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Aluminium (Al^{+3}) Levels in Renal Failure Patients

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Abstract

For the study of aluminium levels in renal failure patients on hemodialysis, 40 patients and 40 normal healthy individuals were selected. Blood urea and serum creatinine were determined in order to differentiate between normals and patients. In patients, the values of these two parameters were consistently higher than those in the normals. Statistical analysis also revealed significantly higher levels of aluminum in patients as compared to the normal individuals. Average serum Al^{+3} level in renal patients was 150 μg/L, much higher than the toxic Al^{+3} level (100 μg/L). In view of frequent use of aluminum containing preparation to combat hyper phosphatemia in chronic renal failure patients the management of hyperaluminemia complication become indispensable. Therefore, useful information obtained from experimental study could be judiciously implemented by the clinicians in perspective of ongoing therapeutic management of such patients. So, clinicians must avoid prescribing aluminium preparations to patients with chronic renal failure over longer period. The suggestive alternative for reducing aluminium toxicity is to use non-aluminium compounds for hemodialysis.

Introduction

Aluminium causes toxic effect on various biological systems particularly in chronic renal failure. It is absorbed from the intestine and is excreted mainly through the kidneys, whereas enteric route of aluminium excretion through the feces is the minor one (Coburn and Robertson, 1989). In individuals exposed to high aluminium intake, renal excretion increases many fold than the normal. But the patients suffering form chronic renal failure are unable to excrete the ingested aluminium through non-functioning kidneys, additionally they are administered oral aluminium hydroxide as a phosphate binder (Coburn and Robertson, 1989). Therefore, the patients of chronic renal failure on hemodialysis are more prone to aluminium intoxication (Sasagawa *et al.*, 1993). In persons having dialysis, it can be expressed as several clinical syndromes e.g. encephalopathy (Russo *et al.*, 1992), osteomalacia (Huraib *et al.*, 1993), cholestasis (Klein *et al.*, 1993), renal osteodystrophy (Sugisaki *et al.*, 1991), hypochromic anemia (Von-Bonsdoff *et al.*, 1990) and increased general morbidity and mortality rate (Gluszek and Adamczak, 1993).

Despite its toxic effect, aluminium is used extensively as phosphate binder in hemodialysis patients in Pakistan. This study was, therefore, designed to find out the probable toxic level of serum aluminium in patients having repeated hemodialysis. It will help the clinicians to control the toxic effect of aluminium, if any, by preventing further administration of aluminium in the form of $Al(OH)_3$.

Materials and Methods

Forty patients suffering from chronic renal failure, exposed for more than one hemodialysis, were selected from different hospitals in Faisalabad District. For control, forty normal healthy adults from 20 to 60 years of age were included in the study. Medical history, general physical examination, blood urea and serum creatinine levels were checked to declare the normal healthy control.

Aluminium estimation: 3 ml blood was taken from antecubital vein, allowed to clot for 30 minutes and serum was collected by centrifuging at 400 rpm for 5 minutes. The serum samples were stored at -20°C till further analysis.

For digestion, 0.5 g serum sample was boiled to dense fumes in 5 ml conc. HCl, 5 ml conc. HNO_3 and 7 ml perchloric acid. The sample was re-boiled after addition of 30 ml water, diluted to 100 ml and subjected to analysis pH was adjusted to 2.5-3.0 with the help of 10 percent NaOH soln. Ten ml buffer complex solution [10 ml thioglycollic acid was added to 2.5 percent $CaCO_3$ soln. (dissolved in dd H_2O with the help of conc. HCl and CO_2 was removed through boiling for 1-2 minutes), diluted to 400 ml and pH was adjusted to 4.2. 14 percent glacial acetic acid and 14 percent sodium acetate (hydrated) to one litre] and 10 ml alizarin red S soln. (1 percent was added to the digested solution, diluted to 100 ml, allowed to stand for 2-3 hours and absorbance was noted at 495 nm using spectrophotometer.

Hematological parameters : Blood urea was determined by enzymatic calorimetric method with salicylate (Boehringer Mannheim Gmb H diagnostic; Fawcett and Scott, 1960). Serum creatinine was measured by Jaffe's reaction without deproteinisation; kinetic method (E. Merck 64, 27, Darmstadt Germany Diagnostic-Merck; Helger *et al.*, 1974).

Statistical analysis: The data obtained from the experimental study on monitoring of serum aluminium level in chronic renal failure patients on hemodialysis were subjected to relevant statistical analysis applying ANOVA study, Z-test and correlation analysis.

Results and Discussion

Pertaining to the data recorded on forty patients with chronic renal failure and multiple hemodialysis treatment, it became evident that the two parameters of the study such

Table 1: Blood urea, serum creatinine, serum aluminium mean ± SD of 40 patients and 40 normals in various age groups.

Age groups	Patients			Normals		
	Blood urea mg/dl	Serum creatinine mg/dl	Serum aluminium μg/L	Blood urea mg/dl	Serum creatinine mg/dl	Serum aluminium μg/L
20-30	181.45 ± 59.32	11.055 ± 3.96	135.44 ± 89.99	28.00 ± 7.90	1.35 ± 0.19	92.33 ± 39.39
30-40	152.66 ± 45.16	8.53 ± 2.11	138.02 ± 90.11	24.97 ± 3.34	1.26 ± 0.196	69.66 ± 39.56
40-50	142.12 ± 30.11	8.84 ± 2.62	109.53 ± 66.50	26.75 ± 6.20	1.23 ± 0.199	76.89 ± 28.45
50-60	116.55 ± 33.06	8.29 ± 3.71	172.27 ± 78.74	29.70 ± 7.32	1.26 ± 0.259	72.08 ± 19.34

In each group of study 10 patients and 10 normals were taken.

Table 2: Table 2 x 2 for relative risk and odd's ratio

	Aluminium level		Crossing limit (100 μg/L)	
		+	−	
Factor patient on haemodialysis	+	28 (a)	12 (b)	40 (a + b)
	−	8 ©	32 (d)	40 (c + d)

General formula

$$P.R. = \frac{a}{(a+b)} \times \frac{(c+d)}{c} \times \frac{28}{40} \times \frac{40}{8} = 3.5$$

$$\text{Odd ratio} = \frac{ad}{bc} \times \frac{28 \times 32}{12 \times 8} = 9.3$$

This table shows that the patients on hemodialysis are at a relative risk of 3.5 times more the normals with respect to aluminium toxicity.

as blood urea and serum creatinine levels were consistently elevated than the upper limit of the normal range of corresponding value. As documented in the relevant literature, these two parameters have been generally recognized as clinical evidence of renalpathy. Therefore, recording of these two parameters to select the typical renal failure is well justified for the experimental study.

Referring to the data given in table 1 on serum aluminium level renal patients on haemodialysis, 28 out of 40 (70 percent) patients showed abnormally high level (> μg/L). Similarly majority of the normal individuals (80 percent) exhibited aluminium concentration level within normal range (< 100 μg/L). It was, however, remarkable to note that 30 percent of such patients had the serum aluminium concentration within the base line level of 100 μg/L. still more surprisingly 20 percent of the normal individuals were found to have serum aluminium level above the base line level.

Analysis of variance study on the data recorded for three parameters of blood urea, serum creatinine and serum aluminium level in chronic renal failure patients as well as clinically individuals ranging from 20-60 years of age revealed that for within each age group, the observations recorded were found statistically significant at 0.05 level of probability. This means that within each group, the data recorded on all three parameters of the study were at lower level for the normal individuals. The statistical evaluation of the data procured for all the parameters of the study on forty patient and forty healthy individuals through application of Z-test indicated consistently high significant difference between values recorded for each parameter o the study comparing healthy and morbid individual together. The logical implication of this statistical findin strengthens the justification for selection of stud parameters in association with relevant clinically findin recorded. The third analytical fact of the data evaluatio was met through correlation studies made simultaneousl The correlation analysis yielded an almost perfect (99 correlation between the parameters selected f experimental studies. Thus fare degree of association higher level of serum aluminium was found with abnorm values of blood urea and serum creatinine in chron renalpathy.

Patients with higher aluminium concentration were receipt of aluminium preparations during hemodialysis w frequency of hemodialysis within 1 to 158. Simi observation was made by Gluzek and Adamczak (19 who reported toxic level of aluminium leading encephalopathy, osteomalacia and microcytic anemia. frequency of hemodialysis was very low in twelve patie and their Al^{+++} level was also within the base line le This observation has also been confirmed by literat (Sasagawa *et al.*, 1993; Klein *et al.*, 1993). Several kn cellular effects of aluminium are: inhibition of enz related replication (Marquis and Lerrick, 1982), interfer with the enzymatic activity of alkaline and acid phospha (Lieberherr *et al.*, 1982), acetyl cholinesterase (Marqui Lerrick, 1982), hexokinase (Trapp, 1980) and calmo (Seigle and Haug, 1983).

Average serum aluminium level in renal patients was found to be 150 μg/L (maximum level even goes upto 293.17 μg/L). As the aluminium toxicity occurs if the aluminium level reaches upto 100 μg/L, the patients in the present studies were having risk of Al^{+3} toxicity. Table 2 shows that the patients on hemodialysis are at a relative risk of 3.5 times more than normals w.r.t. Al^{+3} toxicity (Martin *et al.* 1987). The suggestive alternative for reducing aluminium toxicity is to use non-aluminium containing compounds for hemodialysis. Various non-aluminium preparations have been tried universally for hemodialysis of chronic renal failure patients with successful appeasement of serum aluminium level. One such preparation is the oral dosage of calcium carbonate (Sawyer *et al.*, 1989) that effectively controlled plasma phosphate and calcium concentration and reduced hyper-parathyrodism. Calcium acetate was reported to be even more effective than calcium carbonate (Pflanz *et al.*, 1994) for management of hyper phosphatemia in many chronic dialysis patients. Other recuperative therapies including hemofiltration technique (Sulkova *et al.*, 1991) and Desferrioxamine therapy (Davenport and Ahmad, 1988) were found safe and effective methods for the treatment of aluminium intoxication and accumulation in patients with chronic renal failure. Anti-aluminium compounds like ramitidine (Rodger *et al.*, 1991) and a chelator compound such as 1,2-dimethyl-3-hydroxypyrid-4-one (Kontoghiorghes *et al.*, 1994) also decreased the plasma aluminium levels in aluminium-overload patients on hemodialysis.

It is concluded form the present studies that the management of hyperaluminemia complications become indispensable through the frequent use of aluminium containing preparations to combat hyper-phosphatemia in chronic renal failure patients. Present information can be judiciously implemented by the clinicians in perspective of on going therapeutic management of such patients.

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