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Oxidative stress status in homeless people

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Abstract
Despite the fact that homeless people die quite early from heart disease, our study has shown that widely recognized risk factors for cardiovascular disease (CVD) were in the normal endemic range among people with an unhealthy lifestyle. Recently, an increasing number of studies underline the impact of the pathogenetic role of high-grade oxidative stress in the development of different diseases, including CVD. However, corresponding data regarding homeless people is scarce, and therefore, the aim of this pilot study was to investigate the systemic oxidative stress index via the characterization of two opposite sides of the condition. Blood samples were drawn from 46 homeless (age 44±13 years) and 55 healthy (age 47±4 years) male subjects. Total peroxide and total antioxidant responses were determined from the blood serum and an oxidative stress index was calculated. The comparison between the groups revealed that the homeless group had a significantly ($p < 0.001$) higher oxidative stress index and lower antioxidant marker compared to the control group. Our data demonstrates pathogenetic systemic high-grade oxidative stress in homeless people at the Mustamae District shelter in Tallinn. Considering early diagnostics, prevention and treatment estimations for CVD, it would be worthwhile to conduct a more comprehensive study of oxidative stress markers.

INTRODUCTION

Cholesterol and its fractions are known as common informative markers for cardiovascular diseases (CVD) [1, 2]. However, our study [3] showed that blood markers such as total cholesterol (TC), high- and low-density lipoprotein cholesterol (HDL-C and LDL-C) and triglycerides (TG), which are used in every day clinical practice, were in the normal endemic range among people with an unhealthy lifestyle (homeless people).

In addition, an increasing number of recent studies underline both the need to apply additional new systemic CVD biomarkers and the impact of the pathogenetic role of high-grade oxidative stress in the development of different diseases including CVD [4-9]. Oxidative stress involves any condition in which oxidant metabolites can exert their damaging effects because of increased production or altered cellular mechanisms of protection. Reactive oxygen species (ROS) generated in and around the vascular endothelium appear as important causative factors in endothelial dysfunction underlying the development of atherosclerosis [10].

More specifically it has been shown that lower total antioxidant response (TAR) and higher total peroxide (TPX) levels are associated with cardiomyopathy, atherosclerosis and coronary artery disease (CAD) [8 ,11-14]. Corresponding data regarding homeless people is still scarce. However, it has been recently supposed that oxidative stress seems to play a key role in the impairment of the immune function in homeless people [15]. Therefore, the aim of this pilot study is to investigate the systemic oxidative stress index (OSI) via the characterization of opposite sides of the condition – antioxidant response and peroxide levels in homeless people.

METHODS

Subjects

The study was approved by the Tallinn Medical Research Ethics Committee and written informed consent was obtained from all of the subjects. Nonprobabilistic convenience sampling was used. The study was conducted in early spring, at the end of April, meaning that the subjects had not been exposed to cold or heat stress.

Study group

Recruiting the sample group of homeless people and conducting the procedures took place in the Mustamae District shelter, Tallinn, Estonia, where homeless people can stay for the night (when not intoxicated with alcohol), but where no systematic food provision, medication or any other services are rendered. The pre-recruitment procedure consisted the contingent selection of homeless individuals based on the knowledge of the shelter staff, and 46 men were confirmed as eligible for the study based on prescribed criteria (did not have a definite job, regular income or permanent home; constantly used alcohol or surrogates; did not have systematic eating habits and was not engaged in regular physical activity).

The selection with the assistance of the staff was followed by a questionnaire consisting of questions about education, work, lifestyle (how many years as homeless, eating habits, smoking, drugs and alcohol consumption, physical activity) and medical background.

The mean period of homelessness was approximately 4 years. While one half of the participants denied or doubted they had any illness or pain, the other half mostly claimed to have head, back or leg traumas – 25% of them used painkillers, but they did not obtain the treatment they needed for their condition. Also, to find out the participants' medical background, a medical data search was performed, which did not provide any significant results.

All participants confirmed that they used alcohol or surrogates almost every day but no specific information was given. Even though they all stated that they had approximately two meals a day, this could not be considered systematic eating because no food was rendered by the shelter and the information from the participants was doubtful.

Information about physical activity also seemed contradictory – participants claimed they walked approximately 11 km a day, but based on their physical condition, this was largely questionable.

Considering the abovementioned self-reported data, we could not take the answers into account because the participants lacked credibility (responses contradicted by data from the staff at the shelter, subjects denied, were doubtful or did not remember) except in regard to smoking – 88% of the participants confirmed being smokers.

Control group

All 55 healthy male controls were recruited by random selection from the general population in Tartu, Estonia. Eighty-eight per cent (88%) confirmed being non-smokers. Subjects who were taking regular medication or had a history of serious disease were not included in the study.

Blood collection

Blood collection took place at the Centre of Excellence for Translational Medicine, Tartu, Estonia. Blood samples were collected after an overnight fast between 08:00 and 11:00 a.m. using the standard method from *vena cubitalis* using Vacutainer tubes (BD Vacutainer, Belliver Industrial Estate, Plymouth; Becton, Dickinson and Co., UK). All blood samples were obtained in a sitting position. Guidelines indicating the importance of fasting from food before blood sampling were given to each participant before the testing period.

In the laboratory, samples for serum separation were centrifuged and kept at +4°C until assessed. All determinations were performed on the day of collection and within 12 hours.

Biochemical assay

Total peroxide concentrations were measured using an OxyStat colorimetric assay kit (Biomedica, Vienna, Austria).

The total antioxidant status of the serum was measured using a novel automated colorimetric measurement method for the TAR developed by Erel [16]. In this method, a hydroxyl radical was produced and the rate of the reactions was monitored by following the absorbance of coloured dianisidyl radicals. Antioxidants, present in the sample, suppressed the colour formation to a degree that is proportional to their concentrations. The suppression of the colour formation was calibrated using Trolox, so the results are expressed in terms of millimolar Trolox equivalents per litre.

The ratio of TPX and TAR from the blood serum will give the oxidative stress index (OSI) a marker showing the degree of oxidative stress.

Statistical analysis

Numerical data are presented as mean values ± SD. Differences and correlations were calculated using SPSS version 19 (SPSS Inc, Chicago, IL, USA), and $p < 0.05$ was regarded as a significant variation.

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RESULTS

The data about the homeless people and the healthy controls are given in Table 1.

There were no heterogeneities found within the study groups (homeless and control) based on non-Gaussian distribution (Skewness/Kurtosis stayed between ±2).

The comparison between the groups revealed that the homeless group had significantly ($p < 0.001$) higher oxidative stress indices, TPX and OSI, and lower antioxidant markers, TAR, compared to the control group.

Table 1. The average results (mean ± SD) of measured oxidative stress markers in homeless people compared to control group.

	Homeless (n = 46)	Controls (n = 55)	Significance
Age (years)	43.87 ± 12.47	47.07 ± 3.88	NS
TPX (μM/L)	439.74 ± 169.78	197.80 ± 59.51	$p < 0.001$
TAR (mM Trolox equiv/L)	0.79 ± 0.13	1.54 ± 0.19	$p < 0.001$
OSI	56.15 ± 21.46	13.14 ± 4.45	$p < 0.001$

TPX, total peroxide; TAR, total antioxidant response; OSI, oxidative stress index; NS, not significant.

DISCUSSION

A large number of reports in the literature implicate high-grade oxidative stress (inadequate antioxidant defence, overproduction of peroxides, changed redox status, *etc.*) in the pathogenesis of atherosclerosis [11, 17-19] and major antioxidant components (albumin, uric acid, bilirubin, ascorbic acid, flavonoids) being linked with the risk of CVD [20-26].

Our aim was to examine oxidative stress markers in the homeless population, where CVD is the leading cause of death [27, 28], and to compare the results with healthy participants from the general population. The clear finding was that the homeless group had potent systemic high-grade oxidative stress, where it was especially remarkable that both components of the oxidative stress index (TPX and TAR) were changed dramatically.

Although inflammatory parameters were not tested (we focused only on oxidative stress markers), we still assume that they also contributed to these results. It may be possible that the homeless group suffered from chronic inflammation because of a lack of proper treatment and medication. Chronic inflammatory processes can cause oxidative/nitrosative stress. The release of reactive oxygen/nitrogen species leads to lipid peroxidation, which results in various types of damage to DNA. Through this, the function of protein is changed via structural modifications, and cellular homeostasis is deregulated. Of course, this affects the vascular system – there are several studies showing a link between inflammation and oxidative/nitrosative stress in heart disease [29-31].

Systemic antioxidant status is also closely related to lifestyle choices. Eighty-eight per cent (88%) of the homeless participants claimed that they smoked. Therefore, the results of the study may also be influenced by high nitrotyrosine levels in the blood. There is rapid nitric oxide uptake from exposure to cigarette smoking followed by a rapid loss immediately after smoking [32]. However, two hours after smoking the exhaled levels of nitric oxide are reduced. This sustained reduction can be the result of inflammatory processes and increased peroxynitrite. Peroxynitrite increases nitrotyrosine levels leading to nitrosative stress [33].

We also believe that high oxidative stress levels in this kind of population is correlated with smoking and ethanol co-exposure, because the prevalence of nicotine dependence among alcohol or other substance abusers is extremely high [34], often associated with lower socio-economic status [35] and is well documented among homeless people [36, 37]. Still, statements like this require more dedicated studies including specific information about what type of alcohol/cigarettes, in what quantities and for how long.

Of course there are more factors influencing antioxidant status such as diet, physical activity and psychological stress, which can also function as co-factors increasing oxidative stress. The literature points out that the homeless are often subjected to massive amounts of stress because of the experience of homelessness itself [38]. Still we are dealing with a free-ranging environment, where is hard to achieve experimental control [39]. The same principle applies to accurate nutrition research, which is methodologically difficult to conduct and was also not the aim of this study.

The correlation between physical inactivity and negative cardiovascular events, where ROS also plays a pivotal role, has been stated. Physical inactivity seems to promote nicotinamide adenine dinucleotide phosphate-oxidase (NADPH oxidase) activity resulting in vascular dysfunction and atherosclerotic plaque formation [40]. Our participants claimed they walked approximately 11 km a day, but this was largely questionable on seeing their physical condition. As a result of this apparent contradiction we cannot say if

they were actually physically inactive or not.

Despite this, our findings suggest that more detailed oxidative stress-related research is needed to find ways to increase the quality of life and health status of homeless individuals. The recent data where oxidative stress seems to play a key role in immune function impairment in homeless people [17] also supports such this view.

Our study also exhibits some limitations. Homeless people are not an ideal group for such a study, because credible information about their previous life (results of medical examinations and their medical records *etc.*) is missing and some of the results of the questionnaire seemed contradictory. It is not possible to make any universal generalizations on the basis of this study since the standard of living and general state of health of people in other countries varies considerably.

In addition, due to the study type, the information gathered here is limited. Further research could conduct more specific analyses of the causes via studies involving multiple groups and a more diverse control group, including high alcohol consumers, heavy smokers and combinations of these.

In conclusion, our data demonstrates pathogenetic systemic high-grade oxidative stress in homeless people in the district shelter in Mustamae, Tallinn. Although the small sample size meant that the participants did not constitute a representative sample of the homeless, this study still suggests it would be worthwhile exploring oxidative stress markers with larger groups to consider early diagnostics, prevention and treatment estimations for CVD.

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