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Exposure to alcohol and tobacco smoke causes oxidative stress in rats

Ewa Ignatowicz[1], Anna Woźniak[2], Maksymilian Kulza[2], Monika Seńczuk-Przybyłowska[2], Francesco Cimino[3], Wojciech Piekoszewski[4], Marek Chuchracki[5,6], Ewa Florek[2]

[1]Department of Pharmaceutical Biochemistry, Poznan University of Medical Sciences, Święcickiego 4, PL 60-781 Poznań, Poland

[2]Laboratory of Environmental Research, Department of Toxicology, Poznan University of Medical Sciences, Dojazd 30, PL 60-631 Poznań, Poland

[3]Department Farmaco-Biologico, School of Pharmacy, University of Messina, Viale Annunziata, 98168 Messina, Italy

[4]Department of Analytical Chemistry, Jagiellonian University, R. Ingardena 3, PL 30-060 Kraków, Poland

[5]Department of Maternal and Child Health, [6]Central Laboratory, Gynecology and Obstetrics Hospital, Poznan University of Medical Sciences, Polna 33, PL 60-535 Poznań, Poland

Correspondence: Ewa Florek, e-mail: eflorek@ump.edu.pl

Abstract:
Background: Tobacco smoking and alcohol abuse causes oxidative stress in humans and underlay numerous chronic degenerative diseases. Liver is the main organ exposed to alcohol toxic metabolites, whereas tobacco smoke is chiefly harmful to the lungs.
Methods: The aim of the current study was the assessment and comparison of selected oxidative stress markers, reduced glutatione (GSH), glutathione S-transferase (GST), superoxide dismutase (SOD), catalase, nitrites and protein nitrosylation and DNA damage in the livers and in the lungs of alcohol-addicted rats exposed to tobacco smoke alone or in combination with a single dose of ethanol.
Results: The highest levels of GSH were measured in the liver of smoke only exposed animals and in the lungs of rats exposed to smoke and alcohol. In the liver of animals treated with a single dose of alcohol or with smoke and alcohol, GST was significantly higher than in the group exposed to smoke only. SOD and catalase showed the highest activities in the livers of rats receiving a single dose of alcohol. High concentration of nitrites was observed in the lungs of animals treated with smoke and alcohol in combination, which corresponded to elevated protein nitrosylation in this group, whereas in the livers of these animals relatively low level of nitrites was accompanied with the lowest concentration of nitrosylated proteins. In the liver of alcohol only treated rats the highest nitrites corresponded to the highest protein nitrosylation. In the lungs of all treatment groups the range of DNA damage was higher, than the respective values in the livers. Although alcohol is not considered a specific toxicant to the lungs it was found to cause oxidative stress in this organ.
Conclusions: The obtained results suggest that in the ethanol-addicted rats combined exposure to smoke and alcohol differentially modulate endogenous antioxidant defense system and reactions to oxidative stress.

Key words:
tobacco smoke, alcohol, oxidative stress, rat

Abbreviations: CYP 2E1 – cytochrome P450 izozyme 2E1, GSH – reduced glutathione, GST – glutathione S-transferase, NAD – nicotinamide adenine dinucleotide, NADH – nicotinamide adenine dinucleotide – reduced form, ROS – reactive oxygen species, RNS – reactive nitrogen species, SOD – superoxide dismutase

Introduction

Tobacco smoking and alcohol abuse causes a serious threat to human health. Most often individuals addicted to alcohol are also tobacco smokers. Addiction to alcohol and tobacco may develop through similar mechanisms, moreover, stress, increased tolerance related with the adaptation of the central nervous system to the presence of alcohol [8] and sensitivity to these xenobiotics may enhance addiction [16, 24]. Alcohol is metabolized mainly in the liver, where it undergoes oxidation through the alcohol dehydrogenase [28] and aldehyde dehydrogenase activities. These enzymes require nicotinamide adenine dinucleotide (NAD) as a cofactor and as a result of the reaction a cellular pool of the reduced form, nicotinamide adenine dinucleotide-reduced form (NADH), becomes elevated, which impairs the redox balance. Products of these reactions, acetaldehyde and acetic acid, respectively, are directly responsible for the alcohol toxicity. Ethanol oxidation occurs also in the subcellular fraction of peroxisomes and microsomes, chiefly due to activity of CYP 2E1 isoform of cytochrome P450. Chronic alcohol consumption induces strongly this izoform, which results in generation of reactive oxygen species (ROS) and alcohol-derived radicals, moreover, an increase in CYP 2E1 activity enhances metabolic transformation of numerous xenobiotics into more toxic products [6, 7, 20]. Additionally, chronic alcohol abuse changes morphology of mitochondria membranes, which, together with the NADH increase, raises the electron flow through the complex 1 of respiratory chain and ROS formation [46]. Finally, in the liver, alcohol activates Kupffer cells, capable of pro-inflammatory cytokines induction and ROS and reactive nitrogen species (RNS) generation [44]. In the liver, a common consequence of chronic alcohol abuse is inflammation, cirrhosis or cancer. Despite numerous social drawbacks, alcohol abuse has impact on drinker's individual health and/or life, whereas tobacco smoke is equally toxic to active and passive smokers. Tobacco smoking induces strong addiction and smoke components affect circulation in all tissues and organs causing elevated risk of atherosclerosis, hypertension, chronic obturative pulmonary disease and certain forms of cancer [41, 47]. Tobacco smoke itself is a source of free radicals, moreover, inhalation of particles activates the lung epithelium and fibroblasts and enhances recruitment of inflammatory cells, macrophages and neutrophils to the lung tissue. These cells undergo activation resulting in ROS and RNS synthesis and release and in upregulation of factors involved in inflammation and fibrosis [27]. The deleterious effects of tobacco smoke is observed also in non-smokers, yet exposed to smoke as a contaminant of environment and thus, to protect community health, numerous countries introduce a ban on smoking in public space [29].

A common effect of joint exposure to tobacco smoke and alcohol is oxidative stress, resulting in damage to proteins, polysaccharides, lipids and DNA, leading to the enhancement of pro-inflammatory reactions, accelerated ageing, immunity disturbances and disease development. Smokers abusing alcohol are more prone to develop various cancers [35]. Endogenous antioxidant defense system tends to overcome these unfavorable changes through the enhancement of enzymatic (e.g., catalase, superoxide dismutase (SOD), glutathione peroxidase) and nonezymatic (e.g., albumin, uric acid, reduced glutathione) mechanisms. In the case of insufficiency or depletion of these factors an oxidative stress occurs which forms the basis for numerous pathologies development [45].

The aim of the current study was the assessment and comparison of selected oxidative stress markers, reduced glutathione (GSH), glutathione S-transferase (GST), SOD, catalase, nitrites and protein nitrosylation and DNA damage in the livers and in the lungs of alcohol-addicted rats exposed to tobacco smoke alone or in combination with a single dose of ethanol.

Materials and Methods

All the experiments were conducted according to the Regional Ethics Committee guidelines for animal experimentation, No. of agreement 2/2008, 18th January 2008.