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ASSESSMENT OF THE SERUM ALUMINIUM AND ZINC LEVEL AMONG CHRONIC KIDNEY DISEASE PATIENTS ON CONSERVATIVE MANAGEMENT VS CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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ABSTRACT

Background: Chronic kidney disease (CKD) is one of the major global health problem, not only contributing to increased mortality and morbidity but also responsible for immense economic strain on the health care system.**Material & Methods**: In present prspective study76 patients of either sex ranging in age from 18 to 70 years. The study was planned to evaluate serum zinc and serum aluminium in CKD patients who are on conservative management and also who are on peritoneal dialysis.. After taking detailed history, clinical examination and hematological investigation was done as mentioned in Performa. **Results:** CRF patients on conservative treatment as Group 2 and CRF patients on CAPD as Group 3 , in that order, a significantly higher aluminum levels in Group 2 and Group 3 relative to healthy controls (group 1) were found (20.2 ± 6.60 Vs 89.8 ± 14.49, $p<0.05$; 20.2 ± 6.60 Vs 73.6 ± 10.18, $p<0.05$) but in both group of CRF patients aluminum level were not significant (89.8 ± 14.49 Vs. 73.6 ± 10.18, $p>0.05$).Serum Zinc levels in Group 2 and Group 3 comparative to healthy controls (group 1) were found significantly lower (94.4 ± 24.72 Vs. 40.9 ± 10.92, $p<0.05$, 94.4 ± 24.72 Vs. 39.3 ± 11.76, $p<0.05$) however in both group of CRF patients Zinc level were not significant (40.9 ± 10.92 Vs. 39.3 ± 11.76, $p>0.05$). **Conclusion:** Patients on CAPD showed markedly reduced concentrations of serum zinc, although a slight reduction was also present in CRF patients. Plasma aluminium concentrations were increased in patients on CAPD and CRF patients.

Key words: Chronic kidney disease, Chronic renal failure, continuous ambulatory peritoneal dialysis.

INTRODUCTION:

Chronic kidney disease (CKD) is one of the major global health problem, not only contributing to increased mortality and morbidity but also responsible for immense economic strain on the health care system. In a review, noted that 53 per cent of deaths in India in 2005 were due to chronic disease. Further it is estimated that 1,00,000 new patients of end stage renal disease (ESRD) enter renal replacement programs annually in India **(1)**. Chronic renal failure (CRF) or chronic kidney disease (CKD) is characterized by a gradual and sustained decline in renal clearance or glomerular filtration over many years resulting in permanent kidney failure. The Kidney Disease Improving Global Outcomes (KDIGO) statement has defined CKD

as either kidney damage or glomerular filtration rate (GFR) of <60 mL/min/1.73 m^2 for ≥3 months **(2)**.As GFR falls to values < 25 % of the normal (i.e.30 ml/min), other solutes that are filtered and either reabsorbed or secreted by the renal tubules may accumulate in body fluids.The KDIGO has classified CKD into five stages from mild renal failure to end-stage renal disease (ESRD) as shown inStage 5 CKD is also called established chronic kidney disease and is synonymous with the now outdated terms end-stage renal disease (ESRD), chronic kidney failure (CKF) or chronic renal failure (CRF)**(3)**.Chronic kidney disease is a worldwide public health problem with an increasing incidence and prevalence, poor outcomes, and high cost. Outcomes of chronic kidney disease include not only kidney failure but also complications of decreased kidney function and cardiovascular disease. Current evidence suggests that some of these adverse outcomes can be prevented or delayed by early detection and treatment. Unfortunately, chronic kidney disease is under diagnosed and undertreated, in part as a result of lack of agreement on a definition and classification of its stages of progression **(4)**.Haemodialysis removes trace elements according to the concentration gradient between plasma and dialysate and reduces their concentration in plasma.Recently, the increased use of continuous ambulatory peritoneal dialysis (CAPD) in the treatment of patients with end stage renal failure has indicated the need to expand these studies of trace elements to patients on peritoneal dialysis**(5)**. Theoretically, peritoneal dialysis could lead to a greater depletion of elements than hemodialysis because most elements are protein bound and considerable peritoneal protein loss can occur. On the other hand, the volume of dialysate to which the patient is exposed is less for peritoneal dialysis than hemodialysis, perhaps reducing the absorption of potentially toxic elements.Therefore, we studied trace element concentrations in the blood of patients on CAPD and compared the concentrations to those in normals, patients with CRF but not on dialysis.

MATERIALS & METHODS

The present study was carried out in IPD & OPD of Nephrology department of S.M.S. Medical College, Jaipuron 76 patients of either sex ranging in age from 18 to 70 years. The study was planned to evaluate serum zinc and serum aluminium in CKD patients who are on conservative management and also who are on peritoneal dialysis. Patients with malignancy, gastro Intestinal disorders, Jaundice and Pregnancy were excluded from the study.Written informed consent by the study subjects was taken and ethical approval was appropriately sought before the study. After taking detailed history,clinical examination, subjects of CKD on conservative management were evaluated for the different stages of CKD on the basis of glomerular filtration rate (GFR) and classified. Subjects with CKD undergoing CAPD were apparently having kidney failure which was evident from their GFR falling below 15 mL/min/1.73 m^2.GFR was estimated using Cockeroft-Gault formula. Serum Urea, Creatinine,Total protein,Albumin,Globulin,Electrolytesestimated and estimation of serum aluminium and serum zinc using Atomic Absorption spectrophotometry(ECIL AAS-4141).The data were analyzed using MS Excel 2010, Epi Info v7 and SPSS v22.

RESULTS

In the present study Mean age for control group 50 $\pm$ 5.10, Mean age for CRF group 50 $\pm$ 12.79 and Mean age for CRF group 53 $\pm$ 9.44 years.We had classified all subjects according to GFR which was calculated by Cockeroft-Gault formula and included in different groups.Healthy persons with normal renal function and without any symptoms and with GFR >90 were included in control group.CKD patients with GFR between 15 and 90 were included in second

group of CKD patients on Conservative treatment.CKD patients with GFR <15 were included in third group of CKD patients on Continuous Ambulatory Peritoneal Dialysis (CAPD).

Table No.-1: VARIOUS PARAMETERS IN ALL SUBJECTS

. PARAMETERS	Controls (Group 1) (n=38) (Mean± SD)	CRF on Conservative T/s(Group 2) (n=38) (Mean ± SD)	CRF on CAPD (Group 3) (n=38) (Mean ± SD)	p-value Gp1& Gp2	p-value Gp1 & Gp3	p-value Gp2 & Gp3
GFR(ml/Min)	116.3±27.37	29.51±12.85	10.6±2.52	< 0.05	< 0.05	**< 0.05**
Age (years)	50±5.10	50± 2.79	53±9.44	>0.05	>0.05	**>0.05**
Zn (µg/dl)	94.4 ± 24.72	40.9±10.92	39.3±11.76	< 0.05	< 0.05	**> 0.05**
Al (µg/dl)	**20.2± 6.60**	**89.8±14.49**	**73.6±10.18**	**< 0.05**	**< 0.05**	**> 0.05**

Baseline characteristics of all studied groups are shown in Table 1. The patients with Chronic renal failure were divided into 2 subgroups i.e. CRF patients on conservative treatment as Group 2 and CRF patients on CAPD as Group 3 , in that order, a significantly higher aluminum levels in Group 2 and Group 3 relative to healthy controls (group 1) were found (20.2 ± 6.60 Vs 89.8 ± 14.49, $p<0.05$; 20.2 ± 6.60 Vs 73.6 ± 10.18, $p<0.05$) but in both group of CRF patients aluminum level were not significant (89.8 ± 14.49 Vs. 73.6 ± 10.18, $p>0.05$).
Serum Zinc levels in Group 2 and Group 3 comparative to healthy controls (group 1) were found significantly lower (94.4 ± 24.72 Vs. 40.9 ± 10.92, $p<0.05$, 94.4 ± 24.72 Vs. 39.3 ± 11.76, $p<0.05$) however in both group of CRF patients Zinc level were not significant (40.9 ± 10.92 Vs. 39.3 ± 11.76, $p>0.05$).

GFR significantly low between all groups towards renal failure side because it was a criterion for grouping of all subjects. (116.3 ± 27.37 Vs. 29.51 ± 12.85, $p<0.05$, 116.3 ± 27.37 Vs. 10.6 ± 2.52 $p<0.05$, 29.51 ± 12.85 Vs. 10.6 ± 2.52, $p<0.05$). Same as urea and serum creatinine were significantly high between all groups.

DISCUSSION

Chronic Kidney Diseases (CKD) has become a major cause of global morbidity and mortality.In India the projected number of deaths due to chronic diseases will rise from 3.78 million in 1990 (40.4% of all deaths) to an expected 7.63 million in 2020 (66.7% of all deaths)**(6)**. In the absence of a renal registry, the exact disease burden of CKD/ESRD in the Indian population cannot be assessed accurately. In the most representative population- based study from North India, using a multistage cluster sampling technique in which serum creatinine and urine samples were examined in every subject studied, the prevalence of CKD stage 3 and beyond was found in 0.79% subjects out of 4,972 examined**(7)**.

In our study of 38 patients who were on CAPD we found a number of important alterations in

trace metal concentrations (zinc and aluminum) in the blood and were able to compare these variations to those seen in similarly studied patients with CRF but not on dialysis and normal controls. The most prominent abnormality in patients in CAPD was a marked reduction in serum concentrations of zinc. A moderate to high reduction of serum zinc was also seen in patients with CRF in compare to controls. However, deficiency of zinc in latter group (CRF) of patients was not to the degree seen in patients on CAPD. Our results were accordance to yonova D et al (2012) onZinc status in patients with chronic renal failure on conservative and peritoneal dialysis treatment and observed that continuous ambulatory peritoneal dialysis influences redistribution of zinc in human organism "per se" **(8)**. In renal failure, patients have disturbances in acid- base balance and blood pH is acidic, therefore low Zinc levels in these patients are believed to be due to the shift of zinc into red cells under acidic conditions**(9)**.In CAPD patients, zinc may work as a marker of nutrition showing beneficial effect on serum iron parameters, blood morphology, lipid profile, and elevated vitamin E concentration. Zinc supplementation is needed for CAPD patients, especially older patients and those requiring higher dialysate volumes**(10)**.

The clinical significance of zinc deficiency in our patients on CAPD is unknown. Weakness, anorexia, and taste disturbances are symptoms not uncommon in patients on CAPD. We were unable to correlate the degree of zinc depletion in our patients on CAPD with the presence of these symptoms. Acrodermatitisenteropathica, a feature of severe zinc deficiency, was not seen in any patient on CAPD.The mechanism(s) by which zinc depletion may occur in CAPD is yet to be studied. Zinc is protein bound in the circulation (zinc to albumin) and loss into the peritoneum is possible. However, a correlation between the quantity of protein in the 24-hr effluent dialysate and serum concentrations of zinc was not demonstrable. The hypothesis for zinc deficiency in CAPD that loss of serum protein through peritoneal dialysis fluid causing zinc deficiency is not proved by our study because zinc concentrations in CRF and CAPD group were not significantly different ($p>0.05$), so possible reason for zinc depletion is renal failure which causing protein loss form kidney.

Patients on CAPD have shown increased plasma concentrations of aluminum but not to the degree seen in patients with CRF. Our results were comparable with Napier M. *et al.* study (11). The highest concentrations in CAPD patients were seen in patients on aluminum hydroxide therapy, strongly suggesting that oral aluminum hydroxide is an important, if not the most important, source of plasma aluminum in these patients. It has been previously shown by others that serum aluminum concentration in patients with CRF and not on dialysis may be correlated similarly with oral aluminum hydroxide therapy. Our patients with CRF were taking considerably larger doses of aluminum hydroxide than patients on CAPD. As we have previously reported, patients starting on CAPD were able to reduce the daily dose of aluminum hydroxide by 60 to 100% of the dose required to control hyperphosphatemia while not on dialysis. Other possible factors causing high aluminum concentrations in patients on CAPD include accumulation before beginning dialysis and the absorption of aluminum from the peritoneal dialysate. Peritoneal dialysate used in our patients certainly contains aluminum often at high concentration. However, the proportion of aluminum that is soluble and thus available for absorption is unknown. On the other hand, loss of aluminum (even protein bound) into the dialysate may be a mechanism for removal of excessive aluminum from the body. Aluminum is particularly bound to albumin and two other smaller molecular weight proteins. A study confirms that the widespread distribution of Aluminum in bone, lungs, liver, and other tissues because of the extensive half-life and tissue distribution of Aluminum in a dialysis-dependent population**(12)**. Therefore, in regard to preventing aluminum toxicity, peritoneal dialysis, particularly CAPD, has a major advantage over hemodialysis.

CONCLUSION

Patients on CAPD showed markedly reduced concentrations of serum zinc, although a slight reduction was also present in CRF patients. Plasma aluminium concentrations were increased in patients on CAPD and CRF patients. Moreover, aluminum retention in CAPD patients not taking aluminum hydroxide [$AL(OH)^3$] therapy was significantly less than in those patients requiring $AL(OH)^3$. The clinical significance of serum zinc depletion in CAPD has not yet been determined. The depletion mechanism of zinc and of the accumulation of aluminium in CAPD patients is currently being investigated. There were some limitations in the present study, sample size was small and it was a hospital based study, so can't represent whole population. There is need to perform such studies on larger and community based population.

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