Acidosis in End-Stage Renal Failure

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Acidosis has been identified as one of the uremic toxins. Renal acidosis may contribute to renal osteodystrophy [1] and decreased myocardial contractility [2]. Furthermore, animal experimental studies proved that acidosis plays a pivotal role in the accelerated muscle proteolysis in chronic renal failure by activation of the ATP-ubiquitin proteasome-dependent pathway and will lead to stimulation of branched-chain ketoacid dehydrogenase activity causing degradation of branched-chain amino acids [3-5]. Correction of the acidosis could prevent this catabolism. Also, in clinical practice there is evidence for an impaired nitrogen utilisation and a change of amino acid and protein metabolism due to renal acidosis [6, 7]. It was shown that sodium bicarbonate supplementation improved significantly the nitrogen balance in nondialyzed uremic patients [8]. In another study, the urinary excretion of 3-methylhistidine was used as an indicator of muscle turnover. When in addition to a restricted protein diet bicarbonate supplementation was given to correct acidosis, both excretion of nitrogen and of 3-methylhistidine was reduced, indicating a decrease of catabolism [9]. Reduced levels of branched-chain amino acids in uremic dialyzed patients have also been reported. The

muscle valine level closely correlated with the plasma bicarbonate level [6].

Protein energy malnutrition in maintenance dialysis patients is very common and of multifactorial origin [10]. Low-protein diet and anorexia due to the uremic state are certainly important factors causing malnutrition, but apart from acidosis also the uremic state itself could directly stimulate protein catabolism. The question is: What is the role of renal acidosis and its degree of correction in malnutrition and clinical outcome of dialysis patients?

Prospective studies are warranted to answer this question.

Although the introduction of bicarbonate dialysis resulted in a better correction of the acidosis as compared to acetate dialysis, this correction is still not optimal [11]. Only a few studies showed a postdialysis bicarbonate level of 24-28 mmol/l, and in most studies the predialysis bicarbonate level was below 22 mmol/l [12, 13]. Bicarbonate requirements in hemodialysis patients are dependent on acid production during the interdialytic period, the removal of organic anions during hemodialysis, and on the buffer deficit of the body [14]. When dialysis treatment is initiated, the endogenous buffer system is often exhausted by the long-existing positive hydro-

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gen balance and has to be replenished, thus increasing the bicarbonate requirement. The postdialysis bicarbonate level is dependent on bicarbonate concentration of the dialysate, adequacy of the dialysis treatment, and on ultrafiltration volume [14]. The predialysis bicarbonate level is dependent on buffer deficit, bicarbonate influx, and hydrogen-ion generation rate, which is related to protein intake. Based on nitrogen balance studies and studies on nutritional intakes and nutritional status in dialysis patients, it is assumed that protein requirement in dialysis patients is considerably higher as in normal individuals (1.2 vs., 0.75 g protein/kg/day) [10]. Higher protein intake would lead to even lower predialysis bicarbonate levels.

By individualising the bicarbonate concentration of the dialysate, trying to achieve a postdialysis bicarbonate level of 28-32 mmol/L, and giving the patients in the interdialytic period oral sodium bicarbonate supplementation, it was possible to achieve a mean predialysis bicarbonate level of 24.4 and a mean postdialysis bicarbonate level of 29.9 mmol/L. The protein intake was 1 g/kg body weight per day and the mean ultrafiltration volume was 1.5 liters per dialysis session. The sodium load in these patients was not leading to an increased fluid intake. In 79% of the patients the predialysis bicarbonate level was higher than 22 mmol/L and the postdialysis bicarbonate level between 28 and 32 mmol/L. In 21 % of the studied patients either predialysis bicarbonate was less than 22 mmol/L or postdialysis bicarbonate was less than 27 mmol/L [15]. Postdialysis alkalo-sis was prevented because of its possible complications; decrease of ionized calcium, hyp-oxemia and central nervous system symptoms [14]. An issue that should be addressed is at what level of postdialysis alkalosis are these complications clinically present, and can we increase the predialysis bicarbonate level by

increasing the buffer influx during dialysis, notwithstanding postdialysis alkalosis.

Another technique that has been reported to be associated with a better correction of aci-dosis is the acetate free biofiltration [16, 17]. Also in this technique the goal is an optimal correction of the postdialysis bicarbonate level (30-32 mmol/L). By this way predialysis bicarbonate levels increased significantly. A drawback of this technique is the fact that it is more expensive than regular hemodialysis.

Although individual bicarbonate dialysis and acetate free biofiltration leads to a better correction of acidosis, it is still not known what the optimal pre- and postdialysis bicarbonate levels should be and what the interdialytic bicarbonate profile should be, especially in relation to the effects on protein catabolism.

Acidosis is a uremic toxin which seems to play a role in renal osteodystrophy and malnutrition in dialysis patients. Although the importance of acidosis causing malnutrition in dialysis patients is not fully established, waiting for longitudinal prospective studies on this issue, to correct renal acidosis as well as possible in predialysis and dialysis patients, should be advocated.

References

Lefebvre A, De Veijou MC, Gueris J, Goldfare B, Graulet AM, Morieux C: Optimal correction of acidosis changes progression of dialysis osteodystrophy. *Kidney Int* 1989;36:1112-1118.

Mitchell JH, Wildenthal K, Johnson RL: The effects of acid-base disturbance on cardiovascular and pulmonary function. *Kidney Int* 1972;1: 375-389.

Hara J, May RC, Kelly RA, Mitch WE: Acidosis, not azotaemia stimulates branched-chain amino acid catabolism in uremic rats. *Kidney Int* 1987;32:808-814.

Mitch WE: Cellular mechanisms of catabolism activated by metabolic acidosis. *Blood Purif* 1995;13:361-367.

May RC, Kelly RA, Mitch WE: Mechanisms for defects in muscle protein metabolism in rats with chronic uremia. *J Clin Invest* 1987; 79:1009-1103.

Bergstrom J, Alvestrand A, Furst P: Plasma and muscle free amino acids in maintenance hemodialysis patients without protein malnutrition. *Kidney Int* 1990;38:108-114.

Papadoyannakis NJ, Stefanidis CJ, McGeown M: The effects of the correction of metabolic acidosis on nitrogen and potassium balance of patients with chronic renal failure. *Am J Clin Nutr* 1984;40:623-627.

Jenkins D, Burton PR, Bennett SE, Baker F, Walls J: The metabolic consequences of the correction of acidosis in uraemia. *Nephrol Dial Transplant* 1989;4:92-95.

Walls J, Williams B: The metabolic role of acidosis in uremia. *Contrib Nephrol*. Basel, Karger, 1990; vol 81, pp 136-141.

Bergstrom J: Metabolic acidosis and nutrition in dialysis patients. *Blood Purif* 1995;13:361-367.

Ledebo I: Acetate versus Bicarbonate in Every Day Dialysis. Lund, Gambro, 1990.

Heineken FG, Brady-Smith M, Haynie J, Van Stone JC: Prescribing dialysate bicarbonate concentrations for hemodialysis patients. *Int J Artif Organs* 1988;11:45-50.

Ward RA, Wathen RL, Williams TE, Harding GB: Hemodialysate composition and intradialytic metabolic, acid-base and potassium changes. *Kidney Int* 1987;32:129-135.

Leunissen KML, Kooman JP, Van Kuyk WHM, Van Hooff JP: Bicarbonate dialysis: a review and future perspectives. *Semin Dial* 1994;7: 186-191.

Leunissen KML, Kooman JP, Watterval PW, Claessens PJM, Van Hooff JP: Individualization of the dialysate bicarbonate concentration for an optimal correction of the acidosis; in Man NK, Botello J, Zuchelli P (eds): *Blood Purification in Perspective: New Insights and Future Trends*. Cleveland, ICAOT Press, 1992;pp 177-181.

Zuchelli P, Santoro A, Ferrari G, Spongano M: Acetate-free biofiltration: hemodiafiltration with base-free dialysate. *Blood Purif* 1990;8: 14-22.

Zuchelli P, Santoro A: How to achieve optimal correction of acidosis in endstage renal failure patients. *Blood Purif* 1995;13:375-384.