Relationship between Oxidative Stress, Serum Zinc Level and Systemic Arterial Blood Pressure in Smokers and Non-smokers

Zarchi Theint Theint Hlaing*, Myat Su Bo, Mya Mya Thwin

ABSTRACT
Background and Aim: Either active or passive smoking causes damage to the heart and blood vessels. The aim of this study is to investigate the relationship between oxidative stress, serum zinc level and systemic arterial blood pressure in smokers and non-smokers.

Methods: A cross-sectional comparative study was done. Apparently healthy subjects of age 18-45 years including 40 smokers and 40 non-smokers residing in Magway Township, Myanmar were recruited. Serum zinc level was measured by atomic absorption spectrophotometry method. Serum malondialdehyde level was used as oxidative stress marker and measured by spectrophotometry. Systemic arterial blood pressure was measured by indirect method using mercury sphygmomanometer. Results: Mean serum zinc level of smokers (51.25±7.5 μg/dL) was significantly lower than that of non-smokers (92.91±27.46 μg/dL) (P<0.001). Mean serum malondialdehyde level of smokers (0.76±0.14 μmol/L) was significantly higher than that of non-smokers (0.24±0.09 μmol/L) (P<0.001). Mean Systolic Blood Pressure (SBP) of non-smokers was 120.95±5.02 mmHg and that of smokers was 126.55±6.14 mmHg (P<0.05). There was significant negative correlation between serum malondialdehyde level and serum zinc level (r = -0.75, P< 0.001, n=80). There was also significant negative correlation between serum zinc level and SBP (r = -0.477, P< 0.001, n=80). There was positive correlation between serum malondialdehyde level and SBP (r = 0.487, P< 0.001, n=80).

Conclusion: It could be concluded that smoking increases oxidative stress and decreases serum zinc level and these two changes might contribute to increase in blood pressure in smokers.

Key words: Serum zinc level, Serum malondialdehyde level, Smoking, Systolic blood pressure, Oxidative stress.

INTRODUCTION
Smoking is one of the lifestyle factors that distress the health of human and have been killing millions of human beings for many centuries. It is one of the major risk factors for the development of atherosclerosis, coronary heart disease, acute myocardial infarction and sudden cardiac death.

Cigarette smoke contains over 4700 different chemicals. Many of these are oxidants and pro-oxidants that can produce free radicals and enhance the oxidative stress. Malondialdehyde (MDA) is generated from Reactive Oxygen Species (ROS) and one of the most frequently used indicators of oxidative stress markers.

Oxygen free radicals can directly initiate the process of lipid peroxidation that contributes to cardiovascular diseases.

Cigarette smoke contains reactive peroxyl radicals and acetaldehyde which can increase lipid peroxidation. It can also be connected with the production of free radicals by polymorphonuclear leucocytes. Free oxygen radicals also caused tissues and microvascular damage. Oxidative stress promotes vascular smooth muscle cell proliferation and hypertrophy and collagen deposition leading to thickening of vascular media and narrowing of vascular lumen. Zinc is a vital element in maintaining normal structure and function of cells and which acts as components of antioxidant enzymes. Zinc is actively involved in protecting the body against oxidative stress. In addition, 30 percent of cellular zinc is found within the nucleus of mammalian cells and playing a role in regulation of gene expression. Zinc-dependent metabolic functions are present in every tissue. Severe zinc deficiency can damage on cardiovascular system, gastrointestinal, central nervous system, immune system, skeletal and reproductive system.

In smokers, alterations in the activity of the antioxidant enzyme defense system may lead to smoking-induced oxidant stress. Changes of zinc concentration in smokers may give rise to some of the long-term negative effects on the body. A combination of raised blood pressure and smoking may have a synergistic impact on cardiovascular functions.
Cardiovascular disease is extensively recognized as one of the leading causes of death globally. Smoking is one of the major risk factors for cardiovascular diseases. It is required to explore the link between smoking and cardiovascular diseases. Therefore, this study was designated to find out the incidence of zinc deficiency as well as the relationship between oxidative stress, serum zinc level and systemic arterial blood pressure in smokers.

**MATERIALS AND METHODS**

**Selection of Participants**

Apparently healthy male subjects aged between 18-35 years residing in Magway Township, Myanmar were selected. From these subjects, 40 smokers and 40 non-smokers were selected by simple random sampling method. The procedure was explained and written informed consent was obtained. Detailed smoking characteristics including age at which the subject started smoking, duration of smoking and the number of cigarettes/cheroots smoked per day was recorded.

**Data Collection and Blood Sample Analysis**

Systemic brachial arterial blood pressure was measured in lying position by indirect method using mercury sphygmomanometer. The level of pressure at which Korotkoff sound first heard (Stage I) was taken as Systolic Blood Pressure (SBP) and the level of pressure at which Korotkoff sound disappears (Stage V) as Diastolic Blood Pressure (DBP). The average of three measurements taken one minute interval was used. Ten ml of fasting venous blood was withdrawn from antecubital vein under aseptic condition by using a disposable syringe and needle for each subject. After collection of blood sample, samples were centrifuged 1500 rpm for 10 min to obtain serum. Serum MDA was used as indicator of oxidative stress. Serum MDA level was determined by spectrophotometry at Common Research Laboratory, University of Medicine, Magway, Myanmar. For determination of zinc level, sera were collected in two separate sample tubes and stored at (-20°C) in Common Research Laboratory, University of Medicine, Magway, Myanmar. Serum zinc level was determined by atomic absorption spectrophotometry at Common Research Laboratory, University of Medicine-2, Yangon, Myanmar.

**Statistical Analysis of Data**

Data were analyzed by using SPSS software for Window (version 23, SPSS Inc., Chicago, IL, USA). Data was described by mean ± SD. Independent student's t-test was used to compare the continuous variables. Correlation studies were computed by Pearson's correlation. The significant level of $p<0.05$ was accepted.

**RESULTS**

Baseline characteristics of the subjects were shown in Table 1. Mean serum zinc level of smokers (51.25±7.5 µg/dL) was significantly lower than that of non-smokers (92.91±27.46 µg/dL) ($P<0.001$) [Figure 1]. Mean serum MDA level of smokers (0.78±0.14 µmol/L) was significantly higher than that of non-smokers (0.24±0.09 µmol/L) ($P<0.001$) [Figure 2]. Mean Systolic Blood Pressure (SBP) of non-smokers was 120.95±5.02 mmHg and that of smokers was 126.55±6.14 mmHg ($P<0.05$) [Figure 3]. There was no significant difference in mean Diastolic Blood Pressure (DBP) between smokers (78.9 ± 6.7 mmHg) and non-smokers (77.15 ± 5.4 mmHg). Mean Arterial Pressure (MAP) of non-smokers was 90.95 ± 4.97 mmHg and that of smokers was 93.27 ± 5.68 mmHg ($P>0.05$).

There was significant negative correlation between serum MDA level and serum zinc level ($r = -0.75, P < 0.001, n=80$) [Figure 4]. There was also significant negative correlation between serum zinc level and SBP

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Smokers ($n = 40$) Mean±SD</th>
<th>Non-smokers ($n = 40$) Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.00 ± 7.20</td>
<td>21.20 ± 4.69</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.67 ± 0.04</td>
<td>1.68 ± 0.05</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>55.38 ± 10.04</td>
<td>55.35 ± 7.64</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>19.82 ± 3.54</td>
<td>19.73 ± 2.42</td>
</tr>
</tbody>
</table>

BMI = Body Mass Index; n= number of subjects.
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DISCUSSION

Zinc involves in several metabolic pathways as a cofactor for more than 300 enzymes. Zinc is an essential trace element and vital for many systems in the body. Zinc has antioxidant and anti-inflammatory properties. It participates in various enzyme reactions directly related to the regulation of blood pressure and indirectly related to generation of oxidative metabolic energy and alterations in blood lipid levels. The normal serum zinc concentration is 50-120 μg/dL (0.5–1.2 mg/L). Zinc deficiency can cause endothelial activation that favors all stages of atherogenesis. In the present study, serum zinc levels of the smokers were significantly lower than that of non-smokers ($P < 0.001$). This finding agrees with the findings of Khalid and Numair, 2006; Anetor et al. 2008 and Azzawy and Qaicy, 2011.

Effects of amount of smoking on serum zinc concentration were also assessed in the present study by dividing into two groups. Group 1 contained the subjects who take ≤ 5 cigarettes per day and group 2 contained the subjects who take > 5 cigarettes per day. There were 21 subjects in the former group and 19 subjects in the latter group. Serum zinc level in the former group was 55.81±7.16 µg/dL and that of the latter group was 46.22±3.86 µg/dL ($P < 0.05$). Effects of duration of smoking on serum zinc level were also assessed in the present study by dividing the two groups (< 5 year and ≥ 5 year). There were 23 subjects in the former group and 17 subjects in the latter. Average serum zinc level in the former group was 54.25±8.26 µg/dL and that of the latter group was 47.95±4.99 µg/dL ($P < 0.05$). This finding supposed the finding of Anetor et al. 2008 who found that the negative correlation between the duration of smoking and serum zinc level.

In the present study, mean serum malondialdehyde level of the smokers (0.78±0.14 μmol/L) was significantly higher than that of non-smokers (0.24±0.09 μmol/L) ($P < 0.001$). It was consistent with the studies of Block et al. 2002; Rumley et al. 2004; Bloomer, 2007; Timimi 2010 and Waseem et al. 2012. In the present study, systolic blood pressure of the smokers (126.55 ± 6.14 mmHg) was significantly higher than that of non-smokers (120.95 ± 5.02 mmHg) ($P < 0.05$). However, there were no significant differences between DBP and MAP of the two groups. It was consistent with the study of Primatesa et al. 2001 and Mahmud and Feely, 2003.
In the present study, there were significant negative correlation between serum malondialdehyde level and serum zinc level ($r = -0.75, P < 0.001, n=80$) as well as serum zinc level and SBP ($r = -0.477, p < 0.001, n=80$). It was consistent with the study of Bergomi et al. 1997 who reported that there was inverse correlation between blood pressures and serum zinc. There was positive correlation between serum malondialdehyde level and systolic blood pressure ($r = 0.487, p < 0.001, n=80$). It was consistent with the study of Ahmad et al. 2013.

There is a balance between antioxidants and pro-oxidants (free radicals and other reactive species) under normal condition. If there is an increased level of pro-oxidants leading to potential damage known as oxidative stress. This imbalance can be the effect of depletion of endogenous antioxidants and/or increased formation of free radicals and other reactive species.

It was found that MDA level showed positive correlation with systemic arterial blood pressure. Thus it showed that oxidative stress is associated with hypertension and there is positive correlation between oxidative stress and level of blood pressure. Oxidative stress promotes vascular smooth muscle cell proliferation, hypertrophy and collagen deposition which leads to thickening of vascular media, narrowing of vascular lumen and aggravate vascular damage.

Limitations of the Study

The present study was a cross-sectional comparative study design and it could just describe the relationship between smoking, serum zinc level, oxidative stress marker and systemic arterial blood pressure. To assess the cause-effect relationship of smoking, serum zinc level and cardiovascular risks, more study designs should be carried out among the large populations.

CONCLUSION

This study indicated that smokers had higher oxidative stress marker (MDA), lower serum zinc level and increased systolic blood pressure than non-smokers. It supported that smoking increased free radical production, oxidative stress and increased lipid peroxidation. The excess level of oxidant and pro-oxidant could affect the antioxidants level including serum zinc level and that could also affect the blood pressure.

ACKNOWLEDGEMENT

Nil.

CONFLICT OF INTEREST

There are no conflict of interest.

Ethical Clearance

This research was done after receiving the permission from the academic board of postgraduate studies, University of Medicine, Magway, Myanmar.

ABBREVIATIONS

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MDA: Malondialdehyde; ROS: Reactive Oxygen Species; MAP: Mean Arterial Pressure.

REFERENCES