Original Research Article

Biochemical changes in patients of syndrome "Z" after anti-oxidant treatment

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Abstract

Background: Syndrome "Z" refers to the co-occurrence of obstructive sleep apnea (OSA) and metabolic syndrome (MS). We had reported previously that in patients with OSA syndrome (OSAS), oral intake of N-acetylcysteine (NAC) improved their sleep parameters by decreasing oxidative stress. The present study reports the effect of NAC on some components of MS in these patients. **Materials and methods:** Twenty patients with symptoms suggestive of OSAS and MS underwent overnight polysomnography for confirmation of diagnosis of OSAS. Subsequently, all patients received either NAC (n=10, 600 mg thrice daily) or placebo (n=10) for 30 days. Fasting venous samples were collected and analyzed before and after specific treatments. **Results:** In the NAC group, after the treatment period, compared to their baseline values, there were significant decreases in serum homocysteine, insulin resistance, triglycerides, total cholesterol and LDL cholesterol levels. A significant increase in serum thiol levels as well as a significant decrease in systolic blood pressure was also observed. Such effects were not seen in the placebo treated group. **Conclusion:** Oral intake of NAC for one month showed therapeutic potential in the 20 patients of syndrome "Z in our study. This can form the base for large multicentric randomized control trials to extrapolate the results to the general population.

Keywords: metabolic syndrome, N-acetylcysteine, oxidative stress, sleep apnea

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Introduction

Obstructive sleep apnea (OSA) is a highly prevalent and under diagnosed clinical condition that has been associated with an increased incidence of cardiovascular disease.[1] In northern India, the prevalence of OSA is 13.7%.[2] Along with OSA, when there is excessive day time sleepiness, the condition is referred to as obstructive sleep apnea syndrome (OSAS) the incidence of which is reported to be as 3.8%.[2] This data is comparable to that of the western countries.[3] Risk factors for OSA include obesity, craniofacial abnormalities, smoking, male gender, short neck, alcoholism, and menopause in women.[4] Obesity is one of the main risk factors of OSA as 60% to 90% of these patients are obese and there is a strong positive correlation between body mass index (BMI) and OSA.[5] Metabolic syndrome (MS), also known as insulin resistance syndrome or syndrome X is an assemblage of cardiovascular risk factors like obesity, glucose intolerance, dyslipidemia, and hypertension.[6] The co-occurrence of OSA and MS is termed as syndrome "Z".[7] The presence of both these conditions act synergistically to increase the risk for cardiovascular disease in such patients. The prevalence of syndrome "Z" in India ranges from 4.5% in population-based study[8] to 79% among patients with OSA in hospital-based study.[9]

OSA is characterized by recurrent nocturnal intermittent hypoxia. Following hypoxia, there is a fall in oxygen saturation that normalizes after

cessation of apnea/hypopnea. This cyclical desaturation and reoxygenation mimics ischemia-reperfusion injury. Such damage leads to production of reactive oxygen species (ROS) during reoxygenation.[10,11] Overproduction of ROS initiates a low grade systemic inflammation which is a prominent feature of not only OSA but also MS.[12,13]

Recent studies performed by us and others demonstrated that there was oxidative stress in patients with OSAS.[14,15,16,17] Oral intake of the anti-oxidants vitamins C and E or NAC not only reduced the oxidative stress but also improved the sleep characteristics like sleep efficiency, oxygen desaturation events, snore duration, Epworth's sleepiness score etc.[16,17] Since the patients we investigated had MS also, making them patients with syndrome "Z", we hypothesized that anti-oxidant intake would alleviate the determinants of MS with the result they would be less prone to cardiovascular morbidities. The present investigation throws some light on these issues.

Materials and Methods

The study was conducted in the Department of Physiology, in conjunction with Department of Respiratory Medicine, at Vallabhbhai Patel Chest Institute (VPCI), Delhi, in accordance with the ethical guidelines for biomedical research on human subjects by Central Ethics Committee on Human Research (CECHR), Indian Council of Medical Research (ICMR)-2000 and those as contained in "Declaration of Helsinki".

Subjects: The subjects included in the present study were the same in whom we investigated the effects of oral intake of NAC on the various polysomnography parameters in our earlier study. Patient selection criteria and detailed patient profile could be accessed from the previous study.[17] Briefly, a total of 88 subjects (52 men and 36 post menopausal women) referred to Sleep center, Department of Respiratory Medicine, at Vallabhbhai Patel Chest Institute (VPCI), Delhi, with suspected OSAS were enrolled.

They were screened on the basis of obesity (BMI >25), short neck, history of snoring and excessive day time sleepiness (EDS). All subjects completed the Epworth sleepiness scale (ESS) questionnaire. A score of greater than 10 on ESS was taken as evidence for EDS.[18]

Patients were also asked about their demographics, sleep habits and symptoms, medical history, medication use including intake of anti-oxidants, antidiabetic and antihypertensive drugs, alcohol consumption and smoking habits.

Among the 88 patients screened, 25 patients were eligible for polysomnography as they had features suggestive of syndrome "Z". A patient was considered to have syndrome "Z" if they had three or more of the following risk factors: abdominal obesity of 90 cm for men and 80 cm for women, as recommended by the World Health Organization guidelines for South Asians. Triglycerides ≥ 150 mg/dl, HDL cholesterol<40 mg/dl (male), < 50 mg/dL (female), blood pressure ≥ 130/85 mmHg (or treated for hypertension), and fasting glucose ≥ 110 mg/dl along with OASAS. OASAS was deemed to be present if the apnoea hypopnoea index (AHI) was ⩾5 on performing an overnight polysomnography.

The remaining 63 patients were having either one or any two of the symptoms, and hence, were not included in the study. Out of the remaining 25 patients, 23 agreed to undergo an overnight polysomnography. However, only 20 of them (13 adult males and 7 postmenopausal females) remained for the full length of the study. None of them was a smoker or alcoholic. The purpose of the study and the procedures involved were explained to the subjects and written consent was obtained from all of them.

Polysomnography: The details are given in our previous study.[17] A split-night (diagnostic and continuous positive airway pressure (CPAP) titration done on the same night) polysomnography was performed in all of the subjects. Data acquisition started from 9 pm and continued until 6 am on the following morning. All subjects were acclimatized in the sleep laboratory one night prior to sleep study.

The diagnosis of OSA was confirmed using standard polysomnography (RemlogicTM version 1.1, Embla N7000, Medcare, Netherland) with a standard montage of electroencephalogram (EEG), electro-oculogram (EOG) and electromyogram (EMG) signals, pulse oximetry, respiratory impedance, nasal airflow measurements, thoracoabdominal movements, limb movements, body position and ECG. Sleep studies were analyzed by a technician using computer software. CPAP titration was done using a mask and apparatus (Respironics, PA) according to the

American Academy of Sleep Medicine (AASM) guidelines.

Patients were then put either on N- acetyl cystenine (NAC) (Mucinac, Cipla) 600 mg thrice daily or placebo orally for 30 days. After 30 days, the patients were again assessed by the same sleep questionnaire and ESS. A repeat split night sleep study was performed.

Anthropometry: Height was measured using a wall-mounted stadiometer to the nearest 0.5 cm, and weight was measured to the nearest 0.1 kg with a calibrated scale (Omron digital body weighing machine) without shoes. Waist circumference was measured to the nearest 0.5 cm in duplicate around the smallest circumference midway between the iliac crest and the lowest lateral portion of the rib cage using a nonstretchable tape. BMI was calculated as weight in kilograms (kg) divided by the square of height in meters (kg/m^2). The circumference of the neck was measured at the cricothyroid membrane level. All the measurements were performed by the same observer.

Blood pressure: Systemic arterial blood pressure was measured in supine position before (9 pm) and after sleep study (6 am) after a 5-min rest. It was recorded as the mean of three measurements taken at 2-min intervals, using a periodically calibrated mercury sphygmomanometer, to the nearest 2 mm Hg in accordance with the British Hypertension Society guidelines.[19]

Biochemical investigations: Blood samples were collected by venipuncture before (9 pm) and after sleep (6 am) and after an overnight fasting. Similar protocol was followed when the subjects came for the follow up study after 30 days. All the samples collected were stored at -80^{o}C before subjecting them to biochemical analysis. The measurements were done in triplicate for concordance in values.

Serum fasting glucose: Fasting glucose was measured after an overnight fast in whole blood by colorimetric method using glucose oxidase as described by Chernecky et al (2004).[20] Glucose is determined after enzymatic oxidation in the presence of glucose oxidase. The formed hydrogen peroxide reacts under catalysis of peroxidase with phenol and 4-aminophenazone to form a red-violet quinoneime dye as indicator. The absorbance of the reaction is biochromatically measured at 505 nm.[20]

Insulin resistance: Quantitative measurement of fasting levels of serum insulin was done using commercially available insulin ELISA kits (The Calbiotech, Inc. (CBI) Insulin ELISA kit). The insulin ELISA is a solid phase two-site enzyme immunoassay. It is based on the direct sandwich technique in which two monoclonal antibodies are directed against separate antigenic determinants on the insulin molecule. During incubation insulin in the sample reacts with peroxidase-conjugated anti-insulin antibodies and anti-insulin antibodies bound to microtitration well. A simple washing step removes unbound enzyme labeled antibody. The bound conjugate is detected by reaction with 3,3',5,5'-tetramethylbenzidine (TMB). The reaction is stopped by adding acid to give a colorimetric endpoint that is read spectrophotometrically.[21]

Insulin resistance was assessed from fasting glucose and insulin values using homeostasis model assessment (HOMA) calculations, previously validated against the hyperinsulinaemic euglycaemic clamp.[22] Insulin resistance was calculated via Homeostasis model assessment (HOMA) as follows:

$$\frac{\text{Fasting serum insulin } (\mu U/m) \times \text{serum glucose } (mg/dl)}{405}$$

Measure of oxidative stress - Serum thiol assay: Reaction mixture contained 900ml 0.2M NaHPO4 containing 2mM Na_2 EDTA, 100 ml plasma, 20 ml of 10mM DTNB in 0.2M NaHPO4. Absorbance taken at 412 nm 37°C for 5 min and max absorbance was noted. Similarly absorbance of sample blank and reagent blank were measured. Absorbance of sample blank and reagent blank was subtracted from plasma absorbance values to obtain corrected values. The concentration of thiol was calculated using standard curve obtained using glutathione dissolved in phosphate buffer saline.[23]

Measure of anti-oxidative capacity - Serum homocysteine: Serum homocysteine assay was done using commercially available kits {The Axis® Homocysteine Enzyme Immunoassay (EIA)}. Axis® Homocysteine EIA determines homocysteine in blood.[24] Protein-bound homocysteine is reduced to free homocysteine and enzymatically converted to S-adenosyl-L-homocysteine (SAH) in a separate procedure prior to the immunoassay.[25] The enzyme is specific for the L-form of homocysteine, which is the only form present in the blood.

Lipid profile: Triglyceride, high-density lipoprotein (HDL) cholesterol, and total cholesterol levels were measured in the hospital laboratory by means of a standardized immunocolorimetric assay, and the low-density lipoprotein (LDL) cholesterol level was calculated with the use of the Friedewald equation.[26]

Metabolic Syndrome (MS): MS was diagnosed according to the National Cholesterol Education Program (NCEP) guidelines.[27] Patients had MS if they had three or more of the following risk factors: abdominal obesity of 90 cm for men and 80 cm for women, as recommended by the World Health Organization guidelines for South Asians.[28] Triglycerides ≥ 150 mg/dl, HDL cholesterol<40 mg/dl (male), < 50 mg/dl (female), blood pressure ≥ 130/85 mmHg (or treated for hypertension), and fasting glucose ≥ 110 mg/dl.

Statistical analysis: All the data were expressed as means ± SEM (standard error of mean). Paired t-test with two-tail significance was used to compare the changes in study parameters in the same patient before and after the treatment. Unpaired t-test was used to compare the baseline data in the placebo and NAC groups. The tests were considered significant if they yielded $p<0.05$.

Results

The results presented here are the data collected from 20 OSAS patients with MS who stayed for the full length of the study.

The changes in polysomnography parameters following NAC intake were reported in our previous publication.[17] Briefly, there were significant improvements in the sleep parameters such as an increase in time spent in stage 3 of non rapid eye movement sleep as well as sleep efficiency. There were significant decreases in the apnea-hypopnea index and oxygen desaturation events.

Even the snore characteristics like relative snore time, number of snore episodes and longest snore episode duration, all decreased significantly. [17] The optimal CPAP pressure also decreased significantly post NAC intake.[17] Three patients who required CPAP earlier did not require it after treatment with NAC. [17] Their overall quality of life improved as evident from the significant decrease in ESS. [17]

Effects on anthropometric variables and components of MS: At baseline, the patients in both groups (NAC and placebo) did not differ significantly in age, BMI, neck circumference, waist circumference, pulse rate, blood pressure, insulin resistance and lipid profile.

Whereas after treatment with NAC, there were significant decreases in systolic blood pressure, insulin resistance (due to decreases in fasting insulin as well as fasting glucose), triglyceride, total cholesterol and LDL cholesterol; there was also a significant increase in HDL cholesterol. Even though there was a decrease in diastolic blood pressure, it did not reach statistical significance. These results are presented in Table 1.

Oxidant-anti-oxidant status: We had shown that compared to normal subjects, there was oxidative stress in OSAS patients as evidenced by an increase in lipid peroxidation and a decrease in reduced glutathione levels which improved after oral intake of vitamins C and E or NAC.[16, 17]

In this study, two additional oxidative stress markers namely serum homocysteine and thiol were measured. Serum homocysteine has been reported to be an independent risk factor for vascular disease. [29] Thiols are extraordinarily efficient endogenous anti-oxidants which protect the cells against free radical induced injury. [30]

Serum homocysteine: In the placebo group and the NAC group, the baseline serum homocysteine levels were 28.6 ± 1.5 and 28.7 ± 1.9 µmol/L respectively. In the NAC group, after the treatment period, the homocysteine levels decreased significantly to 19.2 ± 1.8 µmol/L ($p<0.001$, Figure 1). No significant change in the homocysteine level was observed in the placebo group after the treatment period and it remained as 28.9 ± 1.8 µmol/L (Figure 1).

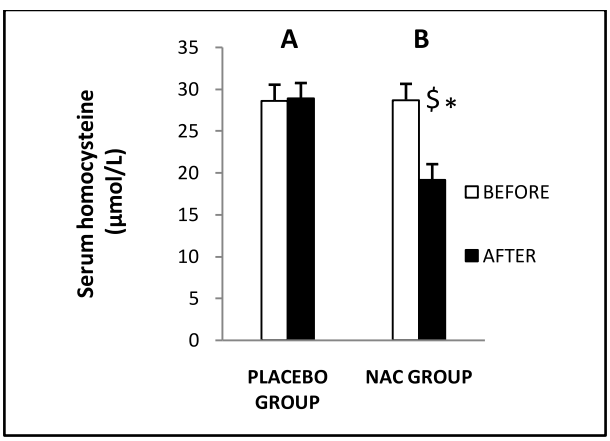
Serum thiol: The baseline serum thiol levels in the placebo group and the NAC group were 201.2 ± 12.6 and 207.9 ± 16.2 µmol/L respectively. After the respective treatment periods, the thiol levels were 207.0 ± 14.2 and 346.4 ± 11.1 µmol/L respectively. The increase observed in the NAC group was statistically significant ($p<0.001$, Figure 2).

Table 1: Effects of treatment with placebo or N-acetylcysteine (NAC) on anthropometric variables and components of metabolic syndrome

Parameters	Placebo group (n=10)		NAC group (n=10)	
	Baseline	Placebo	Baseline	NAC
Age (years)	56.2±3.1		53.1±2.3	
Body weight (kg)	82.8±5.0	82.8±5.0	84.8±4.7	84.6±4.6
Body mass index (kg/m^2)	32.9±2.3	32.9±2.3	34.8±2.4	34.8±2.4
Neck circumference (cm)	39.1±1.2	39.1±1.2	38.9±0.9	38.9±0.9
Waist circumference (cm)	111±1.7	111±1.7	112.5±2.3	112.5±2.3
Systolic blood pressure (mmHg)	130.2±4.8	130.0±4.0	133.8±2.4	128.4±2.1*
Diastolic blood pressure (mmHg)	86.4±2.5	85.2±3.5	86.4±2.2	81.8±1.2$^{\$}$
Pulse rate (/min)	70.5±3.0	71.4±3.0	75.0±2.7	72.2±2.3
Fasting blood sugar (mg/dl)	126.5±6.3	127.5±6.6	129.8±7.0	101.9±2.5**$^{\$\$}$
Fasting serum Insulin (µU/ml)	24.5±0.6	24.6±0.6	24.5±0.7	22.9±1.3*$^{\$}$
Insulin resistance (HOMA-IR)	7.6±1.1	7.9±1.0	7.9±1.1	5.7±0.9**$^{\$\$}$
Triglycerides (mg/dl)	162.8±5.3	161.5±4.6	159.5±8.6	125±4.2**$^{\$\$}$
Total Cholesterol (mg/dl)	215.3±6.1	213±5.0	224±5.7	189±6.9**$^{\$\$}$
HDL (mg/dl)	39±10.2	38±7.2	30±13.5	37±11.2**
LDL (mg/dl)	116±9.6	115±6.6	112±8.1	101±9.9**$^{\$\$}$

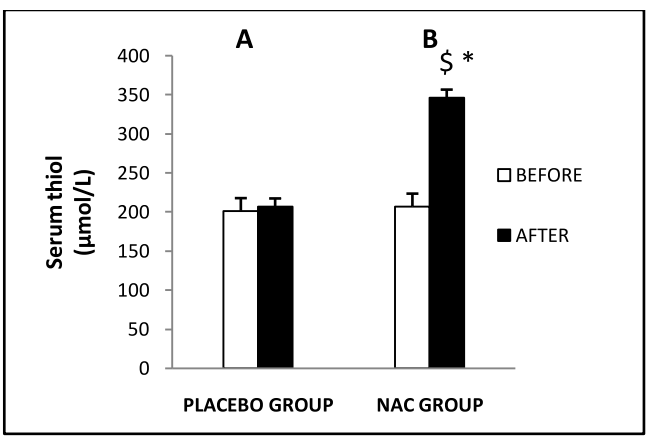
*p<0.05, **p<0.01 vs corresponding baseline. $^{\$}$p<0.05, $^{\$\$}$p<0.01 vs placebo group., HDL = high density lipoprotein; LDL = low density lipoprotein. Values expressed as Mean± SEM; A part of this data was included in our previous publication.[17]

Figure 1: Serum homocysteine levels in placebo and NAC groups



Note the significant decrease after NAC intake in B.*p<0.001, compared to its corresponding baseline value and $^{\$}$p<0.001, compared to placebo group

Figure 2: Serum thiol levels in placebo and NAC groups



Note the significant increase after NAC intake in B. *p<0.001, compared to its corresponding baseline value and $^{\$}$p<0.001, compared to placebo group.

Discussion

This study shows several key findings. All patients of OSAS had MS, thus categorizing them to have syndrome "Z". When these patients were treated with NAC, along with an improvement in the sleep parameters including the quality of life (as reported by us previously),[17] there were significant ameliorations in the various components of MS as evidenced by significant decreases in systolic blood pressure, lipid profile and insulin resistance. Also there was an increase in the antioxidant capacity and a reduction in oxidative stress as noted by an increase in serum thiol and decrease in serum homocysteine levels.

Blood pressure: The presence of hypertension seems to be the factor most closely associated with the presence of MS in a patient with OSA.[31] About 50% of patients with OSA and all patients of syndrome "Z" have daytime hypertension.[32, 33] In the present study, in our patients with syndrome "Z", both the systolic and diastolic blood pressures were raised in accordance with the NCEP guidelines for diagnosis of and the systolic blood pressure in these patients decreased significantly after treatment with NAC (Table 1). There was a tendency for a decrease in the diastolic blood pressure also even though it did not reach statistical significance (Table 1). Even though the changes in blood pressure were reported by us previously,[17] we did not pay much attention to it until we combined it with the other components of MS which are reported now.

This increase in baseline blood pressure observed in patients with OSAS could be due to several reasons. For instance, it could be due to a reduction in nitric oxide (NO) production. Due to the nocturnal desaturations occurring in OSAS patients, there is decreased availability of oxygen which may result in reduced synthesis of NO. Also the nocturnal hypoxia may suppress the transcription of the endothelial NOS gene and the stability of its mRNA as suggested by cell culture experiments performed under hypoxic conditions.[34] Finally, it may be due to decreased availability of NO as NO is scavenged by free oxygen radicals generated under conditions of hypoxia–reoxygenation by circulating neutrophils.[35]

Oxidative stress could have contributed to the blood pressure rise also. Reactive oxygen species (ROS) have been implicated in the experimentally induced hypertension produced by administering N-nitro-l-arginine methyl ester (L-NAME) in rats. Chronic treatment with NAC attenuated the hypertension.[36] Increased ROS production after L-NAME caused augmentation of lipid peroxidation as evidenced by the elevated levels of CD (cluster of differentiation) in the heart and kidney. By lowering superoxide levels, NAC decreased the levels of CD. NAC also enhanced the activity of NOS, probably by protecting its essential cofactor, tetrahydrobiopterin from oxidation by the excess superoxide. Further, it was reported that anti-oxidant treatment with NAC or melatonin, augmented NO-dependent vasodilation in spontaneously hypertensive rats.[37, 38] All these studies indicate that treatment with anti-oxidants reduces blood pressure when there is hypertension. The present results in patients with OSAS support these findings. The failure to observe a statistically significant decrease in diastolic blood pressure could be because of the low sample size or because the NAC treatment was given for a period of 30 days only.

Along with reducing oxidative stress and enhancing NO dependent peripheral vasodilation, anti-oxidant therapy could influence blood pressure by other mechanisms also. It has been reported that the enhanced sympathetic vasoconstriction in rats with L-NAME hypertension results from the inhibition of NOS in the rostral ventrolateral medulla (RVLM).[39] It is known that an increase in NO bioavailability in the RVLM lowers high blood pressure by attenuating sympathetic outflow.[40] Thus, it is proposed that with chronic anti-oxidant intake, there would be an increase in central NO especially in areas such as RVLM which would reduce the sympathetic outflow resulting in a decrease in arterial blood pressure. Indeed, there is evidence that with chronic NAC treatment, there is complete prevention of the development of salt hypertension in Dahl rats due to a strong attenuation of the sympathetic mediated blood pressure rise.[41] Thus, the reduction in blood pressure observed after treatment with NAC in the present study could be due to both the peripheral as well as the central mechanisms.

Free radicals and anti-oxidant status - Serum homocysteine: Moderate hyperhomocysteinemia (>14 μM) has been shown to be an independent risk factor for vascular disease.[29] The deleterious effects of raised homocysteine have been postulated to involve the production of ROS.[42] Further, homocysteine has been shown to influence oxidative stress responsive signal transduction pathways.[43] The anti-oxidant enzyme glutathione peroxidase, catalyzes the reduction of both hydrogen and lipid

peroxides to their corresponding alcohols in a reaction that involves the oxidation of glutathione. By reducing these peroxides to alcohols, glutathione peroxidase prevents inactivation of NO.[44] Homocysteine inhibits glutathione peroxidase activity and leads to a dramatic reduction in steady state mRNA levels for the intracellular NO isoform in endothelial cells.[42] Importantly, these effects occur at concentrations of homocysteine that are pathophysiologically relevant. Jordan et al (2004) [45] reported that untreated OSA patients had raised serum homocysteine. In agreement with Jordan's study, we also found increased levels of serum homocysteine in our patients (Figure 1). We further observed that the serum homocysteine levels decreased after treatment with NAC (Figure 1). These findings are in agreement with Yilmaz et al (2007) [46] who reported that NAC lowered plasma homocysteine levels and improved endothelial function. It is pertinent to mention here that in the present study, the homocysteine level did not decrease below 14 µM with the NAC treatment. It is proposed that there may be a further decrease if the NAC treatment is continued for a longer period.

Serum thiol levels: Thiols protect cells against damage induced by free radicals, due to their ability to react with them.[30] They assist aerobic cells in maintaining a reducing state despite an oxidizing environment.[47] In our study on patients with OSAS, we found decreased levels of serum thiols that increased after treatment with NAC (Figure 2). These findings further support the contention that patients of OSAS have reduced antioxidant capacity.[16, 17]Combining the present results with our previous observations demonstrating that NAC reversed the increased lipid peroxidation and decreased reduced glutathione in patients with OSAS,[17] it is proposed that oral intake of anti-oxidants could reduce blood pressure by decreasing the oxidative stress.

Insulin resistance: Multiple factors promote insulin resistance and glucose intolerance in patients of syndrome "Z". Punjabi *et al.* (2002) reported insulin resistance even in mild forms of sleep apnea.[48] Interestingly Ip and associates observed an association between OSA and insulin resistance, even in non-obese subjects.[49] The patients with OSAS investigated in the present study were clearly obese as their BMI was >30.[50] Treatment with NAC for one month did not change the BMI (Table 1). It remains to be seen whether an increase in the duration of treatment could result in a significant reduction in BMI. This possibility is quite likely as there was a significant reduction in the lipid profile even with 30 days of treatment with NAC.

In our study, the insulin resistance decreased after treatment with NAC (Table 1). Song et al (2005) showed that with chronic treatment with NAC, there was an increase in insulin sensitivity which prevented the blood pressure rise associated with fructose feeding in rats.[51] The mechanism by which NAC produces such an effect may involve the decrease of oxidative stress and alpha-adrenoceptor mediated vasoconstriction. NAC appears to be effective as an insulin sensitizing and testosterone-lowering drug in women with polycystic ovary syndrome.[52] The results of the present study suggest that NAC may also be used as a therapeutic agent to enhance insulin sensitivity in these patients with "Z" syndrome.

Lipid profile: From the above discussion, it is clear that there was an increase in pro-oxidant levels and a decrease in anti-oxidant levels resulting in oxidative stress in our patients with syndrome "Z". Excessive ROS react with protein moieties and disrupt their structure, thus decreasing the cellular uptake of lipids from the blood resulting in dyslipidemia.[53] Following the intake of NAC, as expected, there was an improvement in the oxidative balance with a tilt towards an increase in anti-oxidant capacity. This effect got reflected in the lipid profile also as evidenced by significant decreases in triglycerides, total cholesterol and LDL cholesterol along with a significant increase in HDL cholesterol. These findings are in agreement with a previous study performed in rats.[54]

Limitations of the study: Our small sample size limits the viewing the results of this study with caution, however the results of this study can form the base for large multicentric randomized control trials to extrapolate the results to the general population.

Conclusion

Anti-oxidants are useful as adjunct therapy for patients of syndrome "Z" as we noticed that at the beginning of the study, all the patients with OSAS had MS however by the end of the treatment period, those patients who were treated with NAC, showed significant reductions in their systolic blood pressure, insulin resistance and lipid profile. Since NAC treatment improves their sleep characteristics also, it is proposed that anti-oxidants have beneficial role in these patients.

Acknowledgment: We are grateful to Dr.Vijayan VK for making the sleep lab available and Ms. Kuldeep Patial for the technical support.

Conflicts of interest: Nil

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