ORIGINAL ARTICLE

Malondialdehyde, Selenium & α-Tocopherol in Kidney Stones

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ABSTRACT

Objectives: To determine role of α-tocopherol and selenium and evaluate malonadehyde in calcium stone of kidney.

Study Design: Case-control study.

Place & Duration: Department of Biochemistry, Isra University and Hi-tech Laboratory University of Sindh, Jamshoro July 2013- January 2014.

Material & Methods: Malondialdehyde (MDA), α-tocopherol (α-TP) and Selenium were measured by using spectrophotometeric methods by commercially available kits.

Reslut: Mean± SD of MDA was noted as 26.033±7.8417µmol/l versus 1.882±0.621µmol/l in the cases and controls (p=0.001). The α-tocopherol (α-TP) was low in concentration in the cases compared to controls i.e. 0.38±0.146mg/dl vs. 1.06±0.169 mg/dl (p=0.001). Selenium in cases and controls was found as 38.4± 14.10µg/l vs. 84.5±10.22µg/dl respectively, it showed severe deficiency in cases. (p=0.001).

Conclusion: Present study reports low levels of α-tocopherol and selenium in the subjects with renal stone, and lipid peroxidation plays major role in the pathogenesis of calcium stone of kidney.

Keywords: Selenium, α-tocopherol, Malondialdehyde, Renal Stones

INTRODUCTION:

Selenium is an essential mineral, and a natural antioxidant which delays the oxidation of polyunsaturated fatty acids & preserves elasticity of tissues[1]. Selenium in the form of seleno-cysteine, is a part of the active center of several seleno-enzymes which have antioxidant function e.g., glutathione peroxidase, deiodinases and thioredoxin reductase. Selenocysteine is tightly regulated and any significant modification or change of selenium status would lead to changes in the etiology of seleno-enzymes and thus have important consequences on the susceptibility of tissues to oxidative stress.

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During oxidative stress, free radical chain reaction resulting in lipid peroxidation may occur. α-tocopherol (α-TP), the most important lipid soluble antioxidant protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction[2,3].

The chemical process of lipid peroxidation is mostly initiated by a free radical or any other reactive oxygen species (ROS), which abstracts or removes a hydrogen atom from the carbon chain of an unsaturated fatty acid, leaving a carbonyl radical[4]. This can bind an oxygen molecule, yielding a peroxyl radical. Peroxyl radicals so produced are themselves sufficiently reactive to abstract or remove further hydrogen atoms from an adjacent fatty acid, resulting in the formation of a lipid peroxide. Lipid peroxidation in this way propagates as a chain reaction in which a single initiating free radical can result in peroxidation of large number of unsaturated fatty acid molecules[5]. Lipid peroxidation thus causes functional irregularity of several cellular organelles. Not only can this effect the physical stability of membranes, but the lipid peroxides are themselves unstable and breakdown to yield a range of toxic aldehydes

range of toxic aldehydes that are capable of damaging membrane proteins[6]. Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxide in cells and the serum level of MDA is used as a biomarker to measure the level of oxidative stress in an organism[7].

Oxidative stress, increased lipid peroxidation, and decreased activity of antioxidant system are now recognized to contribute in the pathogenesis of calcium oxalate containing kidney stones. Numerous reports on analysis of stones confirm calcium oxalate to be the most common constituent of kidney stones in Pakistani adults and the western world[8]. The main reason for calcium oxalate to be the most common constituent of kidney stones is its relative insolubility in urine as supersaturation, crystal nucleation, and crystal adherence to the surface of renal epithelial cells[9]. Although tubular fluid in the distal nephron is supersaturated with respect to calcium oxalate ions, it is not known as to why in some individuals calcium oxalate crystals are retained and form the nidus for stones formation. There is strong evidence that tubular dysfunction or damage is involved in binding of calcium oxalate crystals and subsequent pathology[10]. The rationale of present study was to evaluate antioxidants selenium and α-TP and lipid peroxidation indicator, the malonadehyde in kidney stone subjects.

MATERIAL & METHODS:

This study was carried out on 80 cases, in the department of Biochemistry, Faculty of Medicine and Allied Medical Sciences, Isra University and Hi-tech Laboratory University of Sindh, Jamshoro. Case-control studies are used to identify factors that may contribute to a medical condition by comparing subjects who have that condition (the 'cases') with the subjects who do not have the condition but are otherwise similar (the 'controls'). Adult diagnosed cases of kidney stones were included, while subjects having major systemic diseases predisposing to renal stone formation were excluded from the study protocol. 80 cases consist of 40 patients & 40 control subjects.

Five ml of fasting venous blood sample was drawn from ante-cubital vein during luteal phase. The blood was centrifuged at 4000rpm for ten minutes and serum obtained was frozen at -20°C. The serum was used for estimation of Malondialdehyde (MDA), α-TP and Selenium. Malondialdehyde (MDA), α-TP and Selenium were measured by using spectrophotometeric & EIA methods by commercially available kits. Informed written consent was sought from the participants. The data was recorded on a pre-structured proforma. Data was analyzed on SPSS version 21.0. The continuous and categorical variables were analyzed by student`s t-test and chi-square test respectively. The results were presented as mean±S.Dandfrequency(%) respectively. Pearson`s correlation was used to determine association between variables. The significant p-value was taken at = 0.05.

RESULTS:

Demographic characteristics of patients with calcium kidney stones and control subjects are presented in tables I and II respectively. Table II shows gender wise distribution of cases and control subjects. The data shows that 72% of calcium containing k dney stone patients were males. Serum levels of MDA, α-TP and Selenium are shown in Table I and graph 1. Highly significant difference ($p < 0.001$) in the mean serum MDA levels between the patient group (26.033± 7.8417µmol/l) and the control group (1.882± 0.621µmol/l) were found. In contrast to MDA, levels for α-TP in serum were detected to be lower in the patient group (0.38±0.146mg/dl) than in the control group (1.06±0.169 mg/dl) and the difference in the mean values of the two groups were found to be statistically significant ($p<0.001$). Similarly, when serum selenium levels were compared between two populations, selenium levels were found to be significantly lower ($p<0.001$) in the patient group (38.4±14.10µg/l) as against the control group (84.5±10.22µg/dl).Pearson Correlation co-efficient between MDA & α-TP levels in the calcium stone patients was non-significant; r=0.07 and p=0.51 as shown in scatter

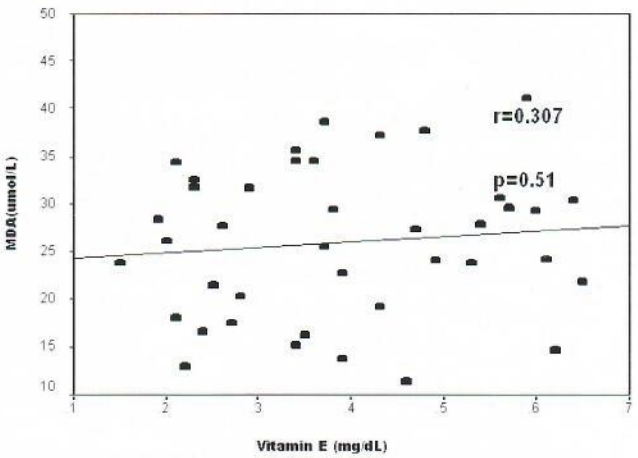
graph 1, similarly MDA and selenium revealed non-significant; r=0.03 and p= 0.82 as shown in scatter graph 2.

Table-I: Demographics characteristics of study population

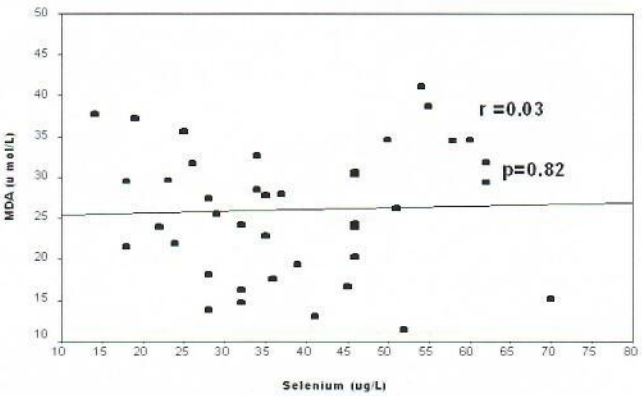
	Patients(n=40)	Controls(n=40)	p-value
Age	34+9.5	35+7.5	0.082
Male	29(72.5%)	24(60%)	0.063
Female	11(27.5%)	16(40%)	0.071

Table-II: Serum MDA, α-TP & selenium concentrations among study population

	Patients(n=40)	Controls(n=40)	p-value
Malonaldehyde (umol/L)	26.033±7.841	1.882±0.621	0.001
a-tocopherol (mg/dl)	0.38±0.146	1.06±0.169	0.01
Selenium (ug/l)	38.4±14.10	84.5±10.22	0.01



Graph 1: Scatter diagram showing correlation of malonadehyde & α-tocopherol



Graph 2: Scatter diagram showing correlation of malonadehyde & selenium

DISCUSSION:

In the present study, calcium containing kidney stones were found to be more common in males than in females. All reports available in literature show that kidney stones predominate in male. The findings are in keeping with previous studies[11,13]. A possible mechanism for high incidence of calcium containing kidney stones in adult males could be increased level of blood testosterone, which cause increased production of oxalate by liver from its endogenous precursors[11-14]. Excessive production of oxalate may cause supersaturation of urine that may lead to crystallization and hence stone formation. This is suggested because oxalate has no metabolic role in human body and is removed from the body via filtering mechanism of the kidneys[14,15], Calcium oxalate, the major component of calcium containing kidney stones has been shown by various investigators to induce free radical generation which results in peroxidation injury to renal epithelial cells[16,17].

Age group of early 20's and late 40's is considered to be most active period in life. Increased physical activity in this age group has been shown to induce several fold increase in plasma xanthine oxidase level that in turn could induce oxidative stress to filtering renal tissue. Oxidative stress, no doubt is a common source of cell injury and results from excessive production of reactive oxygen species[18].

In this study, a significant increase in serum MDA levels (p=0.001) was seen in patient group compared to control group. This finding is in accordance with the reports by other investigators[18,19].

Increase in serum MDA levels could be due to increase in oxidative stress in kidney's caused by increased production of reactive oxygen species or decrease in antioxidant defense mechanism and vice-versa as has been reported previously[18,19]. The α-tocopherol is a well-known chain breaking antioxidant, which protects the cell membranes from oxidative stress[18,19].

In present study significantly lower levels of serum α-tocopherol (p=0.001) and of selenium

(p=0.001) were found in calcium containing kidney stone patients compared to control group subjects. The finding suggests a positive role of lipid peroxidation in kidney stone formation and is accelerated by concomitant deficiencies of antioxidants like a-tocopherol and selenium.

CONCLUSION:

Present study reports the low levels of α-tocopherol and selenium and higher malonaldehye in kidney stone patients. It is concluded that lipid peroxidation owning to decreased antioxidants and / or increased oxidative stress do play a major role in the pathogenesis of kidney stone formation. Further studies are recommended to elucidate the underlying mechanism of lipid peroxidation and antioxidants for proper conclusion.

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