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Glutathione Peroxidase and Its Correlation with the Marker of Lipid Peroxidation in Essential Hypertension Patients

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Abstract: The present study was carried out to estimate the erythrocyte glutathi peroxidase activity, an antioxidant enzyme and malondialdehyde (marker of l peroxidation) in Hypertensive subjects of different grades as per JNC 7th norms an determine their relation with each other in essential hypertensive patients. In the pre study, erythrocyte glutathione peroxidase activity and malondialdehyde levels v measured in 90 hypertensive subjects (30-60 years), categorized into three groups prehypertension, Stage I HT and Stage II HT, depending upon their blood pressure statistically compared it with that of 30 healthy individual, served as control. Correla analysis between aforesaid parameters was performed by using Pearson correlation Erythrocyte glutathione peroxidase activity was found to be significantly low in each pa group as compared to control ($P < 0.001$) where as malondialdehyde levels were increa significantly in each patient group as compared to control ($P < 0.001$) along with subseq increase in blood pressure. Erythrocyte glutathione peroxidase activities were also inver correlated with MDA in essential hypertension patients. To prevent free radical dam body has a defense system of antioxidants which are involved in the prevention of cell damage – the common pathway for vascular ageing and a variety of cardio vasc complications. From our study, it was concluded that increased lipid peroxidation reduced Glutathione peroxidase along with increase in blood pressure can be used a marker for essential hypertension.
Keywords: Glutathione peroxidase, malondialdehyde, oxidative stress, free radical.

INTRODUCTION

Essential hypertension (HT) is a major public health problem worldwide and indeed, associated with increased blood pressure and its related complications. In particular, HT patients have at greater risk for manifestation of stroke and cardiovascular disease (CVD), including myocardial infarction[1]. Although precise etiology of this disease is poorly understood, probability of HT patients to develop future CVD risk appears to be more due to involvement of some common risk factors such as aging, high body mass index, dyslipidemia and sedentary lifestyle[2]. In addition, the increased prevalence and manifestation of CVD in HT patients has renewed the interest of researchers to identify various other unidentified risk factors.

The unidentified risk factors such as oxidative stress have been implicated in the increased burden of HT and its related disorders [3]. Oxidative stress in HT is ensued by excessive production of reactive oxygen species (ROS). These ROS confer their toxic effects through cascade of deleterious events such as DNA strand breakage, damage to endothelium, structural proteins and oxidation of LDL, i.e. lipid peroxidation, which eventually lead not only to uncontrolled blood pressure but also in the development of HT associated various vascular complications as well [4,5]. Malondialdehyde (MDA) is the most abundant product of lipid peroxidation which plays a crucial role in vascular pathology.

In order to prevent these culprit effects of ROS, antioxidant defense system plays a crucial role by incorporating antioxidant enzymes and antioxidants. In this context, Glutathione peroxidase (GSHPx) is a tetrameric enzyme containing selenium. It is not only responsible for the decrease of H_2O_2, but also transforms lipoperoxide and other organic hydroperoxide into their corresponding hydroxylated compounds, which are less reactive. GSHPx is present at higher levels in peroxisomes and vesicles attached to

the plasma membrane, mainly in the liver and erythrocytes [6]. Saxena *et al.* also measured the activity of various enzymic and non-enzymic antioxidants such as vitamin C and superoxide dismutase in patients with HT [7,8]. Reduced activity of antioxidant enzymes have also been described in patients with myocardial infarction, obesity, smokers and other vascular disorders [9]. Previous studies have documented the incidence of oxidative stress in HT patients, however, studies related to association of GSHPx and lipid peroxidation in different stages of HT patients are scanty [7,10]. Therefore, the aim of present study was to evaluate the erythrocyte glutathione peroxidase (GSHPx) activity in different stages of HT and to determine the association of (GSHPx) with the marker of lipid peroxidation.

MATERIALS & METHODS

In the present study, 90 subjects of essential hypertension of either sex were recruited in the patient group and 30 age matched healthy individuals were recruited in control group (30-60 years) after taking their informed consent form and approval of the study from Ethical committee of the college. The patients were classified into 3 groups (50 patients in each group), according to "Seventh Report of Joint National Committee on High Blood Pressure". These include Group I or pre-hypertension [Systolic Blood Pressure (SBP) 120-139 mm Hg and Diastolic Blood Pressure (DBP) 80-89 mm Hg], Group II or Stage I HT (SBP 140-159 & DBP 90-99 mm Hg) and Group III or Stage II HT (S.B.P. $\geq$ 160 mm Hg & D.B.P. $\geq$ 100 mm Hg). Venous blood was collected in EDTA vial from each subject after measurement of blood pressure. In addition, hypertensive patients with other systemic diseases were excluded. Samples were processed immediately.

Erythrocyte glutathione peroxidase (GSHPx) activity was estimated by Beutler's method, after preparation of hemolysate.[11] GSHPx catalyse the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG) by H_2O_2. The rate of formation of GSSG is measured by means of glutathione reductase reaction in which NADPH is oxidized and measured at 340 nm.

Erythrocyte malondialdehyde (MDA) levels were measured as thiobarbituric acid reactive substances, after preparation of hemolysate. The heat induced reaction of malondialdehyde (MDA) with thio barbituric acid (TBA) in the acid solution forms a trimethine coloured substance, which is measured spectrophotometrically at 532 nm[12].

STATISTICAL ANALYSIS

The data collected from patients and control were entered separately in Microsoft Excel sheet of windows 2007 and values were expressed as Mean ± SD. The significance of mean difference between patient and control groups was compared by using Student's t test. The distribution of 't'- probability was calculated depending on 'n' and significance of test was obtained. P value < 0.05 and < 0.001 were considered as significant and highly significant, respectively. P value > 0.05 was considered as insignificant. In addition, correlation analysis between aforesaid parameters was performed by using Pearson correlation test.

RESULTS

In the present study, 150 patients of HT and 50 healthy individuals, served as controls were included. The mean erythrocyte glutathione peroxidase (GSHPx) activity and lipid peroxide level (i.e. malondialdehyde) of the patient and control group are depicted in Table.1.0. The mean erythrocyte glutathione peroxidase (GSHPx) activity in hypertensive subjects were decreased significantly (P<0.001) as compared to controls i.e. 28.2%, 34.2% and 44.3% low in prehypertension, stage I HT and stage II HT patients respectively. On the other hand, erythrocyte malondialdehyde levels were found to be increased significantly (P<0.001) i.e. 38.06%, 51.61% and 69.03% high in prehypertension, stage I HT and stage II HT patients as compared to healthy controls. These variations were increased continuously with increase in blood pressure. In addition, we observed a significant correlation between erythrocyte GSHPx and the marker of lipid peroxidation (MDA) in HT patients, as shown in Table 2. GSHPx activity was negatively correlated with MDA and blood pressure ($p < 0.001$) in HT patients. These results clarify the role of oxidative stress in enhancing the CVD risk in HT patients most probably by its relation with increased blood pressure.

DISCUSSION

Essential hypertension is a major and escalating public-health and clinical challenge worldwide in the wake of urbanization, surplus energy intake, increasing body weight, and sedentary life habits. HT confers a 2-fold the risk of developing cardio vascular disease[1,5]. It has been documented that hypertension also act as a driver of cardio-metabolic risks[9]. Oxidative stress is increased in patients with essential hypertension owing to increase in free radical production. Involvement of free radicals in membrane damage via lipid peroxidation and its resultant products such as lipid radicals (L◦), lipid peroxides (LOO◦), lipid hydroperoxides (LOOH) and highly reactive aldehydes plays a crucial role in the development and progression of disease. In the present study, a highly significant increased levels of malondialdehyde (i.e. marker of lipid peroxidation) were observed in each patient group (P<0.001) as compared to healthy control which rises continuously with increase in blood pressure and clarify the etiopathogenic role of free radicals via lipid peroxidation in HT patients. Our findings were in concordance with the findings of Bhattacharya *et al*.[13] According to them, lipid peroxides are toxic to

the cellular components and lipid peroxidation may be responsible for vascular disorder in HT.

Table-1.0: Erythrocyte Glutathione peroxidase and Malondialdehyde level (µmol MDA/ml) in patients and control group. (Mean±SD)

S.No.	Particulars	Control Group	Patient Group		
			Prehyper--tension	Stage I HT	Stage II HT
1.	No. of Samples	30	30	30	30
2.	Age (years)	30 – 60	30 – 60	30 – 60	30 – 60
3.	Systolic Blood Pressure (mm Hg)	116 ± 2.4	129 ± 3.5	154 ±4.2	165 ± 5.0
4.	Diastolic Blood Pressure (mm Hg)	78 ± 1.37	85 ± 1.65	97 ± 1.53	110 ± 1.45
5.	GSHPx (IU/gm Hb)	32.50 ± 2.24	24.96 ± 1.82*	21.37 ± 1.48**	18.11 ± 1.65**
6.	Malondialdehyde (µmol MDA/ml)	1.55± 0.11	2.14 ±0.13*	2.35 ±0.11**	2.62 ±0.15**

Where: * P < 0.05: Significant; ** P < 0.001: Significant

Table -2.0: Correlation coefficient (r) between erythrocyte Glutathione peroxidase (GSHPx) activity and MDA levels in essential hypertension patients

Particulars	MDA level (Group I)	MDA level (Group II)	MDA level (Group III)
Erythrocyte GSHPx activity	- 0.438	- 0.467	- 0.584

The production of free radicals and its culprit effect on biomolecules is effectively regulated by antioxidant reserves of body. In particular, increased oxidative stress has been found to be associated with decreased antioxidant enzyme activity which can lead to metabolic upsets and changes in cell signaling [14]. In this context, H_2O_2 produced via dismutation reaction of $O_2^{-\cdot}$ is mainly removed by glutathione peroxidase. Erythrocyte GSHPx activity was also found to be decreased and inversely correlated with lipid peroxidation (P< 0.001; Table 1 and 2 respectively) as compared to controls which could be explained either by their decreased synthesis or rapid consumption in protecting the cells from H_2O_2 mediated oxidative damage in HT patients. Our findings were quite similar to the recent findings of Goyal *et al.* who have also reported the marked oxidative damage and altered antioxidant defense system in metabolic syndrome patients having characteristic high blood pressure[15].

CONCLUSION

On the basis of present study and consistent findings of previous studies we can conclude that lipid peroxidation play an etiopathological role in the development of HT and erythrocyte glutathione peroxidase activity is inversely related to increase in blood pressure. Thus, both erythrocyte GSHPx and malondialdehyde levels may be an excellent marker of oxidative stress in essential hypertension. Furthermore, as the blood pressure increases, erythrocyte GSHPx activity decreases continuously not only due to its free radical scavenging action but also in maintaining body's antioxidant reserve and in limiting the lipid peroxidation. Therefore, our study suggests that the diet rich in antioxidants is essential for patients suffering with essential hypertension and consumption of fruit, vegetables and grains should be increased with increase in blood pressure. In addition, adoption of healthy life style with regular physical exercise should be recommended to HT patients.

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