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Effect of sodium fluoride on the rat liver

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Abstract : Sodium fluoride (NaF) is used for caries prevention in the form of fluoridated drinking water etc. Effect of fluorides on various metabolic levels in hard and soft tissues, namely respiration as well as carbohydrate, protein, enzymatic and vascular metabolism, can disturb detoxication of fluorine compounds administered orally. The study objective was to study the effect on liver of young and mature rats exposed to NaF in drinking water from conception till maturity, as well as after its withdrawal. The results observed in the liver, can help determine to what degree of oral fluoride caries prevention is safe and whether it should be implemented.

Keywords : Sodium fluoride, liver, rat

INTRODUCTION

Due to its efficacy in caries prophylaxis and straightforward application, salt (NaF) remains used for caries prevention within the sort of fluoridated beverage, fluoride tablets, fluoridated salt or milk.[1] Effect of fluorides on various metabolic levels in hard and soft tissues, namely respiration also as carbohydrate, protein, enzymatic and vascular metabolism, can disturb detoxication of fluorine compounds administered orally.[2-4]

Fluorine, considered to be one among the environmental toxins, doesn't occur free in nature but because of high affinity for the ions of calcium, sodium, magnesium and tin it forms chemical compounds with them, which are more or less soluble in water.[5,6]

Because of good solubility in water, easy absorption from the alimentary canal also as for economic reasons, salt (NaF) is that the most ordinarily used compound in collective endogenic oral caries prophylaxis. During oral exposure, it can positively affect the oral environment. However, when consumed with food via the alimentary canal it can change, counting on dose and exposure time, cell and tissue metabolism within the further stages. The organ that reacts rapidly to xenobiotics reaching the body from the surface is that the liver. It's there where detoxication processes happen and therefore the resulting pathomorphological changes are the response to the orally administered preparation.

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MATERIALAND METHODS

In the initial stage of the experiment, 30 female rats, 180-200 g body weight, were divided into 3 groups: one control and two experimental groups (I, II). Female rats in the experimental groups received fluorine in aqueous solutions of sodium fluoride (NaF) at a concentration of 10.6 mg NaF/dm^3 (group I) and 32.0 mg NaF/dm^3 (group II), corresponding to a dose of 1.2 mg F/kg b.w. (group I) and 3.6 mg F/kg b.w. (group II). Sodium fluoride (NaF),

was dissolved in tap water. After a two-week adaptation period, during which the rats drank an average amount of 50 ml of water, the females were covered. They received NaF with drinking water 3 days before covering, during pregnancy and lactation. On day 30 of life, young rats were separated from mothers but were still given sodium fluoride with drinking water in the concentrations as above.

Control animals received tap water ad libitum, in which the level of fluorine did not exceed 0.2 mgF/dm^3. On day 90 of life, NaF was withdrawn in groups I and II, and tap water alone was administered to all the animals. The experiment was terminated on day 120 of life.

The animals were kept in standard environmental conditions.[8] The young were subjected to the action of fluoride from conception, through the foetal period, nest period (till day 30 of life) and maturity (day 90). After 90 days of exposure, NaF was withdrawn. The experiment was terminated on day 120 of life. Rats were fed on standard granulated LSM diet.

90 young rats were included in the experiment, 5 in each study subgroup. The animals were weighed and subjected to autopsy at the following age intervals: day 4 (newborn), day 14 (young rat fed on mother's milk); day 30 (young rat, receiving mother's milk, drinking water and standard diet from day 14 to day 30 of life – on that day, the young were separated from mothers but the experimental model was continued), day 60 (mature rat), day 90 (adult rat) and day 120 (NaF was not applied for 30 days).

RESULTS AND DISCUSSION

The animals dissected on day 4 of the experiment, the liver showed the predominance of blood vessels and really numerous haemopoietic system cells that formed islets. Hepatocytes had a foamy, acidophilic cytoplasm. Cell nuclei were well stained, with distinct chromatin lumps and nucleoli. In 14-day-old rats, hepatocytes showed a definite trabecular arrangement and contained acidophilic cytoplasm with markedly stained nuclei and nucleoli. In most fields of vision, lobules were distinct. The haemapoietic cells sporadically formed islets. In 30-day-old animals, the liver structure was already mature. In 60-, 90- and 120-day rats, the structure of the organ was typical for adult animals. Slight vacuolar degeneration might be sporadically seen within the peripheral parts of the lobules.

In the animals of group 1 (NaF concentration in beverage – 10.6 mg) dissected on day 4, pictures of the liver didn't differ markedly from those seen within the control group. In some fields of vision, hepatocytes contained vacuoles. Within the livers of 14-day-old rats, in some hepatocytes the cell wall was blurred. Blood vessels were slightly dilated. In 30-day-old rats, vacuolar degeneration-type changes occurred. Necrotic lesions were sometimes seen in hepatocytes (micro focal lesion). In 60- and 90-day-old rats the liver had a traditional structure. Within the peripheral parts of rare lobules slight vacuolar degenerations were found. In 120-day-old rats during this group, i.e. 30 days after NaF withdrawal, the vacuolar degenerations persisted, particularly in hepatocytes of the peripheral lobules.

In the group II, morphological changes within the liver were more pronounced altogether the animals no matter the time of dissection. Already within the livers of 4-day-old rats an outsized number of hepatocytes with vacuoles within the cytoplasm were seen. Blood vessels were dilated and crammed with clotted acidophilic fluid. On day 14, hepatocytes showed features of injury, visible within the structure of cell and nuclear membranes. Within the vicinity of blood vessels, inflammatory infiltration of neutrophilic granulocytes was observed. Within the livers of 30-day-old rats, the changes were further intensified, and hepatocytes showed distinct vacuolar degeneration and micro necrotic foci. In 60-day-old rats, the image of intoxication within the liver was still present. Within the livers of 90-day-old rats, the changes were becoming weaker. However, vacuolar degeneration-type changes still persisted within the livers of 120-day-old rats despite NaF withdrawal.

According to research surveys conducted by the International Research Agency for Fluorination, the toxicity of fluorine compounds is usually ignored by medical doctors, dentists and paramedical staff involved in healthcare. Therefore, measures should be taken to get undoubted benefits resulting from the appliance of fluorine compounds in caries prevention and to attenuate any side-effects.[6,7,10] Assuming that the liver is involved within the metabolism of toxic compounds produced during systemic transformations and exogenous toxins going to the organism from the environment, we could expect to seek out both patho morphological and metabolic changes as reactions to NaF. Therapeutics or toxins, to which

NaF, counting on its dose, are often included, are likely to impair liver function and induce morphological changes within the liver.[15,16] Hepatotoxic action is manifested by cell respiration disorders that interfere with oxidation and reduction mechanisms, by impairment in protein, carbohydrate and lipid metabolism and by disturbances in intra- and extracellular transport.[9] In consequence, whole cell or its cytoplasmic organelles are often damaged. most often the damage is expressed as parenchymal vacuolar degeneration, necrosis of hepatocytes or disorders within the activity of metabolic enzymes.[14,15] within the livers of newborn rats in group II, slight changes were found in Browicz Kupfer cells at higher fluoride concentration. Distinct vessel dilation could suggest metabolic disturbances within the liver, thus indicating a possible toxic effect of fluoride on the organ as early as within the foetal period. The livers of 14-day old rats exposed to NaF in group I and II, receiving fluorine only with mother's milk, showed vacuolar degeneration-type changes, damage or blurring of cell or nuclear membrane and vessel dilation. The changes were more pronounced in group II, i.e. at higher fluoride concentration.

Lack of distinct morphological and enzymatic changes within the livers of 14-day-old animals of group I (lower NaF concentration) are often explained by the protective role of mother's milk .[16] Since morphological and ultrastructural changes were most pronounced within the livers of 30-day-old rats, Up to day 30 of life, the rats stayed in nests, receiving both mother's milk, standard diet and NaF-enriched water to drink, which resulted together of beverage fluorides with mother's milk fluorides. Already in group I, at the lower NaF concentration, aside from vacuolar degeneration also micronecrotic foci were observed. In group II, at the upper NaF concentration, vacuolar degeneration and various micro- necrotic foci were seen to multiply as compared to group I.

After NaF withdrawal the changes within the liver in both groups were subsiding. the quantity of glycogen increased in hepatocytes, and cell nuclei and endoplasmic reticulum were normal in appearance. Only mitochondrial polymorphism was maintained and damaged endothelial blood cells were sporadically seen.

Endoplasmic reticulum reacts rapidly to the action of toxic compounds. It's rough component undergoes vacuolization (vacuolar degeneration) and loses ribosomes, which results in a decrease in RNA. These changes are related to the impairment in protein synthesis within the cell. The graceful a part of the endoplasmic reticulum also can be subject to vacuolization or proliferation, which causes a substantial decrease within the count of glycogen granules within the affected sites.[17] This has been confirmed by our previous ultra structural findings.[13] The microscope examinations revealed dilation of channels of the rough endoplasmic reticulum in 30-day-old group II animals, i.e. those exposed to the upper concentration of fluoride ions. Similar changes within the liver found within the rough endoplasmic reticulum are described by Lavrushenko.[12] Additionally, in group II rats older than 30 days, the sinusal lumen of the liver sometimes showed collagen bundles amid micronecrosis observed within the morphological examination, which could suggest the start of liver fibrosis.

From day 30 till day 90 of NaF administration, the morphological changes showed a gradual decrease in intensity and only considerable dilation of blood vessels with endothelial swelling was observed. Taking under consideration endless exposure to NaF, the decrease might be the results of adaptive mechanisms of the organism to fluoride, which are discussed by. Hepatic hyperaemia after administration of acetate acid to rats has been observed by Luty.[10] In some systemic diseases, hyperaemia seems to be beneficial, e.g. in myocarditis. The findings of laboratory and epidemiologic studies conducted during water fluoridation period suggest that the deathrate thanks to heart infarct may have decreased thanks to fluorine compounds present in beverage.

Some literature reports as fluorine accumulates within the liver. Its blood level depends on fluoride supply, which refers to all or any fluorine forms in serum. As revealed by Chlebna- Sokó³, thanks to high homeostasis of the serum, blood fluoride levels remain constant even within the case of over dosage.[11]

The NaF-induced morphological changes in rat hepatocytes create an image almost like those observed after intoxications with other toxic compounds administered to experimental animals. It is often assumed that the liver is involved in detoxication of excessive fluorine doses. After NaF withdrawal, the changes within the liver in both groups were subsiding. The glycogen count increased, but during a considerable number of cells vacuolar degeneration persisted. Remission of most

pathomorphological changes after NaF withdrawal may suggest their transitory nature. However, at the time of exposure salt affects the event of the organism both within the prenatal and postnatal period of experimental animals.

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