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Do toxic heavy metals affect antioxidant defense mechanisms in humans?

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ABSTRACT

The aim of this study was to prove whether anthropogenic pollution affects antioxidant defense mechanisms such as superoxide dismutase (SOD) and catalase (CAT) activity, ferritin (FRT) concentration and total antioxidant status (TAS) in human serum. The study area involves polluted and salted environment (Kujawy region; northern-middle Poland) and Tuchola Forestry (unpolluted control area). We investigated 79 blood samples of volunteers from polluted area and 82 from the control in 2008 and 2009. Lead, cadmium and iron concentrations were measured in whole blood by the ICP–MS method. SOD and CAT activities were measured in serum using SOD and CAT Assay Kits by the standardized colorimetric method. Serum TAS was measured spectrophotometrically by the modified Benzie and Strain (1996) method and FRT concentration—by the immunonefelometric method. Pb and Cd levels and SOD activity were higher in volunteers from polluted area as compared with those from the control (0.0236 mg l^{-1} vs. 0.014 mg l^{-1}; 0.0008 mg l^{-1} vs. 0.0005 mg l^{-1}; 0.137 U ml^{-1} vs. 0.055 U ml^{-1}, respectively). Fe level, CAT activity and TAS were lower in serum of volunteers from polluted area (0.442 g l^{-1} vs. 0.476 g l^{-1}; 3.336 nmol min^{-1} ml^{-1} vs. 6.017 nmol min^{-1} ml^{-1}; 0.731 Trolox-equivalents vs. 0.936 Trolox-equivalents, respectively), whilst differences in FRT concentration were not significant (66.109 μg l^{-1} vs. 37.667 μg l^{-1}, $p=0.3972$). Positive correlations between Pb ($r=0.206$), Cd ($r=0.602$) and SOD in the inhabitants of polluted area, and between Cd and SOD in the control ($r=0.639$) were shown. In volunteers from both studied environments TAS–FRT (polluted: $r=0.625$ vs. control: $r=0.837$) and Fe–FRT (polluted area: $r=0.831$ vs. control: $r=0.407$) correlations, and Pb–FRT ($r=0.360$) and Pb–TAS ($r=0.283$) in the control were stated.

The higher lead and cadmium concentrations in blood cause an increase of SOD activity. It suggests that this is one of the defense mechanisms of an organism against oxidative stress caused by environmental factors, whilst non-enzymatic mechanisms marked by TAS are the main antioxidant defense system in relation with Pb concentration in humans from unpolluted area. Simultaneously, the higher CAT activity and TAS can indicate that these mechanisms play a key role in the antioxidant protection in non-stressed environments.

1. Introduction

Reactive oxygen species (ROS) takes part in pathogenesis of many diseases correlated with environmental factors. The relationships between ROS in humans and the morbidity on many diseases (cancers, rheumatoid arthritis, arteriosclerosis, diabetes, diseases of central nervous and alimentary system, hematids, etc.) have been proved (Nohl and Stolze, 1998; Oliński and Jurgowiak, 1999; Schulz et al., 1999; Siems et al., 2000; Beisswenger et al., 2001; Buonocore et al., 2001; Darlington and Stone, 2001; Kawanishi et al., 2001; Sayre et al., 2001).

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The increase of studies focused on the impact of chemical elements on human health and oxidant stress in humans has been observed recently. However, the researches include mostly individuals exposed to the impact of occupational factors, causing changes in the defense mechanisms of an organism against oxidant stress. Among examined elements especially toxic heavy metals are harmful for heath. Simultaneously, the environmental exposure upon these factors is rather not considered in detail. Simultaneously, the investigations describing particular impact of environmental stress on the antioxidant barrier of an organism are poor (Sbrana et al., 1990; Tang et al., 1990; Anwar and Gabal, 1991; Senft et al., 1992; Topaktas et al., 2002; Kobal et al., 2004).

Lead and cadmium are important occupational and environmental pollutants (Nriagu, 1978; Ewers and Schlipköter, 1991). The extraction, smelt, lead purification and production of products containing lead can cause the emission of this metal to the environment. Lead exposure occurs during the production of batteries, cables and wires, in the chemical industry and the beds, printer′s type production, from covers to protect from the radioactive radiation and manufacture of dyes and insecticides (Kabata-Pendias and Pendias, 1984; Kabata-Pendias and Mukherjee, 2007). Lead cumulates in soils and dusts and because it does not decay, this is an essential source of exposure. The consumption of plants farmed in the polluted areas causes the health hazard (Seńczuk, 2002; Kaniuczak, 2004). Cadmium emission to the environment follows mostly from smelters of zinc, nickel and other non-ferrous metals, such as lead and copper (60% of all anthropogenic sources), as well as a result of coal combustion. Environmental pollution with cadmium as a result of industrial activity has often a local character (to about 40 km). The easy movement of this toxic element in the trophic chain causes the health hazard. Moreover, it is more toxic than lead (Bonda et al., 2007). The influence of lead on the ferritin concentration got confirmed with many investigations. These studies include the groups of workers exposed to lead and suggest a direct influence of iron depletion on lead poisoning (Osman et al., 1998; Kim et al., 2002, 2003; Wright et al., 2003; Kwong et al., 2004).

In the areas studied by us there is a sustainable process of penetration into the soil and groundwater with chemicals contained in them, especially cadmium and lead. These metals are derived from both the nearby soda plants, and glass works, and municipal waste treatment plants as well, especially from municipal landfills, active and inactive. Additionally, the investigations were carried out in salted Kujawy Region (northern-middle Poland) in Inowrocław Region of Ecological Danger IRED (salinity, acidification, disturbed Ca, Mg, Na and Fe management, the impact of toxic metals). Thus here it should be taken into account that these environments were of various degrees of degradation where sodium manufacture, wastes utilization, very polluted neighborhoods and industrial manufacture areas with anthropogenic impact are here a constant source of toxic metals, especially cadmium and lead. The separate and independent sources of these metals are here landfill and agriculture itself, areas immediately adjacent, i.e. surrounded districts with dumping grounds of wastes and agricultural cultivation (agrocenoses). Overall environmental effects of these highly unfavorable biogeochemical conditions here are significantly strengthened by a rich network of groundwater, streams, flood waters, stagnant waters and local so-called dystrophic ponds. This favors the leaching of organic matter, both autochthonous and allochtonous, inside the basin (Wilkoń-Michalska, 1971; Cieśla and Dąbkowska-Naskręt, 1984; Czerwiński et al., 1984; Czerwiński, 1996; Rytelewski et al., 1993; Borsuk and Stachowiak, 1994; Niklewska et al., 2000). At the same time the significant effect of iron in the areas we examined should be noted. This element is there in large concentrations in the soil, groundwater in the network, trophic chains, etc. The destabilization of iron compounds economy in these areas is reflected in the form of numerous small ferruginous water tanks, the so-called ''meshes'' that are a source of iron leaching into the environment.

In addition to natural biogeochemical local processes the anthropogenic impact is here significant. The development of saline sodium industry and therefore the activity of industrial giants of this region, leads to imbalance of the environment. Contaminations associated with activity of agricultural production include surface and underground waters, atmospheric air and soil (Rytelewski et al., 1993; Niklewska et al., 2000). The salts of sodium and chlorine combine here with compounds of calcium and potassium, and then are directed to the settlers, the so-called ''white seas'', which are becoming a source of serious instability of the environment. Another source of contamination is spray dried lime sodium–calcium settlers, and damage to wells and pipelines brine (Czerwinski et al., 1984, 1996; Rytelewski et al., 1993). Furthermore, the increase in salinity also causes failures of various devices, such as various hydrological equipment, which results in saline waste entering the emergency ditches watercourses, which leads to formation of saline spills contaminating surface water and arable land (Rytelewski et al., 1993). In enlarging the ''white seas'' also plays a role in geomorphology of land, which influences the direction of water flow and salt deposits conducive to this process (Wilkoń-Michalska, 1971). Human industrial and rural activities in the studied Kujawy region led to secondary soil salinity in the region, namely the formation of soils known as anthropologically saline. The result of this process is to change the properties of soils, which are a result of accumulation of sodium and toxic metals, mainly Cd and Pb, in the complex of absorbent dry-up during drought and form a hard, difficult to grow rock. However, in the state of soil moisture they are boggy, impervious and windproof (Rytelewski et al., 1993).

ROS produced by toxic metals exposure causes tissue damage by a variety of mechanisms (Yetkin-Ay et al., 2007). However, the broad defense mechanisms of an organism exist, targeting to control physiological level of ROS in the organism (Rukgauer et al., 2001; Armutcu et al., 2004; Gacko et al., 2006; Łuszczewski et al., 2007). Antioxidant enzymes activity determines the first line of protection and their charge is the limitation of ROS formation. The mechanism of these antioxidants activity is well recognized and described by many researchers (Harrison and Arosio, 1996; Orino et al., 2001; Rukgauer et al., 2001; Armutcu et al., 2004; Gacko et al., 2006; Łuszczewski et al., 2007). Antioxidant enzymes are very important for aerobic organisms exposed to oxygen. Superoxide dismutase metabolizes reactive oxygen species to hydrogen peroxide. Catalase converts hydrogen peroxide to water and oxygen (Bowler et al., 1992). Thus the influence of heavy metals on the antioxidant enzymes activity became confirmed scientifically.

It should be emphasized that superoxide dismutase and catalase are among the so-called triad of enzyme. Based on the evaluation of changes in the activity of these enzymes we can create the antioxidant status of an organism and the environment, which is complemented by non-enzymatic mechanisms for performance analysis (Fandos et al., 2009; Mansego et al., 2011). Most research confirms that SOD, CAT and non-enzymatic antioxidants can be indicated as the main antioxidant defense mechanisms in humans (Sadowska-Krępa and Poprzęcki, 2005; Corrales et al., 2011; Mansego et al., 2011; Skólmowska and Kmieć, 2011); e.g., the application of CAT and SOD in daily practice encounters many difficulties connected with their loss of activity and with their degradation. These enzymes practically do not penetrate biological membranes, which limits or even makes impossible their protective activity directed against ROS. However, the penetration of the membranous barrier becomes