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Original Research Article

Glutathione Peroxidase, Superoxide Dismutase, and Malondialdehyde Comparison in Urolithiasis Patients before and After Surgery

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Abstract:

Background: Clarifying the pathogenesis of urolithiasis, which affects over 10% of the population in affluent nations, has been the focus of considerable efforts in recent years. As of right now, a number of studies have suggested that free radical oxidation, which is triggered when calcium oxalate crystals interact with renal tubular epithelial cells, plays a major part in the pathophysiology of oxalate urolithiasis, the most prevalent of the active forms of oxygen generated in the kidney. In the current study, the pre- and post-operative oxidant and antioxidant status of patients with complex urolithiasis was evaluated. When complex urolithiasis is surgically treated, oxidative stress is reduced and the capacity for antiradical and antiperoxidative protection is increased.

Aim: Comparative analysis of glutathione peroxidase, superoxide dismutase, and malondialdehyde in patients with urolithiasis

Material and Methods: The study was carried out in the Department of Surgey, the present study was conducted on 50 patients of urolithiasis admitted in the indoor surgical urology ward for surgery.

Results: Malondialdehyde plasma levels have been found to be significantly raised ($p<0.0001$) in pre-operative patients (12.71±1.65 nmoles/ml of plasma) as compared to the post-operative of volunteers (9.00±1.13 nmoles/ml of plasma). Table 1 also shows that there was a significant increase in the values of superoxide dismutase in pre-operative group (5.99±0.91 µmol/l RBC lysate) as compared to the post-operative group values (4.10±0.96 µmol/l RBC lysate).

Conclusion: Enhanced SOD can lessen renal tubular epithelial cell injury and the production of calcium oxalate crystals. The found negative association between MDA and GPx and the positive correlation between MDA and SOD suggest that lipid peroxidation plays a role in the pathophysiology of urolithiasis.

Keywords: Urolithiasis, SOD, MDA, Glutathione Peroxidase and Calcium Oxalate.

Introduction

The history of urolithiasis, often known as stone disease, may extend back to human history. The archaeological examination has clearly shown that stone sickness was a common ailment among prehistoric humans.

In 1901, Sir Grafton-Elliot Smith found one of the oldest known cases of urinary calculus in the pelvic bones of a young man from upper Egypt who lived during the pre-dynastic (7000-3100 BC) era. Numerous such examples can be found among the thousands of mummies that have been unearthed, as well as in other comparable archeological discoveries. Urinary calculi have become more common within the past century. [1,2] The prevalence of stone disease is increasing for a variety of causes, such as dietary changes brought about by lifestyle changes, the use of several chemicals in medications and other preservatives, pollution, and other related circumstances. [3]

Epidemiology of Urolithiasis

Stone sickness has been documented in the literature at various points throughout history, including data derived from archaeological digs. But as socioeconomic conditions have improved in many communities across the globe, the prevalence of stone disease has gone up.

This claim is supported by the observation that, during World War II, when there was a greater degree of poverty and a shortage of food, there was a discernible decline in the incidence of urinary calculi in addition to a decline in the incidence of cardiovascular disorders like MI. [4]

In cases of renal failure, increased oxidative stress and decreased antioxidants alter the composition of lipoproteins, causing low density lipoproteins to oxidize more quickly and hasten the development of atherosclerosis. [5] LDL can be oxidized by a

variety of artery wall cells, including macrophages, vascular smooth muscle cells, and endothelial cells. Lipoxygenases can also trigger this process. [6,7] Thus, in cases of renal failure, cardiovascular disease is the primary cause of death. In addition to being cytotoxic to cells and chemotactic to circulating monocytes, oxidized low-density lipoprotein (LDL) also produces a variety of cytokines and other growth factors, promotes platelet aggregation, and obstructs EDRF. [8] Additionally immunogenic, oxidized low-density lipoprotein (LDL) can produce autoantibodies and kill cells.

These oxidative species, which have a molecular weight of less than 3000 Daltons and are removed with dialysis, have been identified in chronic renal failure.As per the specialized literature of today, it is widely believed that active forms of oxygen produced in the kidneys as a result of oxidative free radicals activated by calcium oxalate crystals interacting with renal tubular epithelial cells play a major role in the pathogenesis of oxalate lithiasis, the most common type of the condition. This theory has been supported by direct and indirect evidence that has been shown in vivo in animal experiments and clinical observations, as well as in vitro in cell cultures that mimic different nephron units. [9] The recurrence of RL is largely due to the pathogenesis of chronic calculus pyelonephritis, which is characterized by the stimulation of cellular oxidation processes and the production of free radicals. The pathophysiology of CPN and the chronic process and recurrence of urolithiasis are both significantly influenced by immunosuppression of immunological state, as numerous authors have shown. [10]

Aim

Comparative analysis of glutathione peroxidase, superoxide dismutase, and malondialdehyde in patients with urolithiasis

Material and Methods

The study was carried out in the Department of Surgery, Division of Urology. The present study was conducted on 50 patients of urolithiasis admitted in the indoor surgical urology ward for surgery at the tertiary care Hospital and Research Center. The samples were taken before and after surgery to investigate the biochemical parameters such as MDA, SOD and GPx.

Statistical Analysis: For analysis of the data the mean values were calculated in each of the groups along with the standard error/deviations for the different parameters. The students't' tests were employed for finding out the statistical significance (p-value) of the results between different groups.

Results

Table 1: Comparison of MDA, SOD and GPx Levels in Post-operative group and post-operative group

Parameters	Post-operative group	Pre-operative group	P-Value
MDA (nmol/ml)	9.00±1.13	12.71±1.65	P < 0.0001
SOD (µmol/L)	4.10±0.96	5.99±0.91	P < 0.0001
GPx (µmol/L)	6.32±0.93	3.16±0.79	P < 0.0001

The pre-operative group patients have shown a marked increase in plasma MDA levels. The different values of the malondialdehyde levels in plasma along with their SD values have been given in table 1. Malondialdehyde plasma levels have been found to be significantly raised ($p<0.0001$) in pre-operative group (12.71±1.65 nmoles/ml of plasma) as compared to the post-operative group of volunteers (9.00±1.13 nmoles/ml of plasma).

Table 1 also shows that there was a significant increase in the values of superoxide dismutase in pre-operative group (5.99±0.91 µmol/l RBC lysate) as compared to the post-operative group values (4.10±0.96 µmol/l RBC lysate). A significantly decreased value of glutathione peroxidase has been observed in pre-operative group (3.16±0.79 µmol/ml of haemolysate) as compared to the post-operative group (6.32±0.93 µmol/ml of haemolysate) as has been depicted in Table 1.

Discussion

According to several findings, renal tissue cells—as opposed to hepatocytes and other cells—are far more vulnerable to the harmful effects of free radicals. [11,12] Based on estimates of 8-OHdG (ROS-induced damaged DNA product) from both in vitro and in vivo experiments employing renal tubular epithelial cell culture line (OK CRL-1840 cells), these observations have been made. [13,14] In the current investigation, we have noted an increase in free radical levels as shown by rising MDA values, an oxidative hazardous metabolite, and falling levels of glutathione peroxidase, an antioxidant that serves as the body's first line of defense. [15] It follows that the generation of free radicals in urolithiasis is likely to cause damage to the endothelial cell lining of the tubules, creating a "nidus" for the settling and subsequent growth of insoluble calcium oxalate salts or other substances of that kind.

Table 1 make it clear that, in comparison to healthy human volunteers, there is a considerable increase

in malondialdehyde levels in urolithiasis patients. More OH* free radicals are created, which damages the lipid bio membrane, mostly polyunsaturated fatty acids (PUFA), creating lipid hydroperoxide, which in turn forms MDA. This is the reason for the rise in MDA levels. A drop in MDA levels indicates a reduction in the production of OH* free radicals as well as reduced damage to the bio membrane, which results in the formation of hazardous metabolites called hydroperoxides. This OH* free radicals are generated from the superoxide anion, O*2 free radicals. Superoxide dismutase (SOD) (EC 1.15.1.1) activity was assessed using the methods outlined in the modification V. Gudumac and coauthors16 by Аубинина Д. Е. and Матяшин Б. Н. The technique relies on SOD's suppression of the nitroblue tetrazolium salt's reduction in the system that includes NADH and phenasinmetasulphate. Formazan with a blue hue is created when NBT is reduced. The intensity of the hue corresponds exactly to the enzyme activity measured in milliliters of serum.

One important enzyme in the removal of superoxide radicals is SOD. As the initial line of defence against ROS, it is employed to scavenge ROS and hasten the mutation of superoxide anion radicals, protecting cells from the hazardous byproducts of aerobic metabolism. Prior work boosted SOD activity to swiftly remove excess ROS for host survival and normal cell function in order to maintain redox equilibrium and build defences against ROS disruption. [17] Kang J et al. 2020 [18] Compared with the Post-operative group, the stone model group showed a significantly higher renal / body mass index with a higher expression of autophagy-ERS- and apoptosis-related proteins LC3B, BECN1, GRP78, CHOP, Bax and Caspase-3; and low levels of p62, bcl-2 protein, and SOD.

Glutathione peroxidase values have been found to be decreased in Pre-operative patients (table 1) as compared to the Post-operative patients. This reflects that there has been a better utilisation or decreased need of the enzyme in the diseased condition. Mahmoud RH et al.2009 [19] found in patients with urolithiasis, the mean serum MDA level increased as compared to the urolithiasis group, and there was a substantial gap between serum MDA in the control group.

Atasayar S. and coauthors' [20] approach was followed in order to assess the level of malonic dialdehyde (MDA). The technique relies on measuring the trimetinic colored complex that results from MDA's interaction with thiobarbituric acid using spectrophotometry.

The formula for calculating MDA content (micromol/l) uses the molar absorption coefficient, which is 1.56 × 105 mol • cm-1.

Conclusion:

The found negative association between MDA and GPx and the positive correlation between MDA and SOD suggest that lipid peroxidation plays a role in the pathophysiology of urolithiasis. Enhanced SOD can lessen renal tubular epithelial cell injury and the production of calcium oxalate crystals.

References

1. Anderson DA. Historical and geographical differences in the pattern of incidence of urinary stones considered in relation to possible aetiological factors. In: Renal Stone Research Symposium. Eds. A Hodgkinson and BEC Norden NY. ChurchilI Livingstone Inc. 1969.
2. Borghi L, Ferretti PP, Elia GF, Amato F, Melloni E, Trapassi MR and Novarini A. Epidemiological study of urinary tract stones in a Northern Italian City. Brit J Urol. 1990; 6:231.
3. Parivar F, Low RK and Stoiler ML. The influence of diet on urinary stone disease. J Urol. 1996; 155: 432- 40.
4. Scott R. The epidemiology of urolithiasis. In: Eds. Wickham JEA, Buck AC. Renal tract stone. Metabolic basis and clinical practice. Churchill Livingstone, NY; 1990.
5. Hasselwander O and Young IS. Oxidative stress in chronic renal failure. Free Rad Res. 1998; 29:1-11.
6. Witztum JL and Steinberg D. Role of oxidized low density lipoprotein in atherogenesis. Journal of Clinical Investigation. 1991; 88: 1785-1792.
7. Reaven PD and Witztum JL. The role of oxidation of LDL in atherogenesis. Endocrinologist. 1995; 5: 44-54.
8. Witztum JL. Susceptibility of low density lipoprotein to oxidative modification. American J urn al of Medicine. 1993; 94: 347-349.
9. Tungsanga K, Sriboonlue P, Futrakul P, et al. Renal tubular cell damage and oxidative stress in renal stone patients and the effect of potassium citrate treatment. Urol Res. 2005; 33(1):65–69.
10. Ceban E. Aspecte contemporane ale etiopatogenezei şi diagnosticului litiazei renale. Curierul Medical. 2012; 5(329):56–63.
11. Buege JA & Aust SD. The thiobarbituric acid assay. Methods in Enzymology. 1978; 52: 306.
12. Mishra HP, Fridovich I. The role of superoxide anion in the a11toxidatio11 of epinephrine and a simple assay for superoxide dismutase. J Biol Chem. 1972; 247:3170.
13. Scott JA, Homey CJ, Khaw BN and Rabitc CA. Quantitation of intracellular oxidation in a

renal epithelial cell line. Free Rad Bio & Medicine. 1988; 4: 79-83.
14. Goswami A, Singhal PC Wagner JD, Univetzky M, Valderrama E and Smith AD. Matrix modu !es uptake qf calcium oxalate c,ystals and cell growth of renal epithelial cells. J Urol. 1995; 153: 206-211.
15. Michiels C, Raes M, To ssaint 0, Remacle J. Importance of Se-glutathione peroxidase catalase and u!Zn SOD for cell survival against oxidative stress. Free Rad Bio & Med. 1994; 17(I): 235-248.
16. Gudumac V, Tagadiuc O, Rîvneac V, et al. Investigații biochimice. Micrometode. Elaborare metodică. Volumul II. Chișinău: 2010.
17. B. Mansuroğlu, S. Derman, A. Yaba, et al., Protective effect of chemically modified SOD on lipid peroxidation and antioxidant status in diabetic rats, Int. J. Biol. Macromol. 72 (2015) 79–87.
18. Kang J, Sun Y, Deng Y, Liu Q, Li D, Liu Y, Guan X, Tao Z, Wang X. Autophagy-endoplasmic reticulum stress inhibition mechanism of superoxide dismutase in the formation of calcium oxalate kidney stones. Biomed Pharmacother. 2020 Jan; 121:109649.
19. Mahmoud RH, Ewadh MJ, Al-Hamadani KJ. Clinical Assessment of glutathione peroxidase and catalase to the status of malondialdehyde in urolithiasis. Pak J Med Sci 2009; 25(5):738-743.
20. Atasayar S, Orhan H, Özgüneş H. Malondialdehyde quantification in blood plasma of tobacco smokers and non-smokers. FABAD J. Pharm Sci. 2004; 29:15–19.