral bicarbonate solution confers clinical benefit in marginally dialysed peritoneal dialysis patients; such patients account for about one fourth of our peritoneal dialysis population.

Introduction

Malnutrition is common in renal failure patients and is associated with increased morbidity and mortality. In peritoneal dialysis patients, dialysis adequacy is important for satisfactory nutrition.[1,2] However, whether increasing 'the dosage' of peritoneal dialysis could improve nutritional status and/or clinical outcome is under dispute.

Acidosis is a major factor responsible for progressive malnutrition in dialysis patients. Theoretically, oral sodium bicarbonate is a convenient therapy. Nevertheless, the effect of oral sodium bicarbonate has not been extensively studied. In a small pilot study, it was effective in improving the nutritional status of peritoneal dialysis patients with a Kt/V of 2.1 (K denotes urea clearance, t dwell time, and V urea distribution volume).[3,4] However, the effect of oral bicarbonate in peritoneal dialysis patients with values below 2.1 (the recommended target of peritoneal dialysis adequacy) has not been studied. It is important to note that although a weekly Kt/V of 2.1 was often regarded as the target of dialysis adequacy, we found that Chinese peritoneal dialysis patients with a Kt/V of 1.7 had excellent outcome. We therefore performed a randomised placebo-controlled study to evaluate the effects of correcting acidosis by oral sodium bicarbonate in peritoneal dialysis patients with weekly Kt/V values below 2.1.

Methods

This prospective randomised placebo-controlled study was conducted from December 2000 to April 2003. We recruited 60 peritoneal dialysis patients with acidosis and a Kt/V of less than 2.1. Patients were randomised to receive oral sodium bicarbonate (0.9 g thrice daily) or placebo and were followed up for 12 months. The major outcome measures were: nutritional status, total number of days in hospital admission during study period, and all-cause mortality. Nutritional assessment included: subjective global assessment (SGA) by the four-item 7-point scoring system; fat-free oedema-free body mass (FEBM) by creatinine kinetics and calculated according to the formula described by Forbes and Bruining[5]; protein nitrogen appearance by Randerson's formula[6] and further normalised to standard body weight (NPNA); and anthropometric measurements (including biceps, triceps, subscapular and supra-iliac skin fold thickness, and mid-arm muscle circumference). Lean body mass (LBM) was computed by standard formula.

Results

Baseline demographic and clinical features of the two groups were highly comparable. Treatment with oral sodium bicarbonate resulted in significantly higher mean plasma bicarbonate level than in the placebo group at 4 weeks

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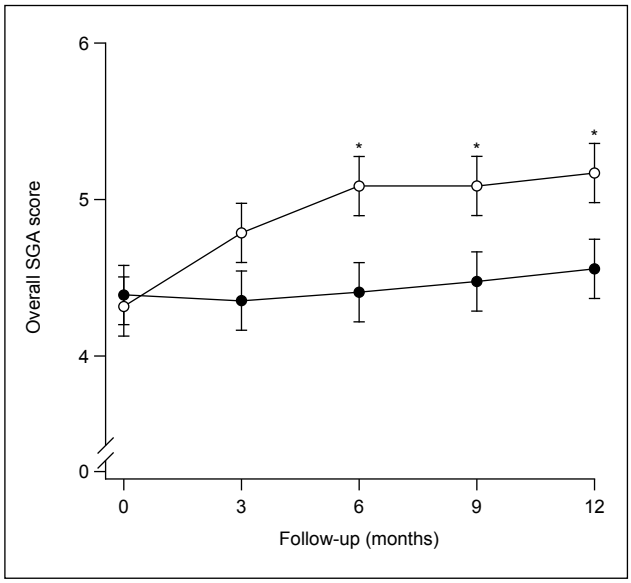

* P<0.05 between treatment and control groups

Fig 1. Overall subjective global assessment (SGA) score at baseline and follow-up of patients on treatment (open circles) and placebos (closed circles)

Error bar denotes standard error of mean

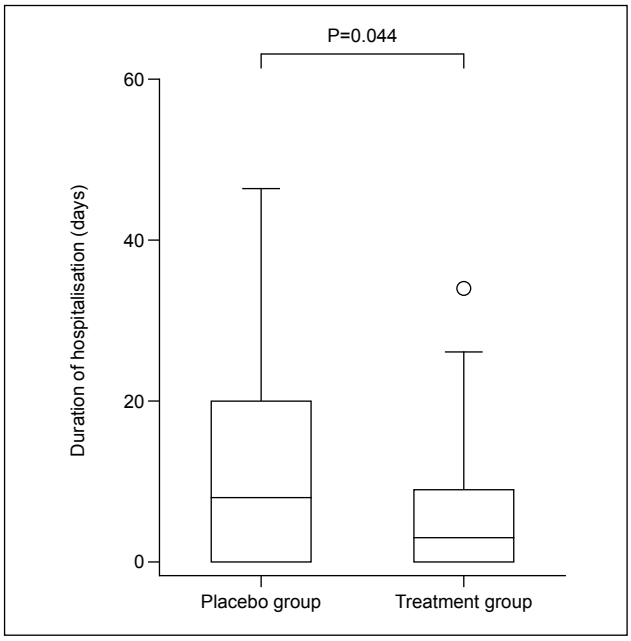

Fig 2. Mean number of days in hospital during the first-year treatment period

Data are illustrated by the Box and Wisker plot

(27.8±2.6 vs 24.7±3.9 mmol/L, P=0.002), and the difference was maintained for 52 weeks.

There was a significant effect of bicarbonate treatment on the change in overall SGA score (repeated measures ANOVA, P=0.0003) [Fig 1]. The mean overall SGA score of the treatment group was significantly higher than that of the placebo group at 24 weeks (5.07±0.94 vs 4.40±1.00, P=0.015), and the difference was maintained thereafter. Similar trends were observed in all item scores of SGA, although only the difference in scores for anorexia and weight loss were statistically significant. Increase in NPNA in the treatment group (1.17±0.32 to 1.28±0.26 g/kg/day, P=0.034) but decline in the placebo group (1.13±0.25 to 1.03±0.28 g/kg/day, P=0.054) was observed. After adjusting for comorbid conditions, there was a significant effect of bicarbonate treatment on the change in NPNA (repeated measure ANOVA, P=0.045). During the study period, FEBM of the treatment group rose from 0 to 24 weeks (30.8±8.4 to 34.3±10.9 kg, P=0.04) and then stabilised, whereas it remained static in the placebo group. The anthropometric LBM remained stable in the treatment group but declined significantly in the placebo group (50.7±7.0 to 48.9±7.1 kg, P=0.002). There was no significant difference in serum albumin level between the groups (ANOVA, P=0.6).

The treatment group had a shorter mean duration of hospitalisation than the placebo group (8.4±17.7 vs 16.8±21.7 days/year; P=0.02) [Fig 2]. After adjusting for comorbidities, those in the treatment group had marginally fewer hospital admissions (1.8±3.1 vs 2.4±2.8 episodes per year, P=0.07) and a significantly shorter hospital stay than patients in the placebo group (8.4±17.7 vs 16.8±21.7 days/year, P=0.02).

Two patients in the treatment group, and five in the placebo group died during the study period, but the difference was not statistically significant (log rank test, P=0.20).

Discussion

Although our trial was small and had limited ability to exclude potential confounding factors, we found that oral sodium bicarbonate improved nutritional status and reduced hospitalisation in Chinese continuous ambulatory peritoneal dialysis (CAPD) patients with Kt/V of 1.7 to 2.1 and plasma bicarbonate below 24 mmol/L.

In this study, serum bicarbonate increased in the control group during the first 4 weeks. We believe the change represents a 'trial effect', as all patients were informed about the nature and causes of acidosis upon enrolment, which might have transiently affected the diet and behaviour of all enrolled patients. After 4 weeks, there was gradual decrease in plasma bicarbonate level in both groups, possibly due to the loss of residual renal function.

We chose SGA as the major outcome measure, because it has proven clinical significance. Although SGA has only been validated as a descriptive and predictive variable, a Canada-US study showed that SGA was related to mortality and hospitalisation of CAPD patients when the score was considered as a time-dependent variable,[1] which suggested that it might be used for monitoring response. However,

our study had limited statistical power to detect changes in other estimates of nutritional status.

The mechanism by which sodium bicarbonate confers benefit is uncertain. Metabolic acidosis causes accelerated proteolysis by enhancing the activity of the ATP-dependent ubiquitin-proteasome system and the enzyme branch-chain ketoacid dehydrogenase.[7] However, we found that bicarbonate supplementation improved the SGA score for anorexia and NPNA, which probably represented a true improvement in appetite and protein intake.

The overall magnitude of benefit noted in our study was similar to that previously reported following use of high-lactate dialysate for the correction of acidosis.[4] The long-term effect of sodium bicarbonate supplements remains uncertain. Clinicians should be cautious regarding the potential for sodium overloading associated with sodium bicarbonate therapy.

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References

1. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol 1996;7:198-207.
2. Szeto CC, Wong TY, Leung CB, et al. Importance of dialysis adequacy in mortality and morbidity of Chinese CAPD patients. Kidney Int 2000;58:400-7.
3. Graham KA, Reaich D, Channon SM, et al. Correction of acidosis in CAPD decreases whole body protein degradation. Kidney Int 1996;49:1396-400.
4. Stein A, Moorhouse J, Iles-Smith H, et al. Role of an improvement in acid-base status and nutrition in CAPD patients. Kidney Int 1997;52:1089-95.
5. Forbes GB, Bruining GJ. Urinary creatinine excretion and lean body mass. Am J Clin Nutr 1976;29:1359-66.
6. Randerson DH, Chapman GV, Farrell PC. Amino acid and dietary status in long-term CAPD patients. In: Atkins RC, Farrell PC, Thomson N, editors. Peritoneal dialysis. Edinburgh: Churchill Livingstone; 1981:171-91.
7. Szeto CC, Lai KN. Metabolic acidosis and nutritional status of patients receiving continuous ambulatory peritoneal dialysis (CAPD). Int J Artif Organs 1998;21:192-5.