Oxidative stress in benign prostate hyperplasia

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ABSTRACT

Benign Prostate Hyperplasia (BPH) is the common health problem in ageing male. Free radicals and reactive oxygen species (ROS) are produced more with advancement of age leads to oxidative stress. This study aims to assess Malondialdehyde (MDA), the marker of lipid peroxidation and vitaminic anti-oxidants e.g. α-Tocopherol (Toc) and Ascorbate (Asc) status in plasma of BPH patients. This is a case control study conducted in Dept of Biochemistry in collaboration with Dept of Surgery, BPKIHS. Forty eight (n = 48) confirmed patients of BPH and forty six (n = 46) healthy age matched controls were enrolled. Plasma MDA, Asc and α-Toc were estimated. Plasma MDA level showed 4.81±1.87 nmol/ml in BPH patients compared to 3.69±1.56 nmol/ml in healthy controls ($p < 0.001$). There were significant decrease in plasma α-Toc and asc level which were 0.85±0.12 mg/dl and 0.93 ± 0.13 mg/dl in BPH patients compared to 1.37±0.31 mg/dl and 1.44±0.38 mg/dl in healthy controls respectively. Inverse correlation of plasma MDA with α-Toc (r = -0.09) and Asc (r = -0.51) was found in BPH patients. There was mild elevation of PSA in BPH patients compared with control but was not statistically significant. Thus, our study showed the evidence of association of oxidative stress in BPH patients.

Keywords: Oxidative stress, prostate hyperplasia, tocopherol, patients, Nepal.

INTRODUCTION

Benign prostate hyperplasia (BPH), a common diseases affecting the aging male, is an endocrine disorder, requires the presence of testicular androgen, growth factors and their receptors for its pathogenesis. The prostatic level of dihydrotestosterone (DHT) as well as androgen receptor remains high with ageing despite the fact that peripheral level of testosterone decreases causing increased proliferation of prostate.[1] BPH occurs in the transitional zone which involves the four major cell types in the prostate smooth muscle cell, fibroblast, acinar and basal epithelium.[2]

Oxidative stress is imbalance of antioxidant to pro-oxidant in favor of pro-oxidant. Antioxidants are substances that are able to compete with the other oxidizable substrate and thus significantly delay or inhibit the oxidation of these substrates. To prevent the series of reaction leads to free radical generation as reactive oxygen species (ROS) and to scavenge these ROS, scavenging system is present in the body system to protect from these devastating free radicals. Enzymatic antioxidant such as Superoxide dismutase (SOD), Glutathione peroxidase (GPx) and Catalase (CAT) as well as non-enzymatic antioxidant glutathione and vitaminic antioxidant namely, α-Tocopherol (Toc) and Ascorbate (Asc) plays a role as a scavenger of free radicals.

Malondialdehyde (MDA) is a physiological keto-aldehyde produced by peroxidative decomposition of unsaturated lipid as a by-product of arachidonate metabolism. MDA is also secondary product of lipid peroxidation and used as an indicator of tissue damage.[3] Increasing evidence has indicated that oxidative stress is associated with aging and several age related degenerative disease including cancer.[4] A wide variety of ROS and reactive nitrogen species (RNS) attack DNA directly and form mutagenic lesion. ROS may cause formation of adducts indirectly by inhibiting autocatalytic lipid peroxidation which generates a large variety of genotoxic breakdown products including alkoxyl radicals, peroxyl radicals and aldehyde such as malondialdehyde.[5]

Therefore, the estimation of MDA, vitaminic antioxidant i.e. α-Toc and Asc level provide the extent of oxidative stress in patients with BPH.

MATERIALS AND METHODS

This hospital based case control study was done in B. P. Koirala Institute of Health Sciences, Dharan, in which 48 male patients with BPH and 46 healthy age matched male control without any systemic disease were enrolled. Those patients with sign and symptoms, positive digital rectal examination and ultrasonography guided biopsy histological examination were included in the study. Informed consent was taken from all participant of the study. The exclusion criteria considered for the study were the presence of liver dysfunction, diabetes mellitus and other infections. Patients with smoking and oral antioxidant supplementation at the time of the enrollment were also not included in the study.

Blood was collected in EDTA vials and centrifuged at 2000 rpm for 15 minutes for separation of plasma. MDA was estimated according to Yagi *et al.* method. This method is based on the formation of red pigment condensation of lipid peroxidation breakdown products like MDA with thiobarbituric acid.[6] α-Toc was estimated by Bieri *et al* method in which α-Toc is oxidized to tocopheryl quinine by ferric chloride and resultant ferrous ion is complex with ethanolic α, α' – Dipyridyl to produce a red colored compound.[7] Plasma Ascorbate was estimated by Sullivan *et al* method depends on the reduction of ferric ion to ferrous ion by ascorbic acid, forming a red-orange, α, α' – Dipyridyl complexin aqueous medium.[8]

Data were analyzed by SPSS – 11.5. The comparison between patients and controls were done by student's '*t*' test and Pearson's correlation coefficient was applied to observe the correlation between variables.

RESULTS

The mean age of cases was 67±12 years and control was 63±8 years. The mean PSA level in serum was found to be 3.71±1.56 ng/ml as compared to 1.61±1.2 ng/ml which was not statistically significant.

Table-1 demonstrates the comparison of different parameters in cases and control. We found statistically significant rise in plasma MDA level in the cases when compared with control. But there was statistically significant decrease in Vitaminic antioxidant α-Toc and Asc in cases than control. Inverse correlation of plasma MDA with α-Tocopherol (r = -0.09) and Ascorbate (r = -0.51) was obtained in BPH patients as shown in Fig. 1 and 2 respectively.

DISCUSSION

As the age advances, the oxidative stress increases and with any pathological condition it may aggravates owing to damage in tissues causing additional complication. The present study shows increased MDA level, indicator of lipid peroxidation and decreased Toc and Asc, indicators of antioxidants in the blood of BPH patients. Increased lipid peroxidation can be destructive to various body tissues if not scavenged by antioxidant defense mechanism. The decreased level of plasma antioxidants indicates that BPH is a disease of increased oxidative stress. There are scanty studies showing the increased MDA level in BPH suggesting oxidative stress in BPH.[9]

Studies have found to express lower level of antioxidant enzymes in BPH prostate than non malignant prostate. SOD and GPx were decreased significantly than in control. With the lower GPx activity CAT alone was probably unable to detoxify H_2O_2 completely. An accumulation of H_2O_2 might occur resulting in higher production of $^{\cdot}OH$ radical. The circulating antioxidant enzymes may be used up in the attempt to counteract the enhanced lipid peroxidation in the affected tissue.[10]

In our study, the level of α-Toc and Asc in plasma of BPH group were lower than in the healthy control group. However, a low level of Toc as well as retinol has also been reported in people living in Terai area of Nepal.[11] The decrease in the levels of these non-enzymatic antioxidant parameters may be due to the increased turnover for preventing oxidative damage in these patients, suggesting an increased defense against oxidant damage. Two vitaminic antioxidant α-Toc and Asc act in synergism in the cytosolic and membrane compartment of the cell. α-Toc scavenges lipid peroxy free radicals and interrupts the chain reaction of lipid peroxidation becoming oxidized itself in the process. Asc present in the aqueous compartments (e.g. cytosol, plasma and other body fluids) and function as a water soluble chain-breaking antioxidant, convert the Toc radical back to active α-Toc there by replenishing antioxidant activity of α-Toc.[12]

Asc with glutathione is first antioxidant to be depleted upon exposure to these environments either by directly scavenging these oxidants or trapping their intermediates. Thus, antioxidants may act in concert to protect tissue undergoing oxidative stress.[13]

With the lowered antioxidants in BPH, an accumulation of free radical such as $^{\cdot}OH$ might occur. These highly reactive oxidant molecules bind and oxidize DNA, lipid and proteins and it reacts with structure from its close neighborhood. Any oxidative lesion that is not repaired can lead to mutations, increasing the risk of carcinogenesis.[14] The enhanced lipid peroxidation occurs as consequence of the insufficient power of depleted antioxidant defense system for a prolonged time. But the alterations in antioxidant status are cause or consequence of lipid peroxidation is still unclear. But no such studies data are available to support this hypothesis.

In addition it has been suggested that antioxidants have protective role against BPH as well as progressive prostate cancer. Thus, Asc and α-Toc supplementation may be helpful for enhancing prostate health of the ageing men. Thus, further research can be designed to see the outcome with the administration of Asc and α-Toc in patients with BPH and ageing male.

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Table-1: Comparison of different parameters of cases with controls

Parameters	**Control (Mean ± SD)**	**Cases (Mean ± SD)**	**P value**
Malondialdehyde (nmol/ml)	3.69 ± 1.56	4.81 ± 1.87	<0.001
α-Tocopherol (mg/dl)	1.37 ± 0.31	0.85 ± 0.12	<0.001
Ascorbate (mg/dl)	1.44 ± 0.38	0.93 ± 0.13	<0.001

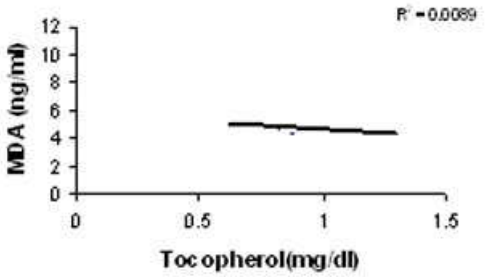

Fig. 1. Scattered diagram of MDA versus Toc level

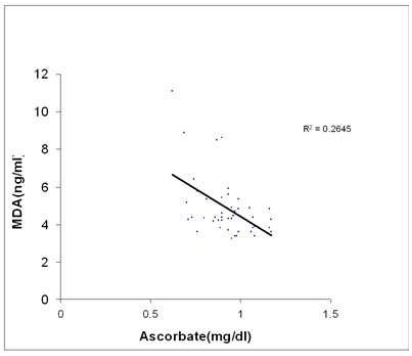

Fig. 2. Scattered diagram of plasma MDA versus Asc level