# Effect of lifestyle modifications on oxidative stress in elderly essential hypertensive patients

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Received November 01, 2015. Accepted February 19, 2016

## Abstract

**Background:** Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in elderly people, while essential hypertension is a major risk factor for CVD. However, extensive experimental data support a role for increased reactive oxygen species levels and altered redox signaling in the pathogenesis of hypertension.

**Objective:** This study evaluates the effects of lifestyle modifications on oxidative stress and blood pressure in elderly hypertensive patients.

**Materials and Methods:** 83 hypertensive patients (49 males and 34 females) were recruited from Santosh Medical College, Ghaziabad, India for 3 months lifestyle modifications program which included morning walk, nadi shodan pranayama, dietary restrictions, and increase uptake of water.

**Result:** Post lifestyle modifications technique values revealed significant reduction of systolic blood pressure (p < 0.0001) and diastolic blood pressure (p < 0.0001) besides all fasting lipids decreased except LDL. Moreover, there was significant increase in the GSH (p < 0.0001) and SOD (p < 0.0001), whereas significant decrease in the MDA (p < 0.0001) was recorded.

**Conclusion:** In this study, lifestyle modification program improved cardiovascular risk factors such as hypertension and dyslipidaemia along with oxidative stress. Modest modification in lifestyle can have substantial effects on human health status which can be achievable and unavoidable in developing countries as it is economical. We emphasize more researches should be done on lifestyle modifications program to make future policies and guidelines.

KEY WORDS: Elderly, hypertension, lifestyle modifications, oxidative stress

# Introduction

Cardiovascular disease (CVD) is one of the leading causes of mortality and morbidity in modern societies, with prevention as well as treatment of the condition is a focus of recent attention.<sup>[1]</sup> Essential hypertension is major risk factor for CVD

Access this article online		
Website: http://www.ijmsph.com	Quick Response Code:	
DOI: 10.5455/ijmsph.2016.01112015383		

in spite of our advance understanding to its pathophysiology and availability of effective treatment strategies.<sup>[2]</sup> Endothelial dysfunction is the most significant pathological factor in producing hypertension; as endothelium is widely considered to be the largest endocrine gland in the human body. While mechanical damage, or loss of functional integrity, disturbs the homoeostasis of microenvironment, leading to the development of pathological states, such as hypertension or atherogenesis.<sup>[3]</sup> However, essential hypertension is a heterogeneous disorder with different patients having different causal factors including insulin resistance, obesity, high alcohol intake, sedentary life, high salt intake, aging, stress, low potassium intake, and low calcium intake. High blood pressure is one of the primary factors for the CVD.<sup>[2,4–6]</sup>

Reactive oxygen species participate in a variety of chemical reactions with biomolecules leading to a pathological condition

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known as oxidative stress.<sup>[7]</sup> Oxidative stress contributes to the process of aging as well as a variety of chronic degenerative diseases.<sup>[8]</sup> Moreover, extensive experimental data support a role for increased reactive oxygen species levels and altered redox signaling in the pathogenesis of hypertension.<sup>[9]</sup> Nevertheless, oxidative stress contributes to mechanisms of atherosclerosis and plaque instability. Biomarkers of oxidative stress, such as malondialdehyde (MDA), may represent independent indicators of risk for patients with stable coronary artery disease.<sup>[10]</sup>

A combination of diet and exercise ameliorates oxidative stress, inflammation, and monocyte-endothelial interaction whereas intensive lifestyle modification may improve novel coronary artery disease risk factors<sup>[11]</sup> as psychological stress increases oxidative stress whereas relaxation decreases it.<sup>[8]</sup> Lifestyle modifications are recommended as a non-pharmacological approach to treatment of hypertension because modifications of lifestyle not only have antihypertensive effects by themselves but also help in reducing the dose of drugs. In addition to dietary modification, exercise, moderation of alcohol consumption, and stopping smoking are important for hypertensive patients.<sup>[12,13]</sup> It has been suggested that yoga effectively reduces blood pressure, heart rate, body mass index, body weight, cholesterol level, blood glucose level along with it increases super oxide dismutase (SOD) and glutathione peroxidase level.[14-18] Similarly, sudarshankriya yoga significantly decreases diastolic blood pressure (DBP) and MDA.[19] Moreover, nadishodhan pranayama considerably reduces basal heart rate and systolic blood pressure.[20,21] Pharmacological treatment for hypertension is effective in reducing blood pressure, morbidity, and mortality from CVD. However, long-term pharmacological therapy can have adverse effects and requires continuous medical supervision. On the other hand, lifestyle modifications can have a real and significant reduction in blood pressure.<sup>[22]</sup> Therefore, this study was designed to analyze the effects of life style modifications on blood pressure changes, oxidative stress in elderly patients suffering from essential hypertension.

## **Materials and Methods**

#### **Study Population**

Study group consisted of 89 elderly patients (51 males and 38 females), between 60 and 80 years of age, suffering from essential hypertension diagnosed on the basis of long-term increase in blood pressure. All the patients were recruited from Santosh Medical College and Hospital, Ghaziabad, India and the research work was done from 20 June 2014 to 20 June 2015. However 6 patients (2 males and 4 females) left the study in between and 83 patients (49 males and 34 females) completed the lifestyle modifications. Inclusion criteria in the study were hypertension >140/90 mm Hg,<sup>[23]</sup> body mass index 18.5–25 kg/m<sup>2</sup>, non alcoholics and non-smokers. None of the subjects was suffering with any type of chronic disease, for example, diabetes mellitus, tuberculosis,

renal failure, thyroid disorder, etc. Subjects were not on antihypertensive medicines, any other medication or hormone replacement therapy.

All of the patients received detailed information regarding the purpose and nature of the study and gave their inform consent before enrolment for the lifestyle modifications program. This study was approved by ethical committee of Santosh University NCR, Ghaziabad, India.

## Lifestyle Modifications

Patients suffering from essential hypertension were asked to modify their day to day life style for 3 months by performing yogic exercise "**Nadi Shodhan Pranayama**" (forced one side nostril breathing) on an empty stomach for 20 min, early morning 6 days in a week, restricting salt intake up to 100 m Eq/day, lowering fat intake up to 44–77g, increasing intake of water 2–3 litres per day, daily sleep of minimum 5–6 h, and morning walk of 2 miles (3.2 km) for 6 days in a week.

#### Measurements

## Blood Pressure

All the measurements and blood samples were collected in the morning empty stomach before and after intervention of life style modifications. Subjects were asked to sit quietly in comfortable position for 10 min and then blood pressure was measured three times by auscultatory method at every 10 min interval by Sphygmomanometer (manufactured by Diamond Regular India).

## **Biochemical Parameters**

Serum concentration of total cholesterol (TC) was estimated by the enzymatic CHOD-POD method.<sup>[24]</sup> Serum concentration of triglycerides (TG) was measured by the GPO-PAP method.<sup>[24]</sup> Serum concentration of high density lipoprotein (HDL) was measured by CHOD-POD/phosphotungstate method.<sup>[24]</sup> Serum concentration of low density lipoprotein (LDL) was calculated by using Friedewald's formula: LDL cholesterol = total cholesterol – HDL cholesterol – [triglycerides/5].<sup>[24]</sup>

Markers of oxidative stress glutathione (GSH) and SOD were estimated in serum sample using enzyme linked immunosorbent assay (ELISA),<sup>[25,26]</sup> whereas MDA in serum was estimated by thiobarbituric acid method (TBA).<sup>[27]</sup> ELISA kits for GSH and SOD manufactured by Qayee-Biotechnology Co. Ltd Shanghai, China were used. TBARS assay kit manufactured by Cayman chemical company, Ann Arbor, USA was used. Elisa Reader of Robonik (India) Pvt. Ltd. and Biochemistry Analyser E-C5VZ(10k) manufactured by Transasia (India) were used for the biochemistry analysis.

#### **Statistical Analysis**

The results were expressed as mean  $\pm$  SD (Standard deviation of Mean). To compare the values obtained before and after lifestyle modifications, paired student's *t*-test was used. Pearson correlation on the entire data was used to test whether GSH, SOD, and MDA were correlated with blood pressure. A *p*-value < 0.05 was considered statistically significant. IBM SPSS Statistics 21 manufactured by IBM USA was used for entire calculations.

## Result

Total 83 patients, aged 66.81 ± 5.22 years completed lifestyle modifications of 3 months. Table 1 shows that lifestyle modifications have significantly decreased SBP (165.08 ± 11.04 vs. 156.77 ± 10.56, p < 0.0001) and DBP (106.75 ± 8.82 vs. 100.67 ± 7.98, p < 0.0001). Beside this, other parameters of cardiovascular disease, heart rate, pulse pressure, and mean arterial pressure showed significant decrease in baseline values after lifestyle modifications [Table 1].

Further, we observed significant changes in lipid profile shown in Table 2. TC, TG, and LDL showed significant decrease of  $9.68 \pm 2.95$ ,  $4.9 \pm 1.1$ ,  $7.12 \pm 0.23$ , respectively, from base line values whereas HDL significantly increased from base line value ( $1.19 \pm 0.51$ , p < 0.0008).

Oxidative stress markers are presented in Figure 1. It shows that baseline values of GSH and SOD significantly increased to (87.77  $\pm$  8.63 ng/mL vs. 95.04  $\pm$  9.31 ng/mL), (68.88  $\pm$  15.02 ng/mL vs. 77.5  $\pm$  15.51 ng/mL), respectively. However, baseline value of MDA significantly decreased (5.99  $\pm$  0.68m mol/mL vs. 4.85  $\pm$  0.86 m mol/mL). The results further revealed that GSH and SOD had negative correlation with

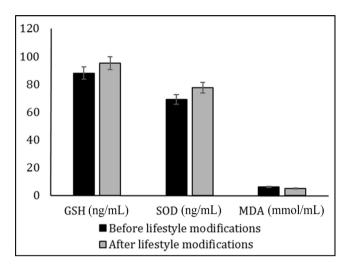


Figure 1: Changes in oxidative stress (GSH, Glutathione total; SOD, superoxide dismutase; MDA, malondialdehyde).

both SBP and DBP. On the other hand, MDA had a positive correlation with SBP and DBP [Table 3].

## Discussion

Hypertension can result in various diseases and there are several lines of treatment for hypertension in early stage;

Table 1: Comparison of pre and post lifestyle modifications values of blood pressure and heart rate

Parameters	Before lifestyle modifications	After lifestyle modifications	P-value	t-value
Systolic blood pressure mmHg	165.08 ± 11.04	156.77 ± 10.56	<0.0001	15.29
Diastolic blood pressure mmHg	106.75 ± 8.82	100.67 ± 7.98	<0.0001	13.33
Heart rate	$77.83 \pm 5.58$	75.76 ± 4.29	<0.0001	6.03
Pulse pressure	58.07 ± 7.43	56.19 ± 7.17	<0.0001	16.78
MAP	126.3 ± 8.72	119.42 ± 8.35	<0.0001	16.78

Values expressed as mean±SD; MAP, mean arterial pressure; SD, Standard deviation of mean.

Table 2: Changes in	lipid profile after	following lifestyle	modifications
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Parameters	Before lifestyle modifications	After lifestyle modifications	P-value	t-value
Total cholesterol (mg/dL)	223.22 ± 28.35	213.54 ± 25.4	<0.0001	11.12
Triglycerides (mg/dL)	137.61 ± 25.58	$133.52 \pm 24.68$	<0.0001	7.43
HDL (mg/dL)	41.17 ± 5.74	42.36 ± 5.23	<0.0008	3.49
LDL (mg/dL)	154.46 ± 22.79	147.35 ± 22.56	<0.0001	9.47

Values expressed as mean±SD; HDL, high density lipids; LDL, low density lipids; SD, standard deviation of mean.

Table 3: Pearson correlation between oxidative stress and blood pressure

Oxidative stress	Systolic blood pressure		Diastolic blo	od pressure
GSH	$r^2 = -0.194$	<i>P</i> <.0001	$r^2 = -0.055$	<i>P</i> <0.0001
SOD	$r^2 = -0.12$	<i>P</i> <.0001	$r^2 = -0.058$	<i>P</i> <0.0001
MDA	$r^2 = +0.046$	<i>P</i> <.0001	$r^2 = +0.024$	<i>P</i> <0.0001

GSH, Glutathione total; SOD, superoxide dismutase; MDA, malondialdehyde.

although, the results vary from person to person. Nevertheless, in last few years, studies have shown that lifestyle modifications can reduce blood pressure in hypertensive patients.<sup>[28,19]</sup> Investigators have suggested though there is a lot of advancement in our understanding of its pathophysiology and effective modus operandi of treatment; most of the hypertensive patients require two or more medicines. Nonetheless, the hypertension and its concomitant remain uncontrolled, especially in elderly, having systolic blood pressure >160 mmHg.<sup>[29]</sup>

Our study recorded significant reduction in systolic and diastolic blood pressure in comparison of baseline values after 3 months of lifestyle modifications. The results of this study are similar to that of Svetkey et al.<sup>[30]</sup> where lifestyle changes significantly reduced systolic and diastolic blood pressure. Likewise Jiro et al.[31] recorded that regular exercise significantly reduces systolic and diastolic blood pressure in mild hypertensive patients. Various researches have suggested diverse mechanism of decrease in blood pressure; as Pal et al. suggested that increased sympathetic activity and vagal inhibition is reflection of autonomic imbalance in prehypertensive patients although yoga and exercise reestablish the sympathovagal imbalance and blood pressure hemostasis in prehypertensive patients.<sup>[32,33]</sup> We observed a significant decrease of heart rate, pulse pressure, and mean arterial pressure in our study as yoga has been found effective in reducing heart rate and blood pressure by affecting baroreflex sensitivity.<sup>[34]</sup>

Increased level of lipid profile is more common in untreated hypertensive than normotensive, and lipid levels are directly related to increase of blood pressure.[35,36] In this study, lifestyle modifications have significantly reduced TC, TG, and LDL concentrations though increased the HDL level. Similarly, Agrawal et al. showed significant reduction in serum TC, LDL, and triglyceride concentrations beside considerable increase in HDL concentrations after 3 months of yoga.<sup>[37]</sup> Agte et al. recorded moderate decrease of serum TC and TG in type 2 diabetic patients after 4 month's Sudarshan kriya yoga.[15] Alike effects of yoga was observed by Lorenzo et al.[38] Decline in lipid profile along with blood pressure may decrease the risk for CVD in elderly hypertensive patients as previous studies revealed that increase in TC level, particularly in the presence of hypertension has been associated with coronary artery disease.[39-41] Moreover, studies have suggested that management of arterial hypertension should focus both on lowering high blood pressure and correcting associated dyslipidaemia.[42,43]

Previous studies have shown that uncontrolled reactive oxygen species are pivot of many pathological conditions; various cardiovascular diseases have been affected by reactive oxygen species to different degrees.<sup>[44,45]</sup> However, alteration in oxidant and antioxidant status in early stage of hypertension is reported. It is found that more than one factor are included in development of hypertension; therefore, hypothetical role of oxidative stress in development of hypertension cannot be ruled out.<sup>[46–48]</sup> We have observed in our study that there is a significant enhancement in SOD activity by 12.57% which is near to the results of Gorden et al. as they observed 24.08% and 20.18% inflation in hath yoga group and conventional PT

exercise group, respectively.<sup>[49]</sup> On the other hand, we recorded increase of GSH level by 8.28% after lifestyle modifications which are nearly to the findings of Cheong et al. and Sinha et al.[50,17] 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.<sup>[50]</sup> Furthermore, both SOD and GSH have shown negative correlation with hypertension in our study which is similar to negative correlation reported in previous studies.<sup>[51,52]</sup> MDA is found elevated in hypertensive subjects as it is produced due to damage of the membrane polyunsaturated fatty acids by reactive oxygen species.[45] In this study, we observed a significant reduction in serum MDA level by 19.03% after lifestyle modifications, which is very similar to the findings of Gordon et al. 18.1% decrease in hath yoga group and 19.9% in conventional PT exercise group. Similarly, Patil et al. observed decline of 20.54% whereas Singh et al. recorded significant decrease after yoga. Moreover, MDA has shown positive correlation with blood pressure in our study which is similar to previous studies.[49,53,54] This decline in MDA level suggests the reduction of cardiovascular risk for elderly hypertensive patients as MDA is the independent risk factor for CVD.<sup>[10]</sup> Finding of this study has demonstrated that lifestyle modifications decrease the adverse effects of lipid peroxidation as MDA had been significantly induced by Yoga may be due to its up regulation.[49,55]

In this study, we observed decrease of lipid profile along with oxidative stress; moreover, decrease level of oxidative stress has shown positive correlation with blood pressure. These evidences are strongly advocating the fact that oxidative stress might be an important factor in developing and maintaining the hypertension as 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 decrease of oxidative stress. That is why antihypertensive treatment should be focused both: on hypotensive effect and oxidative stress.[56] However, dyslipidaemia, hypertension, and lipid peroxidation are directly related to the severity of atherosclerosis. If elimination of free radicals in the plasma takes place before the peripheral tissues take them up, it might reduce atherosclerosis. Therefore, a management strategy aimed at simultaneously reducing lipid peroxidation and increasing total antioxidant status in dyslipidaemic patients may be beneficial.[57]

# Conclusion

In this study, lifestyle modifications program improved cardiovascular risk factors such as hypertension and dyslipidaemia along with oxidative stress. Modest modification in lifestyle can have substantial effects on human health status which can be achievable and unavoidable in developing countries as it is economical. We emphasize further research should be done on lifestyle modifications program to make future policies and guidelines for elderly hypertensive patients.

## Acknowledgment

Our sincere thanks to the Santosh University for their support. We are also very thankful to the staff of physiology department of Santosh Medical College for their assistance and elderly hypertensive participants for their courage and endless efforts for this study.

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**How to cite this article:** Bhatnagar A, Dhar U, Tripathi Y. Effect of lifestyle modifications on oxidative stress in elderly essential hypertensive patients. Int J Med Sci Public Health 2016;5: 1942-1947

Source of Support: Nil, Conflict of Interest: None declared.