

# AIMING FOR THE OPTIMAL CARBONATE PRESCRIPTION FOR MAINTENANCE HEMODIALYSIS THERAPY IN END – STAGE RENAL DISEASE

I. Petrou, A. Bozikas, I. Kiriakoutzik, T. Touroutzis, E. Kitoukidi, P. Pisanidou, N. Georgilas, P. Pangidis, S. Spaia  
Nephrology Department – Hemodialysis Unit, General Hospital of Thessaloniki “Agios Pavlos”, Thessaloniki, Greece

## OBJECTIVES

Both acidemia and alkalemia can be associated with adverse consequences and maintenance of acid – base balance remains an important aspect of renal replacement therapies<sup>1</sup>

Current K/DOQI guidelines recommend predialysis or stabilized serum bicarbonate levels should be maintained at or above 22 mmol/L<sup>2</sup>

Normalization of the predialysis or stabilized serum bicarbonate concentration can be achieved by higher basic anion concentrations in the dialysate and/or by oral supplementation with bicarbonate salts

An oral dose of sodium bicarbonate, approximately 2 to 4 g/d or 25 to 50 mEq/d, can be used to effectively increase serum bicarbonate concentrations<sup>3,4,5</sup>

We compared the effect of higher doses of bicarbonate based dialysate to a standard bicarbonate bath plus oral bicarbonate therapy

## METHODS

| Patients | Sex                  | Mean Age (years) | HD Duration (months) |
|----------|----------------------|------------------|----------------------|
| 60       | 31 male<br>29 female | 72 ± 10          | 59 ± 70              |

60 stable HD patients were evaluated according to their predialysis acid – base status both before the 1<sup>st</sup> and the 2<sup>nd</sup> session of the week with a standard bicarbonate based dialysate of 35 mEq/l, Ca: 1.5 mmol/l and Glu: 100 mg/dl

Those who presented with predialysis HCO<sub>3</sub><sup>-</sup> levels of less than 22 mEq/l were assigned to dialysis against dialysis bath with increased bicarbonate levels (+2 mEq/l) for two weeks (**period A**) and subsequently to dialysis with the standard dialysate bath plus addition of daily oral sodium bicarbonate at a dose of 5 gr per day (t.i.d.) for 2 more weeks (**period B**)

Records of pre and post dialysis acid base status after each study period, along with laboratory tests and evaluation of different parameters (residual diuresis, UF, BMI, BP, dialysis via central catheter, and on – line HDF) were recorded

## RESULTS

Predialysis acid base profile didn't present robust differences, between the 1<sup>st</sup> and 2<sup>nd</sup> dialysis session. In this study, predialysis profile was not correlated with residual diuresis, UF, BMI, BP, dialysis via central catheter, and online HDF

In 25 patients predialysis pH was < 7.35, while 42 patients presented predialysis HCO<sub>3</sub><sup>-</sup> < 22 mEq/L

Those patients were of younger age ( 70 vs. 78 years old, p < 0.05)

However, 18 patients had pH > 7.45 after dialysis session

Overall 25 patients accepted to participate to the subsequent interventional period

During period A (HCO<sub>3</sub><sup>-</sup> +2 mEq/l) postdialysis serum bicarbonate levels were significantly increased (p<0.05)

During period B the postdialysis increment of the serum bicarbonates was less prominent

Patients appeared with predialysis levels of HCO<sub>3</sub><sup>-</sup> in accordance with guidelines, only on period B, after 2 weeks of oral bicarbonate

On the contrary, predialysis levels of serum bicarbonates during period A, were significantly lower than period B

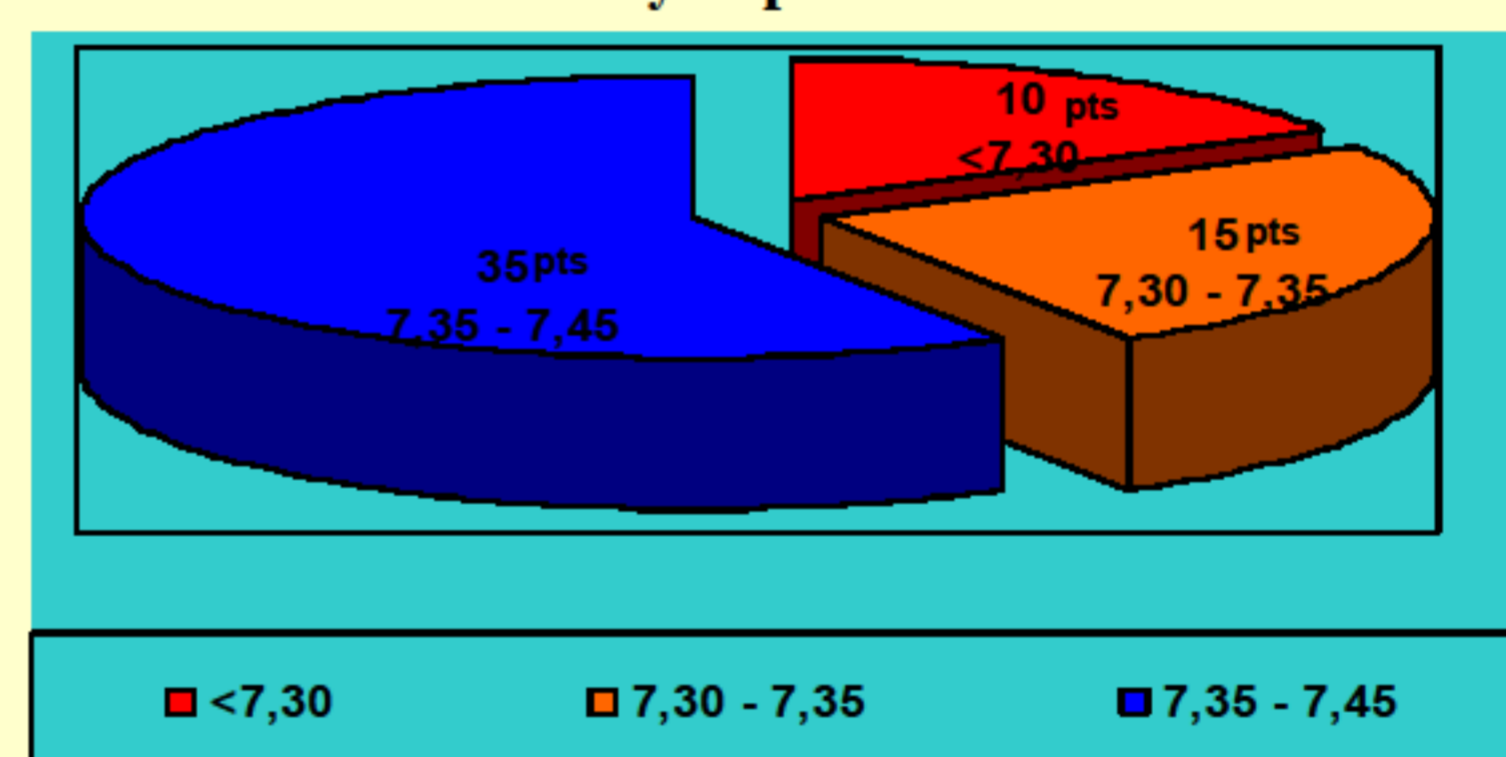
Interdialytic weight was similar, between the two study periods. Three patients could not tolerate symptoms of alkalemia in period A and suffered headaches and muscle cramps

Moreover, several patients resented the frequency and the taste of oral bicarbonate

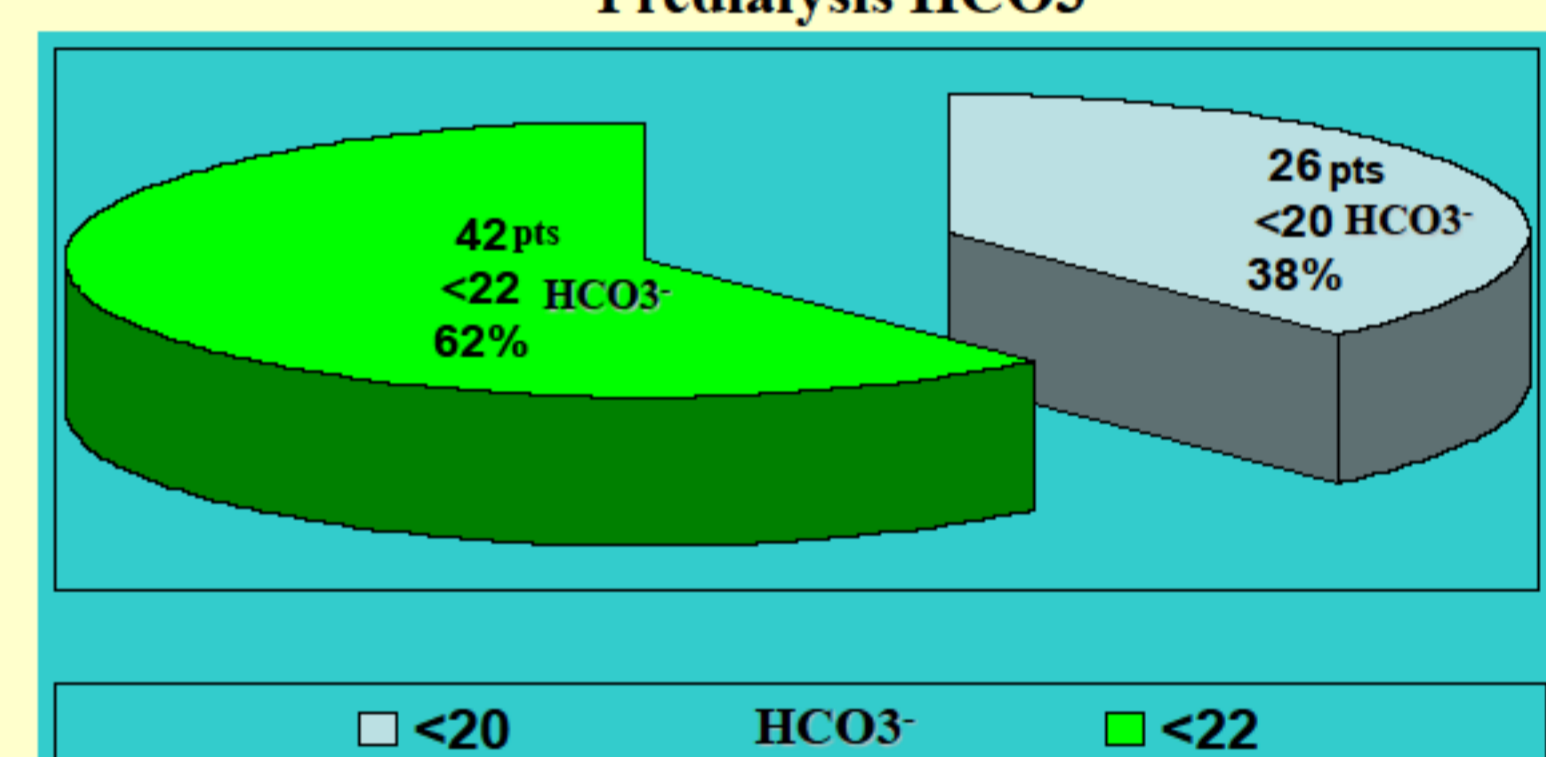
Values prior to 1st and 2nd dialysis session

|  | 1 <sup>st</sup> HD | 2 <sup>nd</sup> HD | p  |
|--|--------------------|--------------------|----|
| pH                                     | 7.34 ± 0.64        | 7.34 ± 0.05        | ns |
| HCO <sub>3</sub> <sup>-</sup> (mmol/L) | 20.5 ± 2.4         | 21.3 ± 1.8         | ns |
| BE (mmol/L)                            | -4.1 ± 3           | -3.5 ± 2           | ns |
| pCO <sub>2</sub> (mmHg)                | 39.2 ± 6.8         | 40.6 ± 5.7         | ns |
| Lactate (mmol/L)                       | 1.1 ± 0.4          | 1.3 ± 0.4          | ns |

Predialysis pH values



Predialysis HCO<sub>3</sub><sup>-</sup>



Comparison of pre HD vs post HD on Period A

|  | pre HD      | post HD     | p     |
|--|-------------|-------------|-------|
| pH                                     | 7.34 ± 0.05 | 7.43 ± 0.04 | 0.001 |
| HCO <sub>3</sub> <sup>-</sup> (mmol/L) | 21.3 ± 1.8  | 25.6 ± 1.3  | 0.001 |
| BE (mmol/L)                            | -3.5 ± 2    | -1.8 ± 1.5  | 0.001 |
| pCO <sub>2</sub> (mmHg)                | 40.6 ± 5.7  | 38.9 ± 4.2  | 0.065 |
| Lac (mmol/L)                           | 1.3 ± 0.4   | 0.9 ± 0.4   | 0.001 |

Comparison of the two study periods

|   | Period A    | Period B    | p    |
|---|-------------|-------------|------|
| HCO <sub>3</sub> <sup>-</sup> predialysis   | 21.51 ± 2.5 | 23.02 ± 2.8 | 0.03 |
| HCO <sub>3</sub> <sup>-</sup> post dialysis | 27.6 ± 1.7  | 26.4 ± 1    | 0.03 |
| pH predialysis                              | 7.36 ± 0.05 | 7.36 ± 0.05 | ns   |

## DISCUSSION – CONCLUSIONS

Our current thrice – weekly HD paradigm necessitates a trade – off of potentially large fluctuations in serum bicarbonate over short periods of time to assure a net physiological acid – base mass balance. This rapid delivery of large quantities of base is obviously non – physiological and not without potential consequences. Increasing bicarbonate dialysis bath results in more prominent postdialysis alkalemia, and still it is not sufficient to maintain acid – base balance in the interdialytic period. Indeed, this study shows that the impact of conventional dialysate bicarbonate concentrations of 35 mEq/L results in a considerable degree of **predialysis acidemia**, followed by significant increase of alkali burden, exposing patients to higher mortality risk. Recently, it has been demonstrated, that low blood levels of bicarbonate may indicate an elevated risk of premature death in generally healthy older individuals.<sup>6,7</sup>

These findings suggest that the use of this blood marker is an important health indicator and that future studies should examine the potential of increasing bicarbonate levels to prolong life.

The addition of oral bicarbonates on a daily basis could neutralize a part of the daily acid load, avoid pre dialysis acidemia and excessive post dialysis alkalemia.

This hypothesis was evaluated in our short term study and it was confirmed that **oral bicarbonate therapy** at a dose of 5 gr per day proved to be **a more physiological approach** and resulted in a balanced acid base status, avoiding excessive postdialysis alkalemia. However, compliance in this study was achieved mainly because of the short term design of period B, since patients were complaining of the additional “medication” in their daily routine as well as the unusual taste. In those patients we have currently reduced the dose of oral bicarbonate and adjusted the dialysate bath.

In conclusion, the ideal scenario for optimal acid – base management in MHD patients includes a multifaceted approach of oral and individualized delivery of bicarbonate rather than a unit – wide prescription that is infrequently changed.

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