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Research Article

Evaluation of Total Antioxidant Activity and Its Relation with Serum Uric Acid in North Indian Elderly

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Abstract: Aging process has been found to be associated with biomolecular destruction which in turn responsible for progression of age related complications. It is conceivable that alteration in plasma antioxidant reserve along with serum acid levels may have a crucial role in aging process. Aim**:** The objectives of present study were to ascertain the plasma levels of Total antioxidant activity (TAA) and serum uric acid (UA) in the subjects of different age groups and to determine their cumulative effect on lipid peroxidation with senescence. Methods: In the present study, 90 healthy subjects were selected and plasma TAA, serum UA and erythrocyte malondialdehyde (MDA) were measured using standard methods. Out of 90 subjects, 60 healthy individuals were categorized into two groups: Group I (40-55 years) and Group II (≥ 56 years) and statistically compared it with that of 30 younger controls (20-30 years) by using student's t-test. Result: Plasma TAA levels were significantly low ($p<0.05$, $p<0.001$) in group I and II as compared to healthy controls. Similarly, erythrocyte MDA levels were significantly high ($p<0.05$, $p<0.001$) in group I and II as compared to healthy controls whereas serum uric acid levels were increased significantly ($p<0.05$) only in group II subjects. However, serum uric acid levels were altered insignificantly ($p<0.1$) in group I subjects as compared to younger controls. Conclusion: Our findings indicate that senescence is closely associated with altered plasma TAA and serum uric acid levels due to augmented oxidative stress and thereby making the elderly more susceptible to develop pathological consequences. Thus, consumption of antioxidant rich diet along with normal uric acid status could be an effective strategy to reduce the culprit effect of aging process.

Keywords: Total antioxidant activity, free radical, inflammation, lipid per oxidation

INTRODUCTION

The incidence and progression of biological system impairment enhances dramatically with advancing of age. Among various risk factors, oxidative stress caused by increased production of reactive oxygen species (ROS) such as superoxide anion ($O_2^{\cdot-}$) and its metabolites or by reduced bioavailability of antioxidant defenses in elderly, forecasting a grim scenario for the evolving age related complications [1].

ROS may act through several mechanisms to mediate apoptosis followed by pathological consequences, which include biomolecular destruction, DNA strand breakage, and protein oxidation, damage to endothelium, cartilage, membrane ion transporters, and lipid per oxidation [2]. Prime target to free radicals attack are the polyunsaturated fatty acids in the membrane lipids, causing lipid peroxidation, has been implicated in the development of various diseases in elderly [3]. Lipid peroxide (malondialdehyde) is the most abundant among the reactive aldehydes derived from lipid peroxidation. It has been suggested that binding to these aldehydes to membrane protein may alter their function, tonicity, permeability, rigidity and integrity, and thereby enhances the aging process [4].

These free radicals are efficiently removed by antioxidant defense system, which includes antioxidant enzymes and antioxidants [5]. Total antioxidant activity (TAA) including co-operative action of non enzymatic antioxidants such as vitamin C, E, A, uric acid and albumin, may have a significant role in the prevention of patho physiological alterations leading to aging and its related complications [6,7]. Amongst various non-enzymic antioxidants, uric acid is an end product of purine metabolism and considered as an effective antioxidant in blood plasma as it scavenges superoxide radical, protects erythrocyte against per oxidative damage and free radical attack [8]. Conversely, its relation with recruitment of circulating inflammatory

markers and vascular injury are well documented [9, 10]. Therefore, the overall objectives of present study were to ascertain the plasma levels of TAA and serum uric acid levels in the subjects of different age groups and to determine their cumulative effect in the progression of lipid peroxidation (via erythrocyte malondialdehyde estimation) as one of the important consequence of aging.

MATERIAL AND METHODS

In the present study, 90 healthy, non-supplemented (do not taking any additional vitamin or minerals) subjects of both sex (15 males & 15 females in each group) and different age groups were included after taking their informed consent and approval of protocol by ethics committee of college. These subjects were selected randomly and categorized into three groups depending upon age i.e. Control group (younger people) includes 30 healthy subjects of age group 20 – 30 years, Group I includes 30 healthy subjects (middle aged people) of age group 40-55 years and Group II includes 30 healthy subjects (elderly people) of age group 56 years onwards. After taking the demographic information, history and limited physical examination, a fasting blood samples were collected in plain vial (for serum minerals estimation) and in EDTA vial from antecubital veins avoiding venostasis from each subject after collecting the information of age, sex, height, weight, blood pressure and confirmation of healthy state. Height and weight were measured with subject barefoot and light dressed. The body mass index (B.M.I.) was calculated as B.M.I. = weight (Kg) / Height (metre^2). Obese (B.M.I > 25), hypertensives (B.P. >120/80 mmHg) and smokers were excluded from the study.

Samples were processed immediately for plasma and serum separation. Plasma total antioxidant activity was estimated spectrophotometricaly by the method of Koracevic *et al.;* Two milliliter of blood samples was collected in EDTA bottles. Plasma was separated immediately by centrifugation and TAA is measured. This method is based on the principle that the standardized solution of iron EDTA complex reacts with hydrogen peroxide by a Fenton type of reaction, leading to the formation of hydroxyl radicals. This reactive oxygen species degrades benzoate, resulting in the release of TBARS. Antioxidants from the added plasma cause the suppression of production of TBARS. The reaction is measured spectro photometrically at 532 nm [11].

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

Serum uric acid levels were estimated by Caraway's method in which uric acid reacted with phosphotungstic acid in alkaline medium forming a blue color complex which was measured at 700 nm [13].

Statistical analysis

The data collected from study group subjects were entered separately in Microsoft Excel sheet of windows 2010 and values were expressed as Mean ± SD. The significance of mean difference between study group subjects was compared by using Student's t test and distribution of probability (P).

RESULT

The mean blood pressure and anthropometric indices of the study group subjects are depicted in Table 1. The observations made reveal significant changes in plasma TAA, erythrocyte malondialdehyde and serum uric acid levels of different age group subjects as represented in Table 2. Plasma total antioxidant activity was found to be significantly low ($p<0.05$ & $p<0.001$) in both the study groups i.e. 22.6% and 35.2% low as compared to controls. Conversely, erythrocyte MDA levels were 24.8% and 43.5% high in Group I and Group II respectively as compared to healthy controls. Significant increase in serum uric acid levels were observed only in Group II (29.4% high; $p<0.05$) subjects whereas in Group I subjects, serum uric acid levels were not significantly altered (14.3% high; $p<0.1$). These levels statistically reveal continuous variation with senescence; however, on comparing Group I and Group II, these values were altered insignificantly.

Table-1: Demographic profile of different age group subjects (n=90)

S No	Particulars	Control group (n=30)	Group I (n=30)	Group II (n=30)
1)	Age (years)	26.4 ± 4.0	48.0 ± 5.0	63.0 ± 5.0
2)	M:F ratio	1:1	1:1	1:1
3)	Height (meter)	1.58 ± 0.09	1.55 ± 0.08	1.60 ± 0.08
4)	Weight (Kg)	54.5 ± 4.)	57.0 ± 4.0	61.8 ± 3.8
5)	B.M.I. (Kg/m^2)	22.5 ± 2.5	23.3 ± 2.8	23.0 ± 2.6
6)	Systolic blood pressure (mmHg)	104 ± 4.2	112 ± 5.8	116 ± 4.0
7)	Diastolic blood pressure (mmHg)	72.0 ± 3.6	75.5 ± 4.2	76 ± 3.8

Table 2: Plasma Total antioxidant activity (TAA), Malondialdehyde (MDA) and serum uric acid levels in different age group subjects. Mean ± SD

S No	Particulars	Control group (n=40)	Group I (n=40)	Group II (n=40)
1)	TAA level (m mol/L)	1.32 ± 0.23	1.03 ± 0.17**	0.86 ± 0.15***
2)	Uric acid (mg %)	4.39 ± 1.30	5.0 ± 1.62*	5.7 ± 1.74**
3)	Malondialdehyde (µmol MDA/ml)	1.68 ± 0.12	2.09 ± 0.14**	2.41 ± 0.15***

Where,
* p<0.1: Non-significant; ** p<0.05 : Significant; *** p<0.001 : Highly significant

DISCUSSION

It has been well accepted that enhanced production of free radicals is associated with physiological changes that compromise functional deterioration of organs and thereby shaping the elderly more susceptible to develop disease [14, 15]. In addition, the prevalence of oxidative stress with senescence has attracted increasing attention amongst epidemiologists, clinicians and experimental researchers. The mechanisms whereby free radicals may exert cytotoxic effect related to aging process include damage to cell membrane via lipid peroxidation and protein oxidation. Lipid per oxidation contributes local membrane destabilization that alters the proper trafficking of intracellular vesicles, phagocytosis, degranulation, antigen presentation, receptor mediated ligand uptake and many other process leading to age related deterioration [16, 17]. In this context, we observed that erythrocyte malondialdehyde levels were significantly high in both middle aged and elderly subjects (p<0.05 and p<.001; Table 2) which authenticate the hypothesis that aging is closely associated with lipid peroxidation mediated destruction in cell, sub cellular organelles and biomolecules. Our findings were in agreement with the findings of Bhattacharya et al. who also observed enhanced production of MDA in elderly osteoarthritis patients [18]. Moreover, lipid peroxidation initiates a complex cascade that promotes aging effects such as atherosclerotic plaque formation followed by myocardial infarction, inhibition of NO and prostacyclin synthesis, enhancement of cytosolic free calcium and peripheral vascular resistance leading to Hypertension; and leakage of lysosomal hydrolases via breakdown of lysosomal membrane which cause dystrophic changes in muscle fibers leading to weakness of muscles with growing age [1, 19, 20].

Increased production of MDA may be associated with alteration in antioxidant defense system as characterized by alteration in total antioxidant activity [21, 22]. In the present study, plasma TAA levels decrease continuously with increase in age (p<0.05, p<0.001) along with increase in MDA levels in middle aged and elderly people which clarify the contributory effect of reduced antioxidant status due to augmented oxidative stress that could not be compensated by increase in some other antioxidants such as uric acid as observed in present study. However, uric acid levels were found to be significantly high (p<0.05) only in elderly subjects while insignificant elevated levels were observed in middle aged subjects which suggests that body is trying to protect itself from the deleterious effects of free radicals with continuous increase in age by increasing uric acid production. Recently, marked reduction in TAA along with elevated levels of serum uric acid in older people, hypertensive smokers and other age related diseases have been well documented [23, 24, 25].

CONCLUSION

Considering the above culprit events and documented evidences of previous studies, it can be inferred that free radical production increases with increase in age; and depletion of total antioxidant status due to their free radical scavenging action may be an indirect markers of oxidative stress during aging. Moreover, it contributes aging process by inducing lipid peroxidation. In addition, present study also suggests that consumption of diet rich in antioxidants should be increased with advancing of age which may prevent or postpone the onset of aging and its related complications.

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