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Antioxidant profile, carbonyl and lipid oxidation markers in the parotid and submandibular glands of rats in different periods of streptozotocin induced diabetes

Anna Zalewska [a,*], Małgorzata Knaś [b,1], Mateusz Maciejczyk [c,1], Napoleon Waszkiewicz [d], Anna Klimiuk [a], Magdalena Choromańska [a], Jan Matczuk [e], Danuta Waszkiel [a], Halina Car [f]

[a] Department of Conservative Dentistry, Medical University Bialystok, Sklodowskiej M.C. 24a Str., 15-274 Bialystok, Poland
[b] Institute of Health Care Higher Vocational School, Noniewicza 10 Str., 16-400 Suwalki, Poland
[c] Students' Scientific Group "Stomatological Biochemistry" at the Department of Conservative Dentistry, Medical University of Bialystok, Sklodowskiej M.C. 24a Str., 15-274 Bialystok, Poland
[d] Department of Psychiatry, Medical University Bialystok, Plac Brodowicza 1 Str., 16-010 Choroszcz, Poland
[e] County Veterinary Inspection, Zwycięstwa 26B Str., 15-959 Bialystok, Poland
[f] Department of Experimental Pharmacology, Medical University Bialystok, Szpitalna 37 Str., 15-767 Bialystok, Poland

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ABSTRACT

Objective: The aim of this study was to estimate the antioxidants barrier, and the oxidative stress in the salivary glands of rats in different periods of streptozotocin induced diabetes.
Design: Rats were divided in: 4 control (C2/4/10/14) and 4 experimental (DM2/4/10/14) groups. Salivary glands were removed 2/4/10/14 weeks after streptozotocin injection. Peroxidase (Px), uric acid (UA), total antioxidant status (TAS), superoxide dismutases (SODs), catalase (CAT), malonylodialdehyde (MDA), advanced glycation end products (AGE) concentrations were examined.
Results: TAS, Px were lower in the parotid diabetic glands throughout the whole experiment. TAS in the submandibular diabetic glands was lower in 2nd and 4th and higher in 14th week. Px in the submandibular diabetic glands was reduced in 4th and increased in 14th week. UA was lower in parotid, elevated in submandibular diabetic glands in 4th, 10th, 14th weeks. In the submandibular as compared to parotid glands an increase in TAS and UA was observed in 10th and 14th, Px in 14th week.

In all periods, a significant increase in AGE was observed in both diabetic salivary glands. An increase in MDA was observed in the parotid diabetic glands in the 4th, 10th, 14th of the study. In the submandibular glands this increase was observed in the 2nd, 4th, 10th week, in the 14th week, the MDA level was significantly reduced in comparison to the control.

* *Corresponding author*. Tel.: +48 606614245.
E-mail address: jmatczuk@yahoo.com (A. Zalewska).
[1] The second and the third author had equal participation, their surnames in alphabetical order.
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Conclusion: The antioxidants of parotid glands are deficient throughout the whole experiment. In the last period submandibular glands copy with free radicals, becoming the main antioxidant's source.

1. Introduction

Diabetes mellitus type 1 is a metabolic disease which is characterized by hyperglycemia resulting from disturbances of insulin secretion or its action in target cells.[1] A chronic hyperglycemia in the course of diabetes type 1 results in morphological changes and dysfunction various organs including salivary glands. It was described that diabetic parotid, but not sublingual and submandibular, swelling was caused by the hydropic degeneration of its ductal and acinar cells. Moreover Carda et al.[2] showed that this increase in glandular size was due to adipose parotid stroma infiltration and ductal dilatation. This morphological disturbances of the salivary glands structure result in changes in the salivary flow rate and composition of the human saliva.[1,3–5]

There is convincing scientific and clinical evidence that pathogenesis of salivary glands and oral cavity complications in the course of diabetes type 1 is closely associated with oxidative stress.[1,3,6,7] Oxidative stress is a condition resulting from an imbalance between production and neutralization of reactive oxygen species (ROS), potentially leading to damage.[8]

Physiologically and in the most diseases, including all type of diabetes, mitochondria are the main source of ROS and consequently oxidative stress.[9] Under normal condition mitochondrial glucose oxidation generates ATP and it also produces small amounts of superoxide anion, which can be converted to other ROS.[10] In health the body is protected from oxidative effects of ROS by an antioxidant defense system. However, as it was proven, this system becomes deficient in diabetes mellitus, and is further exacerbates by hyperglycaemia.[11–13] Under the conditions of hyperglycemia, higher oxidative glucose metabolism itself generates the formation of large quantities of superoxide anion, which cannot be completely neutralized by SOD, resulting in oxidative stress. Moreover hyperglycemia results in formation of glycation end products (AGEs). There exists accumulating evidence that AGEs intensify existing oxidative stress by binding to specific receptors (RAGE) located within the surface of many cells. Activation of RAGE receptors located on macrophages results in the development of inflammation, which activates NADPH oxidase and the production of ROS.[14] AGEs are also considered as a marker of carbonyl stress, which is irreversible form of non-enzymatic oxidation.[15] Other less significant sources of ROS include autoxidation of glucose,[16] increase the activity of ROS generating enzymes[17] and the lack or deficiency of insulin.[18] The targets of ROS injury include proteins, lipids and DNA. It was shown that products of lipid peroxidation (among others malonodialdehyde, MDA) are an important pathological indicator in diabetes mellitus.[19–21]

It was shown that short term hyperglycaemia increased the catalase (CAT) and glutathione peroxidase (GPx) activities in the parotid glands, however the MDA level was significantly higher only in the submandibular glands of streptozotocin rats in comparison to the control.[19] However similar study of Deconte et al.[20] showed: an increase in superoxide dismutase (SOD) and GPx activities as well as in the MDA content and any differences in total antioxidant status (TAS) and CAT in parotid glands of rats 30 days after streptozotocin (STZ)-injection in comparison to the control. It was also shown that streptozotocin induced diabetes affects salivary glands SOD (dismutase type was not specified), CAT and GPx as well as changes in the MDA concentration and that alterations depend on the duration of diabetes and type of the salivary gland.[21] However there is no available study on the behaviour of the most important components of antioxidant barrier of the salivary glands: salivary peroxidase (Px),[22] uric acid (UA)[22] and TAS[23] depending on the duration of STZ induced diabetes. TAS is the sum of whole antioxidants, regardless of the source, it can, therefore, evaluate the efficiency of the entire antioxidant system of the salivary glands instead its individual components in the fight against free radicals.[23] Px the only one component of the antioxidative barrier which is synthesized exclusively in the salivary glands and can therefore reflect the efficiency of the salivary glands themselves in combating oxidative stress. UA–plasma-born, non-enzymatic and it is defined as the most important salivary antioxidant.[22]

The aim of this study was to estimate the capacity of the antioxidant barrier (including Px, UA, TAS as well as superoxide dismutase 1 (SOD1), superoxide dismutase 2 (SOD2), (CAT)), as well as the assessment of the effects of oxidative stress (including lipid peroxidation marker MDA and carbonyl oxidation marker-AGEs) in the parotid and submandibular glands of rats in different periods of streptozotocin induced diabetes.

2. Materials and methods

The protocol of this study was approved by Local Committee on the Ethical Use of Animals of the Medical University in Bialystok, Poland, number 52/2013.

2.1. *Animals*

Healthy male Wistar rats weighted 200–250 g were obtained from the Department of Experimental Pharmacology, Medical University, Bialystok, Poland. They were caged separately under standard conditions (20–21 °C, in a cycle 12 h light/12 h dark). The animals had free access to water and to a standard laboratory rat chow (Agropol, Motycz, Poland). Two days after their arrival, the rats were divided randomly into control (C, 32 rats) and experimental groups (DM, 32 rats), followed by a subdivision into four subgroups (the eight rats in each