Determining Serum Zinc and Magnesium Levels in Hemodialysis Patients Could be Helpful for Clinicians

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Abstract Trace element determination is requested rarely for critically ill patients in Iran, due to the underestimation of the trace element determination by Iranian physicians. The aim was to compare the levels of Zn and Mg in a group of hemodialysis patients and normal individuals. This study shows that trace element determination is helpful for management of hemodialysis patients. Fifty-three hemodialysis patients and 51 control individuals were randomly analyzed for Zn and Mg serum levels. Comparison of before or after dialysis and with normal individuals was done and receiver operating characteristics (ROC) curves were plotted to evaluate the analytical sensitivity and specificity of Zn and Mg determination. Confidence interval for all statistical methods was 95 %. Zinc serum levels were decreased after hemodialysis insignificantly ($P = 0.201$) but Mg levels were decreased significantly ($P = 0.000$). Both Zn and Mg levels, before and after hemodialysis were meaningfully lower than normal controls ($P < 0.05$). ROC analysis showed that the area under the curve was high for Zn levels

both before and after hemodialysis but it was high for Mg only before hemodialysis. Current study shows that serum Zn and Mg measurements can have clinical importance. Both before and after hemodialysis, serum Zn = 297.5 µg/L and Mg = 2.295 µg/L are proposed as cut-off values with about 90 % specificity, for monitoring of these two element in hemodialysis patients. It is suggested that clinicians consider the measurement of these trace elements for hemodialysis patients routinely or periodically as clinical chemistry tests.

Keywords Trace elements · Renal dialysis · Sensitivity and specificity · Zinc · Magnesium

Introduction

Determination of essential trace elements is important for hemodialysis patients. It is because of treatment interventions, hemodialysis facilities and patient's life style [1–3]. Unfortunately, such important monitoring approach is not attended for Iranian hemodialysis population, routinely or at least periodically. Hemodialysis is a frequent interventional treatment method in Iran; because of high prevalence of chronic kidney disease (CKD) [4]. It is reported that hemodialysis results into the loss of some trace elements such as manganese, selenium and zinc [2]. On the other hand, the importance of trace elements measurement for monitoring the effect of long-term hemodialysis on the trace elements blood level, is suspicious. Iranian physicians hesitate to order trace element determination for hemodialysis patients. Two main causes of such hesitation may be: (1) Limitation of medical laboratory facilities, such as atomic absorption apparatus in most Iranian diagnostics laboratories; (2) Physician's unfamiliarity with or

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underestimation of the importance of trace elements measurement for hemodialysis patients. Investigators have shown that determination of trace elements for breast cancer patients may have clinical importance [5–8]. Moreover, clinical significance of trace element determination was shown for hemodialysis or critically ill patients [1, 9–12]. In the current study the status of serum zinc (Zn) and magnesium levels have been investigated in a group of Iranian hemodialysis patients and a group of normal individuals to evaluate the usefulness of Zn and Mg measurement in end stage renal disease (ESRD) patients.

Materials and Methods

Fifty-three hemodialysis patients and 51 control individuals were randomly analyzed for Zn and Mg serum levels. Before and after hemodialysis, the samples were gathered from hemodialysis patients or normal individuals from Qaemshahr city of Mazandaran province, North of Iran. All cases and controls fulfil the consent form of study. Cases and controls were matched for age range that was between 23 and 79 years old. Serum samples were separated and analyzed using atomic absorption technique and according to the instruction of apparatus (Shimatzu AA670G Atomic Absorption; Japan). Wavelengths, using air-acetylene flame were $W_{Zn} = 213$ nm and $W_{Mg} = 279$ nm.

Statistical Analysis

Data were analyzed using IBM Statistical Package for Social Sciences (version 20; SPSS). Distributions of data were not normal; then, for comparing before and after

hemodialysis serum levels of Zn and Mg Wilcoxon test, and for comparing case and control's, Mann–Whitney test were used. Correlation calculation was performed between before and after hemodialysis using Pearson correlation (R-value). Receiver operating characteristics (ROC) curves were plotted to evaluate analytical sensitivity and specificity of Zn and Mg determination in hemodialysis patients. The area under the curve (AUC) was calculated with 95 % confidence interval (CI) to detect the best cut-off value. The optimal cut-off values which will be presented involves both highest sensitivity and specificity.

Results

Both male and female were included in the study. The case group was consisting of 25 males and 28 females while 23 males and 28 females were included in the control category. Table 1 shows descriptive statistics of Zn and Mg serum levels. Zn serum levels were decreased after hemodialysis, but not significantly (CI 09.5; $P = 0.201$). Mg serum levels were decreased significantly after hemodialysis (CI 0.95; $P = 0.000$). Comparison of serum Zn or Mg concentrations of cases, both before or after hemodialysis, with control individuals, shows significant differences (with 0.95 CI: for Zn before hemodialysis $P = 0.003$; for Zn after hemodialysis $P = 0.000$; for Mg before hemodialysis $P = 0.000$; for Mg after hemodialysis $P = 0.041$) (Table 1). The correlation of Zn serum concentrations before and after hemodialysis was high (R-value = 0.852; $R^2 = 0.726$; CI 0.99; $P = 0.000$); it was also true for Mg serum concentrations (R-value = 0.568; $R^2 = 0.322$; CI 0.99; $P = 0.000$). ROC analysis showed

Table 1 Wilcoxon analysis for comparison of zinc (Zn) and magnesium serum concentrations of cases before and after hemodialysis: Mann–Whitney statistical analysis used to comparison of cases and controls serum levels of Zn and Mg

	Statistical indices	Zinc (before) N = 53	Zinc (after) N = 51	Mg (before) N = 53	Mg (after) N = 53
Case	Median ($\mu\text{g/L}$)	283	174	2.84	1.890
	Minimum ($\mu\text{g/L}$)	2	14	1.570	1.300
	Maximum ($\mu\text{g/L}$)	3578	1524	9.810	9.090
	<i>P</i> value for comparison of before and after hemodialysis	0.201		0.000	
	Statistical indices	Zn		Mg	
Control	Median ($\mu\text{g/L}$)	127		2.080	
	Minimum ($\mu\text{g/L}$)	36		1.000	
	Maximum ($\mu\text{g/L}$)	346		3.160	
Comparison	Before hemodialysis	After hemodialysis		Before hemodialysis	After hemodialysis
<i>P</i> value for comparison of case and control categories	0.003	0.000		0.000	0.041

Fig. 1 ROC curve of Zn and Mg serum levels before and after hemodialysis

that the AUC for Zn concentrations before and after hemodialysis was equal to 0.680 ($P = 0.002$) and 0.742 ($P = 0.000$), respectively. AUC for Mg concentrations before and after hemodialysis was equal to 0.910 ($P = 0.000$) and 0.348 ($P = 0.009$), respectively (Fig. 1). Determination of cut-off values for the measurement of Zn and Mg before and after hemodialysis helps to evaluate the clinical significance of such measurement. According to ROC analysis when at least considering 90 % specificity, the cut-off and sensitivity values would be as shown in Table 2.

Discussion

In total, current study proposes the measurement of Zn and Mg for hemodialysis patients. Hemodialysis affects the blood levels of Zn and Mg meaningfully. In addition, their measurement could be important for clinical monitoring of Zn and Mg blood levels. Comparison of Zn and Mg levels between case and control groups showed that these essential trace elements have higher concentrations in cases than control individuals. Hemodialysis decreased serum Zn and Mg levels. Good correlation between before and after hemodialysis confirmed the reductive effect of hemodialysis on the serum levels of both metal elements. However, such reduction was not so impressive in a way that resulted to the

normal category values (compare P -values of Table 1). ROC analysis confirms that measurement of Zn and Mg in hemodialysis patients could be sensitive and specific. According to AUCs, measurement of Zn, both before and after hemodialysis, is of worth but Mg measurement is only worthy before hemodialysis. Considering 90 % specificity of Zn and Mg measurement for hemodialysis patients the cut-off values would be 297.5 and 2.295 $\mu\text{g/L}$, respectively. The best sensitivity value was obtained for Mg measurement before hemodialysis. The lowest sensitivity value was obtained for Mg measurement after hemodialysis.

Sensitivity and specificity estimation of trace element measurement, for monitoring of disease status, has been proposed or evaluated by some researchers. Kuo et al. [6] recommended the application of ROC method for determination of trace elements measurement in normal and malignant breast cancer persons. Silva et al. [5] have used ROC analysis for essential or trace elements measurement in breast cancer patients and propose their measurement as prognostic or even tumor biomarkers. The current study showed that Zn and Mg had higher serum levels in hemodialysis patients than normal individuals, significantly. Then, it is probable to use their concentration measurement as the kidney function failure or insufficiency biochemical markers. Anyway, such suggestion needs more confirmatory investigations. The cut-off values which are presented in the current study could be helpful as a measure for comparison and critical decision in clinical investigations.

Table 1 shows that Zn concentration value before dialysis was lower than after dialysis (2 against 14 $\mu\text{g/L}$). Such finding may emphasize that hemoconcentration could occur owing to dialysis. Nevertheless, this effect is not so considerable and hemodialysis has mostly a reductive effect on Zn serum levels (compare median and maximum Zn levels before and after dialysis; Table 1).

Some investigators have reported a reduction [13, 14] and others acute toxicity or increased levels of essential trace elements in hemodialysis patients [15–17]. Such discrepant discussion was present also in a review article by Tonelli et al. [2]. Reported serum levels of Zn and Mg of normal and hemodialysis patients from different parts of the world are variable [13]. This evidence suggests these important points: (1) Normal serum/blood levels of trace elements should be determined for normal/patient

Table 2 Cut-off values and sensitivity of Zn or Mg measurement when considering at least 90 % specificity

Essential element	Cutoff value ($\mu\text{g/L}$)	Sensitivity (%)	Specificity (%)
Zn before hemodialysis	297.5	49	90
Zn after hemodialysis	297.5	41.2	90
Mg before hemodialysis	2.295	84.3	90
Mg after hemodialysis	2.295	15.7	90

population of any country; (2) Routine determination of trace elements should be considered in the clinical evaluations by physicians, especially in countries such as Iran; (3) Determination of trace elements such as Zn and Mg, maybe of worth before or after dialysis and could be an indicator of trace element imbalance status.

Most cited studies in review articles are focused on the importance of zinc, copper, manganese, aluminum, lead and so forth [2, 18]. However, a few studies on hemodialysis considered the toxicity or essentiality of magnesium. Kasama declares that investigations are needed to clarify the importance of Mg in hemodialysis patients [18]. The present investigation addressed this clarification, at least in a group of Iranian population.

Then, it could be concluded that the measurement of Mg is of worth for hemodialysis patients, especially before dialysis. Periodical monitoring of trace metals could be helpful for the evaluation of hemodialysis patients considering trace elements toxicity or loss. We intensively declare the importance of trace elements measurement for Iranian hemodialysis patients. In the current study, the clinical significance and some critical cut-off values were presented that may be helpful for physicians to make decision about Mg and Zn blood levels in hemodialysis patients.

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Compliance with Ethical Standards

Conflict of interest All authors declare that there is not any conflict of interest about their role in the current study.

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