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Effect of lifestyle interventions on oxidative stress in elderly hypertensive and in normal individuals

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Abstract---Introduction: Oxidative stress has emerged as one of the important factors of aging as well as various diseases including hypertension. A Few changes in lifestyle like food habits and exercise leads to significant decrease in the oxidative stress and inflammation which in turn improves the endothelium functions. Aim: The present study was designed to assess and compare the effect of lifestyle modifications on oxidative stress in elderly essential hypertensive patients as well as in normotensive elderly subjects. Materials and Methods: One hundred four normotensive elderly subjects of group I and one hundred eighty-six elderly hypertensive patients of group II between 60 to 80 years of age successfully completed three months lifestyle modifications program conducted in the department of physiology, Santosh Medical College Ghaziabad. Oxidative stress markers GSH, SOD, MDA and blood pressure were measured before and after lifestyle modification program. Results: The findings of the present study showed that SBP ($p<0.001$), DBP ($p<0.001$), MAP ($p<0.001$) were significantly low in group II hypertensive patients in comparison of group I normotensive subjects. Value of SOD increased significantly in group II hypertensive patients in comparison to group I normotensive subjects. There were statistically insignificant changes in GSH and MDA in group II patients compare to group I subjects. Conclusion: The Present study concluded that lifestyle modifications are effective for both the elderly population essential hypertensive and

normotensives. However, current study showed that lifestyle modifications are more beneficial for essential hypertensive elderly patients in comparison to elderly normotensive subjects.

Keywords---Yoga, Blood Pressure, Antioxidants, Geriatric Population.

Introduction

Oxidative stress has emerged as one of the important factors of aging as well as various diseases including hypertension. Reactive oxygen species (ROS) has been found to be associated with the onset as well as progression of various chronic diseases including cardiovascular diseases (CVD).¹ Oxidative stress is one sided increase of ROS; it may be due to increased ROS production or deterioration of antioxidants defence.² Reactive oxygen species are double edged sword as it plays an important role in normal physiological functioning of various organs including haemostasis, cellular defence and aging; nonetheless, excessive production of ROS leads to cellular dysfunction.³ Hypertension is known to be one of the important causes of mortality and morbidity worldwide. In addition, hypertension may induce a variety of diseases; however, different treatments for hypertension have emerged with variation of success from subject to subject.⁴

In addition, oxidative stress has been found to be elevated in hypertension due to increased production of ROS which further induces atherosclerosis.⁵ ROS lead to oxidation of low-density lipids (LDL) which in turn induces production of cytokines from smooth muscles and escorts endothelial dysfunction.⁶ Dysfunction of endothelium along with inflammatory pathways has been demonstrated to be associated with atherosclerosis.⁷ Hypertension is associated with increased vascular oxidative stress; oxidative stress induces injury of the vascular wall which further leads to infiltration of platelets, leukocytes, and collagen fibres; consequences in increased size of smooth muscles escorting to narrowing of the vascular lumen.⁸ Effective control of blood pressure may combat with various future complications of hypertension.⁹ Heterogeneous aetiological factors induce the genesis of hypertension; therefore, changes of lifestyle factors along with diagnosis and treatment of secondary causes is essential to prevent CVD.¹⁰ Nevertheless, in last few years, investigators have shown that life style modifications can reduce blood pressure in hypertensive patients.^{4,9}

Physical exercise as well as physical fitness cause significant decrease of blood pressure.¹⁰ Studies have shown nadi-shodhana pranayama meaningful decreases heart rate and blood pressure.^{11,12} Further, few changes in lifestyle like food habits and exercise leads to significant decrease in the oxidative stress and inflammation which in turn improves the endothelium functions.¹³

Therefore, the present study was designed to assess and compare the effect of lifestyle modifications on oxidative stress in elderly essential hypertensive patients as well as normotensive elderly subjects.

Materials and Methods

It was an interventional type of study conducted in the department of physiology, Santosh Medical College Ghaziabad, NCR, Delhi. Study population was divided into Group I which included one hundred nineteen elderly normotensive subjects (69 males & 50 females) and Group II which incorporated two hundred seventeen elderly essential hypertensive patients (133 males & 84 females) between 60 to 80 yrs of age. All the group I and group II participants of the study were recruited from Santosh Medical College Ghaziabad, NCR, Delhi. Fifteen normotensive subjects (12.6%, 11 males & 4 females) of group I whereas, forty-one hypertensive patients (18.89%, 29 males and 12 females) of group II left the lifestyle program in between due to various reasons. One hundred four normotensive elderly subjects (58 male & 46 female) of group I and one hundred eighty-six elderly hypertensive patients (114 male and 72 female) of group II successfully completed three months lifestyle modifications program. Body mass index (BMI) 18.5-25 kg/m², non- alcoholic, non-smokers were inclusion criteria for both groups except blood pressure <140/90 mm Hg¹⁵ for group I (Normotensive subjects) and blood pressure >140/90 mm Hg¹⁵ for group II (Hypertensive patients). Participants suffering from chronic disease, taking any type of medicines, hormonal replacement therapy or any kind of physical disability were excluded from the study.

The study was started after approval of the ethical committee in the month of July 2014 and was completed in the month of April 2017. All the research participants were narrated about the cause and purpose of the research program. Inform written consent of the participants was obtained in the local language before being included in the three months lifestyle modification program. All of the normotensive subjects of Group I as well as hypertensive patients of Group II were divided into the subgroups of 25 to 30 subjects to follow lifestyle modifications program. An orientation program was organized for both Groups before starting the lifestyle modifications. All of the participants completed their yogic exercise under the supervision of trained yoga instructors; on the other hand, daily morning walk was supervised by trained instructors. Health of every participant was monitored during the course of study on every alternate day. Moreover, various orientation programs were organized for each group every month to sustain their interest in the research program.

Methodology of Lifestyle Modifications in group I and II

Elderly patients suffering from essential hypertension of group II as well as normotensive elderly subjects of group I were asked to modify their day-to-day life by performing the lifestyle modifications for three months.¹⁵ All the participants were asked to perform yogic exercise Nadishodhan Pranayama¹¹ for twenty minutes followed by daily morning walk of 2 miles¹⁶ for six days in a week. They were advised for daily sleep of minimum 5 to 6 hours¹⁷, restrict salt intake up to 2.3 gm/day¹⁸, lowering fat intake up to 40 to 50 gm/day¹⁸ and increase intake of water 2 to 3 litres per day.¹⁹ All the elderly hypertensive patients and normotensive subjects were asked to come with empty stomach early in the morning up to 6 am.

Measurements

Blood pressure was measured by auscultatory method.²⁰

Biochemical Estimations

Estimation of Oxidative Stress

Oxidative stress markers GSH and SOD were measured by Enzyme Linked Immunosorbent Assay (ELISA) method using assay kits and ELISA reader manufactured by Qayee-Biotechnology Co. Ltd and Robonik (India) Pvt. Ltd. correspondingly.²¹ MDA was investigated by TBARS method using TBARS kit and biochemistry analyser E-C5VZ(10k) manufactured by Cayman chemical company, Ann Arbor, USA and Transasia, India respectively.²²

Statistical Analysis

The results of the present study were expressed as Mean \pm SD (Standard deviation). To evaluate statistical significance of data in each group before and after lifestyle modifications paired students t-test was used. Unpaired t-test was used for intergroup comparison. A p-value < 0.05 was considered statistically significant. IBM SPSS Statistics 21.0 manufactured by IBM USA was used for entire calculations.

Results

Values of all the parameters were expressed in Mean \pm SD. It is clear from the Table 1 that there was a significant decrease in systolic blood pressure (SBP) 126.88 ± 6.59 mm Hg vs 123.35 ± 5.82 mm Hg, $p = < 0.0001$ and diastolic blood pressure (DBP) 81.25 ± 4.64 mm Hg vs 79.5 ± 4 mm Hg, $p = < 0.0001$ in comparison to baseline values in elderly normotensive subjects of group I. Further, a significant decrease was observed in mean arterial pressure (2.25 ± 0.57 mm hg, $p = < 0.0001$), pulse pressure (1.73 ± 0.73 mm hg, $p = < 0.0001$), and heart rate (0.79 ± 0.24 BPM, $p = < 0.0087$) of normotensive elderly subjects of group I after following three months lifestyle modifications program. (Table 1)

Table 2 shows blood pressure, mean arterial pressure, pulse pressure and heart rate of elderly hypertensive patients of group II following lifestyle modifications. It is evident from the table 2 that there was a significant decrease in the baseline values of SBP from 166.16 ± 10.07 mm Hg to 157.2 ± 9.84 mm Hg, $p = < 0.0001$ and DBP from 106.83 ± 8.97 mm Hg to 100.28 ± 8.51 mm Hg, $p = < 0.0001$ in hypertensive patients of group II ($n = 186$). Further, significant decrease of mean arterial pressure (7.38 ± 0.31 mm hg, $p = < 0.0001$), pulse pressure (2.27 ± 0.3 mm hg, $p = < 0.0001$) and heart rate (1.79 ± 1.07 BPM, $p = < 0.0001$) were observed in hypertensive patients of group II. (Table 2) In the Figure 1 GSH and SOD of group I normotensive elderly subjects and group II elderly hypertensive patients have been presented. It is evident from the Figure 11 that there was a significant increase of total glutathione (88.83 ± 9.57 ng/ml vs 94.26 ± 9.39 ng/ml, $p = < 0.0001$, 6.11%) and superoxide dismutase (78.96 ± 11.04 ng/ml to 85.63 ± 10.26 ng/ml, $p = < 0.0001$, 8.44%) in elderly normotensive subjects of group I. Whereas,

a significant increase in baseline values of glutathione from 87.16 ± 9.25 ng/ml to 93.15 ± 11.41 ng/ml, $p = < 0.0001$, 6.87% and superoxide dismutase from 71.1 ± 13.35 ng/ml to 79.14 ± 13.17 ng/ml, $p = < 0.0001$, 11.3% were observed in group II elderly hypertensive patients after following three months lifestyle modification program. (Figure 1)

It is evident from the figure 2 that a significant decrease was observed in the baseline values of melanodialdehyde in comparison of values after three months lifestyle modifications in normotensive subjects (5.26 ± 0.49 m mol/ml vs 4.54 ± 0.63 m mol/ml) Similarly, a significance decreases in baseline values of melanodialdehyde in elderly hypertensive patients (5.9 ± 0.77 m mol/ml vs 5.08 ± 0.91 m mol/ml). The p value was < 0.001 for hypertensive elderly patients

Table 3 shows the comparison of the changes observed between pre lifestyle modifications values and post lifestyle modifications values in group I and group II. SBP ($p < 0.001$), DBP ($p < 0.001$), MAP ($p < 0.001$) was significantly lower in group II hypertensive patients in comparison of group I normotensive subjects. There were statistically insignificant changes in PP and HR of group II hypertensive patients compare to group I normotensive subjects. (Table 3)

Data presented in table 4 shows that value of SOD increased significantly in group II hypertensive patients in comparison to group I normotensive subjects. There were statistically insignificant changes in GSH and MDA in group II hypertensive patients compare to group I normotensive subjects.

Table 1
Comparison of blood pressure pre and post lifestyle modifications values in normotensive subjects of group I.

Group I (normotensive subjects, n = 104)				
Normotensive Subjects, Age 65.18± 4.25	Before Lifestyle modifications	After Lifestyle modifications	P value	Changes (%)
Systolic blood pressure mm Hg	126.88± 6.59	123.35± 5.82	<0.0001**	2.78%
Diastolic blood pressure mm Hg	81.25± 4.64	79.5 ± 4	<0.0001**	2.15%
MAP mm Hg	96.4 ± 4.47	94.15 ± 3.9	<0.0001**	2.33%
PP mm Hg	45.46 ± 6.22	43.73 ± 5.49	<0.001**	3.81%
HR (BPM)	78.25 ± 5.59	77.46 ± 5.83	<0.0087**	1.01%

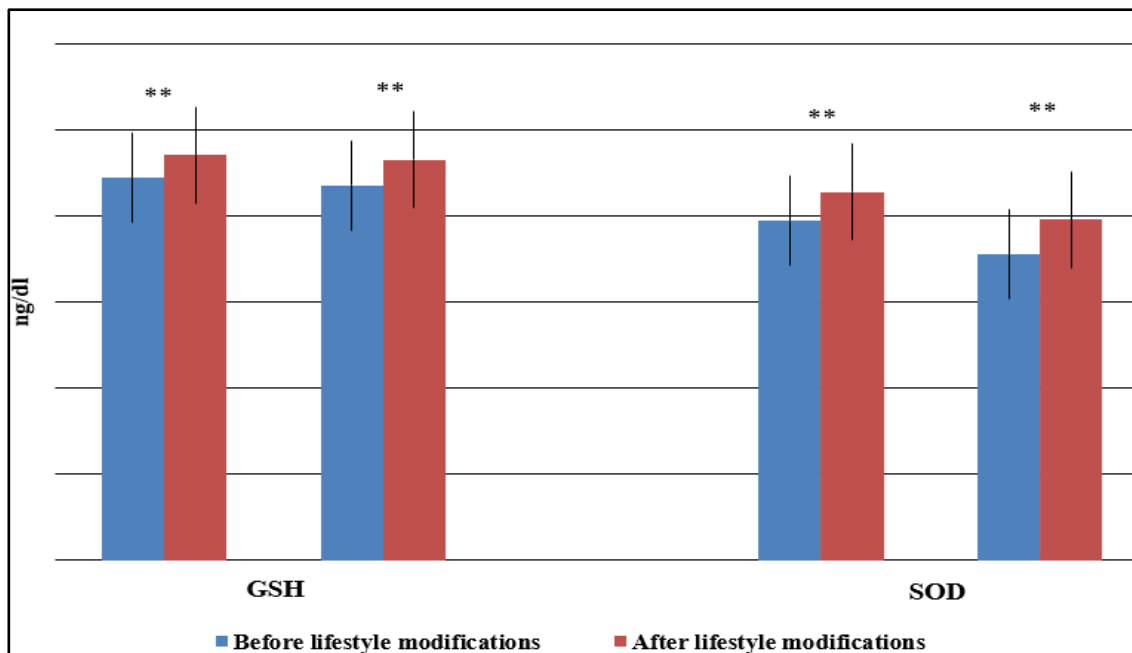
Values expressed as Mean+/-SD. MAP=mean arterial pressure, PP=pulse pressure, HR=heart rate, SD= Standard deviation of Mean, BPM = beats per minute. ** = ($p < 0.01$) highly significant (comparison of post value with pre value).

Table 2
Comparison of blood pressure pre and post lifestyle modifications values in hypertensive patients of group II

Group II (hypertensive patients, n = 186)				
Hypertensive patients, Age 65.58 ± 4.63	Before Lifestyle modifications	After Lifestyle modifications	P value	Changes (%)
Systolic blood pressure mm Hg	166.16± 10.07	157.2± 9.84	<0.0001**	5.39%
Diastolic blood pressure mm Hg	106.83± 8.97	100.28 ± 8.51	<0.0001**	6.13%
MAP mm Hg	126.65 ± 8.61	119.27 ± 8.33	<0.0001**	5.83%
PP mm Hg	59.24 ±7.69	56.97 ± 7.39	<0.0001**	3.83%
HR (BPM)	77.39 ±6.07	75.6 ± 5	<0.0001**	2.31%

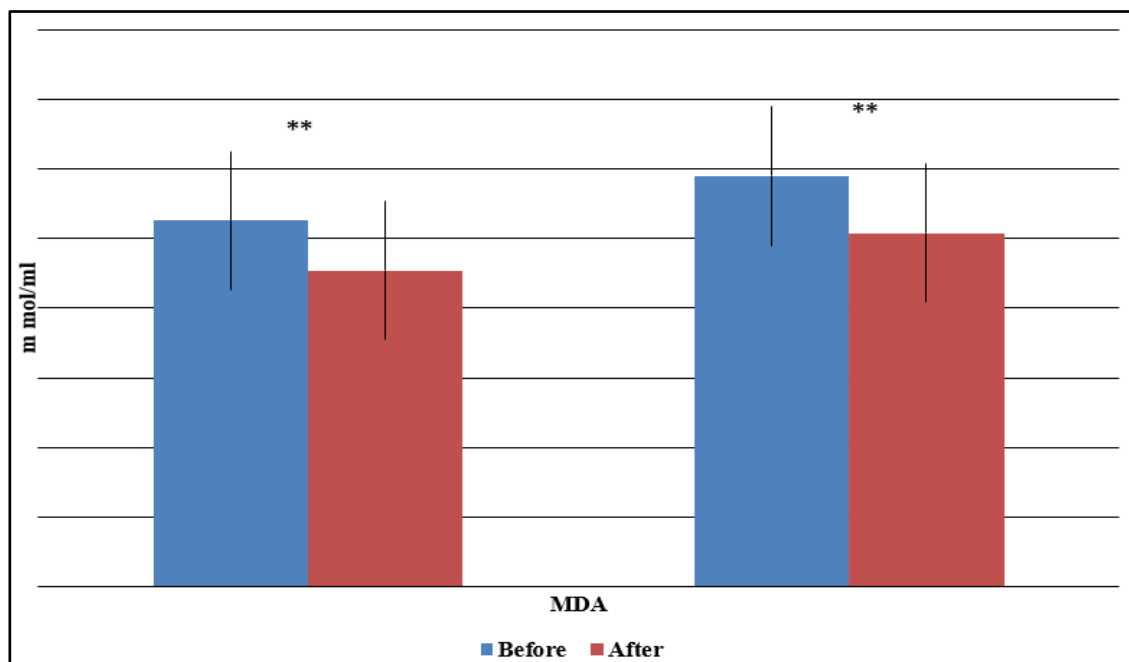
Values expressed as Mean+/-SD. MAP=mean arterial pressure, PP=pulse pressure, HR=heart rate, SD= Standard deviation of Mean, BPM = beats per minute. ** = (p<0.01) highly significant (comparison of post value with pre value).

Fig. 1
Changes in oxidative stress of normotensive subjects of group I and hypertensive patients of group II after following lifestyle modifications.



Values expressed as Mean+/-SD. GSH= Glutathione total. SOD= superoxide dismutase, SD= Standard deviation of Mean. ** p = <0.01 (comparison of post value with pre value).

Fig. 2
Changes in MDA of normotensive subjects of group I and hypertensive patients of group II after following lifestyle modifications



Values expressed as Mean \pm SD. MDA= malondialdehyde. SD= Standard deviation of Mean. ** p = <0.01 (comparison of post value with pre value).

Table 3
Intergroup comparison of cardiovascular markers changes in group I (Normotensive group) and group II (Hypertensive group).

Variants	Group I (Normotensive subjects)	Group II (Hypertensive patients)	p value
Systolic blood pressure mm Hg	3.24 \pm 4.24	8.96 \pm 4.52	<0.001 ^{***}
Diastolic blood pressure mm Hg	1.73 \pm 3.71	6.55 \pm 3.66	<0.001 ^{***}
MAP mm Hg	2.25 \pm 3.16	7.38 \pm 3.5	<0.001 ^{***}
PP mm Hg	1.73 \pm 5.21	2.3 \pm 4.3	<0.31 ^{NS}
HR	1.6 \pm 2.76	2.24 \pm 3.31	<0.09 ^{NS}

Values are expressed as Mean \pm SD. *** = p<0.001, Comparison of after lifestyle modifications values with before lifestyle modifications values. NS= Nonsignificant (p>0.05), Comparison of after lifestyle modifications values with before lifestyle modifications values. MAP= mean arterial pressure, PP= pulse pressure, HR= heart rate.

Table 4
Intergroup comparison of oxidative stress improvement in group I
(Normotensive group) and group II (Hypertensive group).

Variants	Group I (Normotensive subjects)	Group II (Hypertensive patients)	p value
GSH (ng/ml)	5.42±4.27	6.44±4.37	<0.057 ^{NS}
SOD (ng/ml)	6.67±4.04	8.03±4.1	<0.01 ^{**}
MDA (m mol/ml)	0.72±0.59	0.81±0.6	<0.22 ^{NS}

Values are expressed as Mean ± SD. ** = p<0.01, Comparison between changes of pre and post lifestyle modifications values. NS= Nonsignificant (p>0.05), Comparison between changes of pre and post lifestyle modifications values. GSH= glutathione, SOD= superoxide dismutase, MDA= malondialdehyde.

Discussion

Cardiovascular diseases are one of the leading causes of the death worldwide and hypertension occupies first place. Development of hypertension is triggered by various factors including imbalanced diet, sedentary lifestyle, obesity and high cholesterol levels.²³

Hypertension is one of the major causes of cardiovascular diseases which ultimately lead to mortality, worldwide. However, effective control of blood pressure can avoid various complications of hypertension like coronary artery disease, congestive heart failure, renal failure, heart enlargement, stroke etc.^{9,10,14} The outcome of this study disclosed that lifestyle modification resulted in a significant decline in SBP as well as DBP in group I normotensive elderly subjects. Similarly, Elmer PJ et al,²⁴ showed a significant decrease in SBP as well as DBP of normotensive subjects after following lifestyle modifications. Likewise, Ingole A et al²⁵ and Bhatnagar A et al¹² recorded a significant decrease in blood pressure of healthy subjects after following lifestyle interventions.

The present study demonstrated a significant reduction in systolic and diastolic blood pressure of group II elderly essential hypertensive patients in comparison of baseline values after participating lifestyle modifications program. These results were consistent with the prior studies of Paeolatti V et al,²⁶ and Svetkey LP et al,²⁷ in which they observed a significant decrease in both SBP and DBP after following lifestyle modifications. Alike, Cohen D L et al,²⁸ and Appel LJ et al⁴ exhibited a significant decrease in SBP and DBP after following lifestyle modifications program.

This decrease of blood pressure in elderly normotensive subjects and elderly essential hypertensive patients seems to be due to increased physical exercise along with restricted intake of energy through lifestyle modifications induce loss of weight as well as the decrease of BMI.²⁴ Further, obesity and increased BMI cause higher incidence of hypertension.^{10,18} The risk for cardiovascular diseases and blood pressure can be decreased by increasing physical activity and decrease alcohol consumption in elderly hypertensive patients.²⁹ Exercise improves the

endothelium functions and leads to decrease in peripheral resistance along with reducing in cardiomegaly in patients with stable chronic heart failure.³⁰ Furthermore, lifestyle modifications have been found effective in reducing blood pressure even modest physical exercise along with restricted dietary intake can cause a moderate decrease in blood pressure. In addition, multiple lifestyle interventions can lead to sustained blood pressure within normal limits.³¹

The findings of the current study revealed that there was a significant increase of GSH in elderly normotensive subjects which was consistent with the findings of the previous studies of Hegde SV et al,³² and Cheong KJ et al,³³ as they recorded a significant increase of GSH in normotensive subjects after following lifestyle modifications.

This study showed a significant increase of SOD in normotensive subjects which was similar to the findings of the previous studies of He LIU et al ³⁴ and Bhattacharya S et al.³⁵

In addition, the current present study demonstrated a significant increase of GSH level of group II elderly essential hypertensive patients. Jatuporn S et al³⁶ also observed a significant increase of GSH in patients with coronary artery disease. Findings of the present study exhibited a significant increase of SOD in elderly essential hypertensive patients which was similar to Bhatnagar A et al³⁷ as they demonstrated a significant decrease in GSH and SOD levels of elderly essential hypertensive patients.

This increase of GSH and SOD in normotensive elderly subjects seems to be due to exercise leads to increased consumption of oxygen which induces oxidative stress; however increased oxidative stress due to exercise, in turn, stimulate the production of antioxidants SOD and GSH.³⁸ Increased physical activity leads to decrease oxidative stress.³⁹ In addition, the present study was a combination of various lifestyle modification factors including yoga module. Yoga enhances the calm stage of mind and improves the vagal sympathetic balance.³⁸ Improve sympathetic and parasympathetic balance leads to decrease of oxidative stress.^{25,35} Furthermore, physical exercise induces increased oxygen consumptions resulting in increased ROS production, which further stimulate SOD generation.^{13,34} Moreover, lifestyle modifications decrease the weight which in turn decreases the LDL level and increase the HDL level; further, this decrease of LDL and increase of HDL prevent lipid peroxidation which results in decreased production of ROS.⁴⁰ Enhancement of GSH and SOD may be helpful in diminishing the consequences of chronic disease like hypertension as GSH and SOD have been found effective against harmful oxidative stressors.³³

MDA is a highly toxic molecule produced by oxidation of lipids.²⁵ Hypertension has been found associated with high level of MDA as it is produced by damage to the membrane polyunsaturated fatty acids via reactive oxygen species.⁴¹ A significant decrease of MDA was manifested in the present study which is consistent with the previous studies of Ingole A et al²⁵ and Hegde SV et al³² as they recorded significant decrease of MDA in normotensive subjects after following lifestyle modifications.

Further, in the present study a significant decline in serum MDA level of elderly essential hypertensive patients has been recorded which was consistent with the previous study of Agte VV et al,⁴² and Bhatnagar A et al³⁷ as they observed significant decrease of MDA in essential hypertensive patients after following various lifestyle interventions. Contrary to the current study Jatuporn S et al³⁶ did not observe any significant change in serum MDA level of coronary artery disease patients after following lifestyle modification program.

The findings of this study have demonstrated that lifestyle modifications decreased the adverse effects of lipid peroxidation reflected by a significant decrease of MDA as the practice of yoga improve the antioxidant defence of the body.⁴³ Regular physical exercises enhance antioxidant level via various signalling pathway results in decreased production of ROS.⁴⁴ This decrease of MDA as observed in the present study seems to be due to the increase of antioxidant level as it causes improvement in antioxidants defence which in turn leads to decreasing of reactive oxygen species resulting in decreased lipid peroxidation reflects as the decrease of MDA.⁴⁵ Regular practice of yoga facilitates calm stage of mind which further improves the balance of sympathetic and parasympathetic nerves activities.⁴⁶ Increased sympathetic activity is associated with higher BMI.⁴⁷ Further, improved balance of nervous system leads to decrease of metabolism and serum cholesterol which results in a decrease of free fatty acid as well as MDA.³³

These evidence are strongly advocating the fact that oxidative stress might be an important factor in developing and maintaining hypertension as a reduction of the oxidative stress is correlated with regression of target organ disease and normalization of metabolic activities; furthermore, hypotensive effects of medicines are not related with a decrease of oxidative stress. That is why antihypertensive treatment should be focused both: on hypotensive effect and oxidative stress.⁴⁸

However, a decrease in blood pressure as observed in the present study was more significant in elderly essential hypertensive patients in comparison of normotensive subjects. This higher decrease of blood pressure in hypertensive patients in comparison of normotensive subjects may be due to better improvement of oxidative stress in hypertensive in comparison of normotensive subjects as increase in antioxidant level may lead to decrease of lipid peroxidation which can result in decrease of blood pressure.^{39,43} Further, significant difference in improvement in hypertensive groups may be due to GSH and SOD are negatively whereas, MDA is positively correlated to blood pressure.⁴⁹ Increased antioxidant level leads to increase in bioavailability of NO which further helps in decrease of blood pressure.^{15,50}

Findings of the present study showed improvement in oxidative stress was more significant in hypertensive patients as SOD increased significantly in group II hypertensive patients compares to group I normotensive subjects. An insignificant change of GSH and MDA were observed in group II hypertensive patients in comparison of group I normotensive subjects.

This decrease in oxidative stress markers of hypertensive patients may be due to comparatively significant improvement of blood pressure in hypertensive group as

hypertension has been found associated with increased oxidative stress.⁶ Further, hypertension leads to increase level of ROS and decrease antioxidants level.¹

Conclusion

In this way, a decrease in oxidative stress along with hypertension as observed in the present study might decrease further deterioration of cardiovascular system and prevent cardiovascular diseases in elderly normotensive subjects and elderly hypertensive patients as increase oxidative stress is an impartible cause of hypertension. Further present study concluded that lifestyle modifications are effective for both the elderly population essential hypertensive and normotensive. However, current study showed that lifestyle modifications are more beneficial for essential hypertensive elderly patients compare to elderly normotensive subjects. Nevertheless, studies on larger populations are required to illustrate more precise and elaborate effect of lifestyle modifications on geriatric population both normotensive and essential hypertensive patients.

Limitation

The small size of study population was one of the most important limitations of the present study. Further, study does not assess the effects of lifestyle modifications individually in male and female of both essential hypertensive and normotensive elderly subjects.

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