

The Evaluation of serum Zinc, Copper, Sodium and Potassium levels in hemodialysis patients

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الخلاصة:

الهدف من الدراسة هو تقدير مستويات الزنك، النحاس، الصوديوم والبوتاسيوم في مصل مرضى الفشل الكلوي المزمن والذين يخضعون لعملية غسيل الكلى. تم دراسة تأثير الفترة الزمنية لعملية غسل الكلية على تلك العناصر. المجاميع التي تم دراستها تكونت من 32 مريض مصاب بعجز الكلية المزمن ممن يخضعون لعملية غسل الكلية، و32 من مجموعة السيطرة. تم تقدير مستويات الزنك والنحاس بواسطة تقنية الامتصاص الذري للهدبي بينما تم تقدير مستويات الصوديوم والبوتاسيوم بواسطة جهاز تحليل الأيونات. أظهرت النتائج انخفاض مستويات الزنك والنحاس والصوديوم لدى المرضى المصابين بعجز الكلية المزمن (P<0.01)، أما زيادات مستويات البوتاسيوم يومياً فهي غير معنوية (P<0.05) بالمقارنة مع مجموعة السيطرة. لم تظهر النتائج أي تأثير للفترة الزمنية لعملية الغسيل الكلوي على مستويات العناصر النزرة.

Abstract:

The aim of this study was to determine serum zinc (Zn), copper (Cu), sodium (Na) and potassium (K) levels in patients with chronic renal failure (CRF) undergoing hemodialysis (HD) and to investigate the influence of HD duration on these trace elements. The study group included (32) HD patients and a control group of (32) healthy subjects.

Blood samples were drawn for determination of serum (Zn) and (Cu) levels which measured by atomic absorption spectrophotometry, and serum (Na) and (K) levels measured by electrolyte analyzer.

The mean age was (50.5 ± 12.7) yr in the (HD) group and (48.1 ± 20.3) yr in the control group. Laboratory findings showed the following mean values: Zn (43.12 ± 12.81) micro.gm/dl in the HD group (vs. 72.59 ± 4.8) micro.gm/dl in the control group, Cu (65.3 ± 10.2) micro.gm/dl in the HD group (vs. 120.1 ± 46.3) micro.gm/dl in the control group, Na (133.9 ± 10.53) mmol/ L in the HD group (vs. 145.8 ± 25.35) mmol/ L in the control,

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K (4.77 ± 0.68) mmol/ L in the HD group (vs. 3.59 ± 0.44) mmol/ L in the control group. The serum Zn, Cu levels of the HD group was significantly lower than that of the control group ($P < 0.01$). The serum Na level of HD group was significantly decreased than that control group ($P < 0.05$), While serum (K) level in HD significantly increased ($P < 0.05$) than that control group.

NO significant differences in the serum Zn, Cu, Na, and K levels between long term and short term dialyzed patients ($P > 0.05$). Because the levels of trace elements (Zn, Cu) of the HD group were significantly low, we recommend that (Zn, Cu) should be given to patients with (CRF) undergoing HD.

Introduction:

For human beings trace elements are essential nutrients with a gamut of functions. They are for instance indispensable component of many enzymes. So they have some regulatory functions and they may affect immune reactions and free radical generation. Abnormality of trace elements are primary the result of uremia and they may be further modified and sometimes greatly exacerbated by the dialysis procedure(1).

The essentially of zinc (Zn) in the growth and well – being of both plants and animals is well established. Since Zn deficiency was first described in humans in the early 1960s, research has elucidated many of its specific metabolic interactions(2). Moreover, the discovery of a variety of zinc-related clinical disorders has directly demonstrated the importance of Zn in human nutrition.(3)

Copper (Cu) is an integral component of many metallo – enzymes. The major functions of Cu metallo - proteins involve oxidation – reduction reactions; most known copper – containing enzymes bind and react directly with molecular oxygen. A number of pathological conditions have been attributed to the loss of cupro – enzyme activity.(2,3)

Chronic renal failure (CRF) is a clinical syndrome that results in the permanent loss of renal function due to the progressive loss of nephrons. Whatever it is that causes the renal damage in the CRF, it is ultimately the progressive loss of nephrons that leads to end stage renal disease (ESRD).(4)

Hemodialysis (HD) remains the most common technique for the treatment of patients with (ESRD). A deficiency of trace elements has been described in patients with CRF undergoing HD(4). Causes of this deficiency may be related to a low dietary intake of these trace elements

, a decrease of their intestinal absorption, and their loss to the dialysate. (4,5)

Potassium is one of the electrolytes that with sodium is involved in the maintenance of normbalance, osmotic equilibrium, acid – base balance, and it is crucial to cardiovascular and nerve. It is the primary positive cation found within the cells, and along with calcium serves an important heart muscle contractions, skeletal muscle contraction, nerve impulse transmission, and the energy from food. (6)

Sodium incorporated into tissues such as bone and has a slow turnover rate. Most of the exchangeable sodium is in the extracellular fluid (ECF) which comprises both the plasma and the interstitial fluid. Sodium losses are just as variable and most sodium excretion is via kidney. (7)

Subjects and Methods

Subjects:

The study group consisted of (32) HD patients (20 males ,12 females) who received chronic maintenance hemodialysis (approximately 4 hours per treatment, 2times per week) in the HD care unit Hilla hospital during period December 2004 – June 2005 . The control group consisted of 32 health subjects (18 males , 14 females). The mean age of those in the HD group was (50.5 ± 12.7 year) (range 20 to 67 year), and in the control group (48.1 ± 20.3) (range 18 to 55 year). The study subjects were all in the same socioeconomic class and had similar nutritional habits. Each patient was medical stable. Informed written consent was obtained from each subject.

Methods:

Blood samples were drawn sterile, disposable plastic syringes for determination of serum Zn, Cu, Na, and K levels, urea concentration will be measured by enzymatic method by kit, urae – kit enable end point enzymatic determination of urea concentrations (urease- modified breathelot reaction) in human urine, serum or plasma urease hydrolyzes urea by producing ammonium. In alkaline medium, the ammonium ions react with the salicylat and hypochlorit to form a green colored indophenol, the color intensity is proportional to the urea concentration in the sample (8). In HD patients, blood samples were drawn after dialysis. All plastic and glassware used in the experiments were treated with deionized water and then dried. The serum was separated by centrifuge ($1500 \times g$) at $25^{\circ}C$ and stored at ($-22^{\circ}C$) until analyzed. Serum samples were diluted with deionized water (1:5 v/v). Zn and Cu levels

were then measured on atomic absorption spectrophotometer(Pye UNICM) Model S P2900 equipped with burn and air acetylene flame (9). Na and K level were then measured by Electrometer in clinical chemistry laboratory in Dywanyia maternal and children hospital. The vitros analyzer (Johnson and Johnson company use a single – direct ISE system . Each disposable slide contains a reference and measuring electrode. A drop of sample fluid and a drop of reference fluid are simultaneously applied to the slide and the potential different between the two is measure with a voltmeter(10).

Statistical analysis:

Comparative analysis between HD and control groups were done using (t- test) for paired value and Chi square test. Results were expressed as the mean \pm standard deviation (SD). The correlation coefficient were calculated . P – value (< 0.05 and < 0.01) were considered to be statistically significant.

Results:

Clinical characteristics of the study patients are summarized in *Table(I)* There were no significant differences in age or diastolic blood pressure between the HD patients and the controls. There was a significant difference in serum urea and systolic blood pressure ($p < 0.01$) between the HD and control group.

Serum Zn and Cu levels of the groups are shown in *Table (II)* and in *Figures (1,2,3 and 4)* . Serum Zn levels in HD group were (43.12 ± 12.8) $\mu\text{g/dl}$ vs. (72.59 ± 4.8) $\mu\text{g/dl}$ in the control group. Serum Cu levels for the HD group were (65.3 ± 10.2) $\mu\text{g/dl}$ vs. (120.1 ± 46.3) $\mu\text{g/dl}$ for the control group thus, serum Zn and Cu levels were significantly lower ($p < 0.01$) in the HD patients than in the control group. *Figures (3,4)*

Serum Na and K level of the groups are in *Table(II)* serum Na level for HD group were (133.96 ± 20.53) mmol/L vs. (145.8 ± 23.35) mmol/L in the control group. Serum Na level were significantly lower ($p < 0.05$) in the HD patients than the control group. Serum K levels for HD group (4.77 ± 0.68) mmol/L vs. (3.59 ± 0.44) mmol/L in the control group but the change in the normal range. Serum Zn , Cu, Na , and K levels according to HD duration are shown in *Table(III)*, fifteen patients (46.8%) had been on hemodialysis less than 8 month ; seventeen (53%) had been on hemodialysis between (9 month and 30 month). The mean HD duration was 15.6 month. There was difference in serum Zn, Cu, Na and K levels among the patients based on dialysis duration ($P > 0.05$).

Table (I) Clinical characteristics of the HD group (n = 32) and of the control group (n =32) expressed as the mean \pm SD

characteristics	Hemodialysis	control
age (yr)		
mean	50.5 \pm 12.7	48.1 \pm 20.3
range	20 - 67	18 - 55
urea (mg /dl)	91.5 \pm 27.08	43.9 \pm 6.78
systolic BP (mmHg)	143 \pm 28	120 \pm 32
diastolic BP (mmHg)	75 \pm 12	70 \pm 70

Table (II) Serum Zn , Cu , Na, and K levels of the HD group (n=32) and of the control group(n= 32).

Parameter Mean \pm SD	Hemodialysis	Control	P - value
Zn(μ g/dl)	43.12 \pm 12.8	72.59 \pm 4.8	S
Cu(μ g/dl)	65.3 \pm 10.2	120.1 \pm 46.3	S
Na(mmol/L)	133.96 \pm 10.53	145.8 \pm 25.35	S
K (mmol/L)	4.77 \pm 0.68	3.59 \pm 0.45	S

Table(III). Serum Zn ,Cu , Na , K levels of HD group by hemodialysis duration (mean \pm SD).

Dialysis duration (month)	Serum Zn (μ g/dl)	Serum Cu (μ g/dl)	Serum Na (mmol/L)	Serum K (mmol/L)	P- value
< 9 month (n = 15)	40.5 \pm 17.9	68.3 \pm 14.4	135.2 \pm 8.4	4.5 \pm 0.51	S
\geq 9 month (n = 17)	42.6 \pm 12.3	64.5 \pm 14.9	134.1 \pm 9.1	4.52 \pm 0.31	S

Discussion:

There have been many studies regarding serum Zn and Cu levels in patients with (CRF) undergoing HD (10) (11). In a study involving 15 HD patients and 11 health subjects , Karayayli et al (11) reported that serum Zn levels in HD patients of (67.1 \pm 10.3 μ g/dl vs .100.1 \pm 9.5 μ g/dl. In the control group, which represented a significant difference controls, whereas serum Cu levels were significantly higher in the controls than in the CFR patients. Paydas et al (12) found that serum Zn and Cu levels

were lower in patients with HD after dialysis. Our study also indicates that serum Zn and Cu levels are lower in patients with CRF undergoing HD than in controls.

In some studies, it was reported that serum Cu levels were higher in HD patients (10, 13), while in others the serum Cu levels in patients with CRF were normal ranges or lower (14, 15). In the present study, serum Cu levels were significantly lower in the HD patients than in the controls. A number of authors have investigated the influence of HD on serum trace element levels in patients with CRF. Many of those studies suggested that HD increased serum Zn and Cu levels (10, 12, 13). However, in another study it was claimed that HD decreased serum Zn and Cu levels in patients with CRF, Kaminska – Galwa et al (15) did not find any difference in serum Zn and Cu levels between long term and short – term dialyzed patients. Our study is in agreement with this study.

Some investigators attributed that low levels of Zn and Cu to protein – calories malnutrition which frequently develops in patients because of dietary restriction (16, 17, 18). Loss of appetite and poor absorption by the intestines may also be contributing factors (19, 20, 21, 22). In addition to the above, a third possible cause for low serum Ca and Zn levels in these patients may be excessive loss of trace elements into the dialysate (23). Also low levels of serum Zn levels may be due to a specific Zn transport defect, and absence of an intestinal Zn ligand. Zn and Cu supplementations have been recommended when protein is restricted in CRF patients (15, 24). In another studies, it was claimed that the cause of Zn deficiency was an inadequate amount of Zn intake (25) (26).

In our study showed the Na levels were lower in HD patients, while the K levels were higher than control group. Most CRF patients retain the ability to reabsorb Na ions but the renal tubules may lose their ability to reabsorb water and also concentrate urine (6)

Hyperkalemia is a feature of advanced CRF and poses a threat to life. The ability to excrete potassium decrease as the CRF falls, but hyperkalemia may not be a major problem in CRF until the CRF falls very low levels. Then a sudden deterioration of renal function may precipitate a rapid rise in serum potassium (16)

Conclusion:

Serum Zn and Cu levels are significantly lower in HD patients, while Na levels were decreased and K levels will increased than in the control. There is no significant difference in serum Zn, Cu, Na and K levels

between long – term and short term dialyzed patients. We recommend that Zn and Cu should be given to patients with CRF undergoing HD.



Fig(1)Mean serum Zn of hemodialysis(HD) and control groups by gender

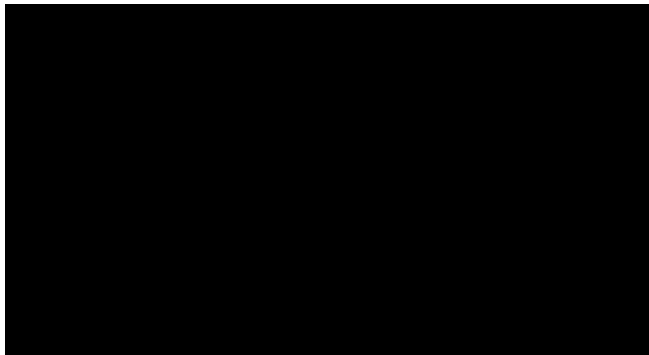
(I) in males(n=20 HD,18control) , (B) in females(n=12 HD, 14control)



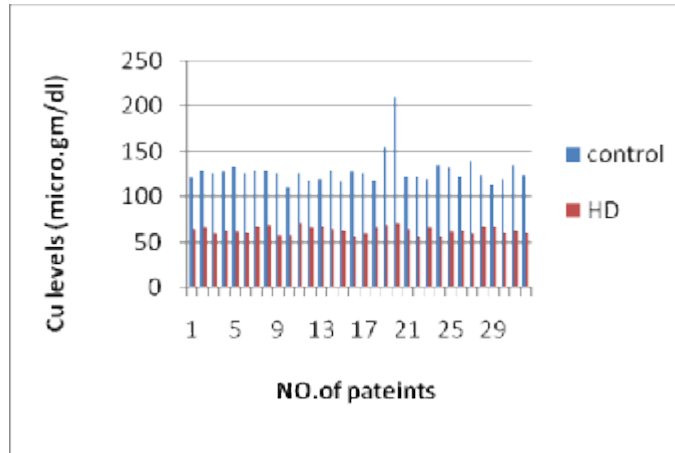
A

B

Fig(2)Mean serum Cu levels of hemodialysis and control groups by genders. (A) in males(n=20 HD, 18 controls), (B) in females(n= 2 HD, 14control).



Fig(3) Mean serum Zn levels of pateints undergoing hemodialysis (n=32)as compared with controls(n=32)



Fig(4) Mean serum Cu levels of patients undergoing hemodialysis (n=32)as compared with controls(n=32).

Reference:

- 1- Zima T, Tesar V, Mestek O, et al. Trace elements in end stage renal disease. Clinical implication of trace elements .1999; 17:1-2.
- 2-Burtis CA , Ashwood ER(eds). Clinical chemistry(2nd Ed). Philadelphia : W. B.Saunders Co.,1994.
- 3-Jacop RA (ed). Textbook of clinical chemistry. Philadelphia : W. B.Saunders Co.,1986.
- 4-Lazararus JM , Hakim RM. Medical aspects of Hemodialysis . In: The kidney(Vol. II, 4th Ed.).Brenner BM, Rector FC(eds.) Philadelphia : W. B.Saunders Co.,1991: 2223 –2265.
- 5-Ronald R. Acu – cell Nutrition , Zinc & potassium. Copy right 2002 – 2005: 1-7.
- 6-Gaw A, Cowan RA, O’ Reilly DS., et al. Clinical Biochemistry 2nd edition , CHURLTILL LIVINGSTON company 1999: 14- 21.
- 7-Fawcett JK, Scott JE. A rapid and precise methods for the determination of urea. J. Clin. Path. 1960;13: 156- 159.
- 8-Wills M.R., Savory J. Biochemistry of renal failure. Ann. Clin.Lab.. Sci. 1981;11:292 –299.
- 9-Roby JF, White B. Biochemical techniques.10 edition, Books/Cole Publishing Company. 1987::213.
- 10- Atlihan F , Soylemezoglu T, Devecioglu C. Serum Zinc and copper in chronic renal failure. In: Trace elements in Health and

- Disease (Trace 89), Yuregir GT, Donma O, Kayrin L (eds). Adana : Cukurova University Medical Faculty Press , 1991 : 517 – 522.
- 11-Karayaylali I, Tamer L, Gurbuz E.Kronic hemodiyalize hastalarinda serum ve trombosit Zn, Malonildialdehit duzeyleir ile C ve E vitamin duzeyleri. XIV. Ulusal Bobrek Hastalıkları, Diyalize ve Transplatasyon Kongresi. Antalya (poster summary), 1997:35.
- 12-Paydas S, Albayrak A, Yuregir G. Trace elements in hemodialysis patients.In: Trace Elements in health and Disease (Trace 89), Yuregir GT, Donma O, Kayrin L (eds). Adana : Cukurova University Medical Faculty Press , 1991 : 615 – 618.
- 13-Lin TH, Chen JG, Liaw JM, Juang JG. Trace elements and lipid peroxidation in uremic patients on hemodialysis. Biol Trace Elem Res 1996; 51:277- 283.
- 14-Ongajiooth L, Ongajiooth S, Likidlilid A, Chatachum Y, Shayakul C, Nilwarangkure S. Role of lipid peroxidation, trace elements and antioxidant enzymes in chronic renal disease patients. J Med Assoc Thia 1996;79:791 – 800.
- 15-Kaminski – Galwa B, Grzeszczak W, Jedryczko A, Pachekski J. Influence of long – term hemodialysis on serum trace elements cocentration in patients with chronic renal failure. Prezegl Lek 1994; 51: 9 –14.
- 16-Lacey L, Papp L: Study trace elements in patients on hemodialysis. Intern Urol Nephrol 1983;15: 207 – 210.
- 17- Antonio LD, Shalhoud RJ. Zinc and sexual dysfunction. Lancet 1980;11:843 –851.
- 18-Craig Gm, Evans SJ, Brayshaw BJ , et al. Study of serum Zinc, albumin, alfa – 2 macroglobulin and transferring levels in acute and long stay elderly hospital patient. Postgrad Med J 1990;66:205 – 209.
- 19- Parasd As, Rabbani P, Abbasi A, Bowersox E, Fox MRS: Experimental Zinc deficiency in humans. Ann Int. Med 1978;89:483 – 490.
- 20- Parasd AS: Clinical endocrinological biochemical effects of Zinc deficiency Clin Endo Metab 1985,14(3): 567 – 559.
- 21-Mahajan SK,parasd AS, Rabbani P, et al. : Zinc deficiency : a reversible complication of uremia. Am J Clin Nutr. 1982;36:1177- 1183.
- 22-Bor NM, Karabiyikoglu A, Dereagzi H: Zinc in treatment of psoriasis. J Islam Acad Sci 1991;4:78 –82.
- 23-Blenndis LM, Ampil M.,Wilson DR, et al.: protein in the Zinc deficiency of uremia. Am J clin Nutr 1981;34:2658-2661

- 24-Hadi M, Fujii H, Saloh T. Vitamin and mineral status in chronic renal failure: The effect of protein restriction. *Nippon Jinzo Gakkai Shi* 1994;36(6): 740- 745.
- 25-Paniagua R, Claure R, Amato D, Flores E, et al. Effects of oral administration of zinc and diiodohydroxyquinoline on plasma Zinc levels of uremic patients. *Nephron* 1995 ;69:147-150.
- 26-Foreman JW, Abitbol CL , Trachtman H, et al . Nutritional intake in children with renal insufficiency. *J Am Coll Nutr* 1996; 15:579-585.