CLEARENCE OF ZINC AND COPPER DURING HEMODIALYSIS Preliminary Study

SANIYE SEN*
NACI M. BOR*
MURAT COLAKOGLU*
AYSE GULTEKIN*

SUMMARY: It has been shown that patients in end stage renal disease maintened on hemodialysis program develop zinc and copper deficiency. In order to explore the causes of this important complication, this investigation was planned and conducted on 28 patients. It was observed that the mean serum zinc levels during (6I.92±13.05 µg/dl) and at the end (62.92±7.92 µg/dl) of the procedure were not significantly different from the initial value. But zinc concentration of the exit line of the dialyser at the end of 2 hours revealed a statistically significant difference (P<0.5). The mean serum copper levels in the entry line of the dialyser was 93.0±17.0 µg/dl at the end of the procedure (P<0.05). These differences are believed to present concentration of patients blood due to ultrafiltration. It is concluded from these findings that during hemodialysis the end stage renal disease patients do not lose significant of zinc or copper in to dialysis.

Key Words: Zinc, copper, hemodialysis, clearences.

INTRODUCTION

It is known that serum zinc and copper levels of patients with end stage renal disease (ESRD) maintened on hemodialysis (HD) program are reduced compared to their normal values (1-6). We in a recent series of experiments confirmed these results (17).

Some investigators attributed this serious complication to protein-calory malnutrition which frequently develops in these patients because of dietary restriction (8, 18, 19). Loss of appetite and poor absorption by the intestinocytes may also be contributing factors (1, 2, 12, 20, 21). In addition to the above a third possible cause for low serum Cu and Zn levels in these patients may be excessive loss of trace elements into the dialysate. In order to investigate the latter possibility we conducted the experiments presented in this communication.

MATERIALS AND METHODS

This investigation was carried out on 10 female and 18 male patients all of whom were on maintenance hemodialysis program at the Hemodialysis Center of Social Security Ankara Hospital. They were hemodialysed 3 times per week for 4 hours and 40 minutes with a blood flow rate of 220 ml/min and dialysate flow rate 500 ml/min using either Cobe C2000 or B. Braun Secura machine with 1 m^2 exchange with celulosic membrane (cuprophan). All patients were heparinized.

During 4 hour hemodialysis period 1 liter of dehidration was produced for each patient corresponding to 4.75 ml ultrafiltration per minute. The dialyser was washed using 1000 ml of physiologic salt solution before hemodialysis. Samples of blood were removed from the inlet and outlet of dialyser before dialysis began, 2 hours after initiation and at the end of the perfusion. Samples of dialysate were also removed from the inlet and outlet of dialyser simultaneously. In all samples Zn and Cu was measured using Cathodeon Alpha-4 atomic absorption spectrophotometer.

All glassware and equipment used in these procedure were routinely washed with detergents followed by acid solution and were additionally rinsed several times with de-ionized water.

The results were subjected to statistical analysis using Student t test.

*From Hemodialysis Center of Social Security Ankara Hospital, Ankara, TURKEY.

Table 1: Serum zinc and copper levels during single session of hemodialysis.

μg/dl	Zn (mean±SD)	Cu (mean±SD)
Predialysis arterial	60.17±8.40	93.00±7.86
2 hour arterial	61.92±13.05	96.65±20.92+
2 hour venous	63.67±9.24 +	93.25±23.32+
End of dialysis arterial	62.92±7.92	96.50±20.06+

Statistical compared to the initial value (+) $p < 0.05$.

RESULTS

The mean serum Zn level was 60.17±8.40 μg/dl (inlet line of the dialyser) and the mean copper level was 93.0±7.86 μg/dl at the initiation of the hemodialysis. By the end of the second hour serum Zn was 63.67±9.24 μg/dl of the sample obtained from the venous blood of the dialyser (returning to the patient). This was statistically different from those of the inlet line of the dializer at the beginning of dialysis. The mean serum copper levels was 96.50±20.06 μg/dl at the end of the procedure and appeared on the other hand significantly different ($P<0.05$) from that of the corresponding initial value (Table 2). Serum Cu 96.50±20.06 μg/dl at the end of the procedure was on the other hand significantly different ($P<0.05$) in the inlet line to the dialyser compared to its original figure. Cu levels of dialysate samples removed zero throughout the procedure. Zn levels of the samples obtained from both entry and exit lines of the dialyser are seen in Table 2.

DISCUSSION

Studies reported earlier by Mansouri *et al.* (7) have indicated that Zn and Cu are not dialysed during hemodialysis. From this point of view the Zn deficiency of these patients with ESRD maintened on chronic hemodialysis program may easily be attributed to protein-calory malnutrition (8,18,19). Loss of appetite, and poor absorption by intestinocytes may also be contributing factors (1, 2, 12, 20, 21).

In a former study conducted by us serum Zn and Cu levels of a series of ESRD patients also maintained on hemodialysis were found significantly below normal values (17). We advised these patients to increase their protein uptake by 1 gr/kg/day. Subsequent measurement two months later revealed serum Zn levels %9 higher compared to the former findings. This insufficient recovery raises the probability of loss of these essential elements during hemodialysis.

The results of the present series however indicate that hemodialysis did not significantly influence ($P>0.05$) the serum Zn levels of these patients during the first 2 hours of application (Table 1). We observed however that the blood returning from the dialyser to the patient obtained significantly higher levels ($P<0.05$) at the end of 2 hours. This could possible be due to loss of water secondary to ultrafiltration. In fact a significant, nevertheless minimal rise in serum Zn at the outlet of the dialyser after 4 hours of application appears as a serious indication of the fact that Zn is not lost from the patient to the dialysate.

This is perhaps due to the fact that Zn in the blood is combined to albumin forming a large particle unable to pass through the pores of the dialyser memrane (7, 22-25).

Serum Cu levels at the end of first and second hour are higher compared to the beginning of dialysis (Table 1). This also appears to be due to hemoconcentration secondary to ultrafiltration in the hemodialysis. Our results seems to agree with the conclusions of the former investigations who apparently indicated that no Zn or Cu loss occur during hemodialysis (7, 22). From this angle the Zn and Cu deficiency observed in patients with ESRD appears to be not because they are undergoing hemodialysis three times weekly but perhaps due to nutritional reasons and/or because of poor gastrointestinal absorption. Etiology and pathogenesis of this reduction and its consequences however are at present not sufficiently understood.

In summary it can be stated that patients undergoing hemodialysis were studied to find out whether Zn or Cu is lost in to dialysate during a cession of 4 hours. It was observed that in the dialyser exit line (return to the venous system of the patient) Zn and especially Cu concentrations increases to a moderate degree ($P<0.05$). This is believed to be due to hemoconcentration.

Table 2: Dialysate zinc values during single session of hemodialysis (μg/dl).

	Time: Predialysis (mean±SD)	1-2 hour Outlet (mean±SD)	1-2 hour Inlet (mean±SD)	Post D (mean±SD)
Zn Value	11.9±4.38	9.16±3.94	9.87±3.81	8.18±3.23 x

Statistical compared to the initial value (x) $p < 0.001$

REFERENCES

1. Prasad AS, Rabbani P, Abbasi A, Bowersox E, Fox MRS : Experimental zinc deficiency in humans. Ann Int Med 89: 483-490, 1978.

2. Prasad AS : Clinical endocrinological and biochemical effects of zinc deficiency Clin Endoc Metab l4(3): 567-589, 1985.

3. Aggett PJ : Zinc metabolism in chronic renal insufficiency with or without dialysis therapy. Contr Nephrol 38: 95-102, 1984.

4. Sanstead HH : Trace elements in uremia and hemodialysis. Am J Clin Nutr 33:1501-1508, 1980.

5. Smythe WR, Alfrey AC, Craswell PW : Trace elements abnormalities in chronic uremia. Ann Intern Med 96: 302-310, 1982.

6. Atkin-Thor E, Goddord BW, O'Nion J, Stephan RL, Kolff WJ : Hypogeusia and zinc depletion in chronic dialisis patient. Am J Clin Nutr 36:403-409, 1982.

7. Mansouri K, Halsted JA, Gombos EA : Zinc, copper and calcium in dialysed and non dialysed ureamic patients. Arch Intern Med 125:88-93, 1970.

8. Locsey L, Papp L : Study of trace elements in patients on hemodialysis. Intern Urol Nephrol 15(5): 207-210, 1983.

9. Mahajan SK, Abbasi AA, Prasad AS, Rabbani P, Briggs WA, McDonald FD : Effect of zinc therapy on gonadal function in hemodialysis patients. Ann Intern Med 97:357-361, 1982.

10. Antoniuo LD, Shaldhoub RJ, Sudhakar T, Smith Br JC: Reversal of uremic impotence by zinc. Lancet 11:895-899, 1977.

11. Mahajan SK, Prasad AS, Rabbani P, Briggs WA, McDonald FD : Zinc deficiency: a reversible complication of uremia. Am J Clin Nurt 36:1177-1183,1982.

12. Mahajan SK, Prasad AS, Briggs WA, McDonald FD: Effect of zinc therapy on sexual dysfunction in hemodialysis patients. Trans Am Soc Artif Intern Organs XXVI: :139-143, 1980.

13. Brook AC, Jhonston DG, Ward MK, Watson MJ, Cook143 DB, Kerr DNS : Absence of a therapeutic effect of zinc in the sexual dysfunction of hemodialysis patients. Lancet 11: 618-620, 1980.

14. Rodger RSC, Sheldon WL, Watson MJ, Dewar JH, Wilkinson R, Ward MK, Kerr DNS : Zinc deficiency and hyperprolactinemia are not reversible cause of sexual dysfunction in uremia. Nephrol Dial Transplant 4:888-892, 1989.

15. Antoniou LD, Shaldhoub RJ, Schecter GP : The effect of zinc on cellular immunity in chronic uremia. Am J Clin Nutr 34:1912-1917, 1981.

16. Allen JI, Korhic W, Kay EN, McClain CJ : Zinc and T-Lymphocyte function in hemodialysis patients. Am J Clin Nutr 36:410-415, 1982.

17. Sen S, Bor NM, Colakoglu M, Ercan A : Zinc and copper deficiency in maintenance hemodialysis patients with end stage renal disease. J Islam Acad Sci 4:71-73, 1991

18. Antoniou LD, Shalhoud RJ : Zinc and sexual dysfunction. Lancet 11:843-851, 1980.

19. Craig GM, Evans SJ, Brayshaw BJ, Raina SK : A study of serum zinc, albumin, alfa-2 macroglobulin and transferrin levels in acute and long stay elderly hospital patient. Postgrad Med J 66:205-209, 1990.

20. Bor NM, Karabiyikoglu A, Dereagzi H : Zinc in treatment of psoriasis. J Islam Acad Sci 4:78-82, 1991.

21. Blendis LM, Ampil M, Wilson DR, Kiwan J, Labrance J, Jhonson M, Williams C : Protein in the zinc deficiency of uremia. Am J Clin Nutr 34:2658-2661, 1981.

22. Martins EO : Flow-through dialysis of zinc (11) from modal and human sera. J Inorg Biochem 33:237-245, 1988.

23. Freeman RM, Carl MD, Richard S, Rames LK : Zinc metabolism in aminonucleoside induced nephrosis. Am J Clin Nutr 28:699-703, 1975.

24. Lindeman RD, Baxter DJ, Yunice AA, Karaikitpanitc S: Serum concentration and urinary excreations of zinc in chrosis, nephrotic syndrome and renal insufficiency, Am J Med Sci 275(1): 17-31, 1978.

25. Stec J, Podracka L, Pavcovcekova O, Kollar J : Zinc and copper metabolism in nephrotic syndrome. Nephron 56: 186-187, 1990.

Correspondence:
Saniye SEN
Hemodialysis Center of
Social Security,
Ankara Hospital,
Ankara, TURKIYE.