CORRELATIONS BETWEEN FLUORIDE CONCENTRATIONS AND FREE RADICAL PARAMETERS IN SOFT TISSUES OF RATS

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SUMMARY: In previous studies we investigated the impact of subchronic exposure of rats to sodium fluoride administered in their drinking water as it affected selected biochemical parameters in their soft tissues and organs. The activity of glutathione peroxidase and the concentrations of fluoride, reduced glutathione (GSH), substances reacting with thiobarbituric acid (TBARS), and carbonyl groups were determined in kidney, liver, brain, testis, and blood or serum. To ascertain if there is interdependence between fluoride concentrations and these free radical parameters, respective correlation coefficients were calculated. Strong positive and negative correlations in the tissues investigated were found. The results of this study increase the evidence for free radical involvement in fluoride toxicity.

Keywords: Carbonyl groups; GSH and glutathione peroxidase; Negative fluoride correlations; Positive fluoride correlations: Rat soft tissues; Reduced glutathione (GSH); Thiobarbituric acid (TBARS) and carbonyl groups.

INTRODUCTION

In previous studies[1-3] we determined the effect on selected biochemical parameters in various soft tissues of subchronic exposure of rats to sodium fluoride administered in their drinking water. Among parameters characterizing antioxidant defenses, the activity of glutathione peroxidase (GPx)[4] and concentration of reduced glutathione (GSH)[5] were determined.

The impact of fluoride on free radical parameters in soft tissues has been investigated by many authors.[6-8] Recently several reviews have appeared on this subject.[9,10] In our experiments with rats to determine free radical damage, the concentration of substances reacting with thiobarbituric acid (TBARS)[11] and the concentration of carbonyl groups[12] were selected. The already mentioned parameters of these substances, as well as the concentration of fluoride,[13] were determined in kidney, liver, brain, testes, and serum. The protocol for these experiments has already been reported.[3] Results of fluoride determinations, as well as values concerning antioxidant defenses and free-radical mediated tissue impairments in the investigated tissues were also presented earlier.[1-3]

In this report, in order to ascertain if interdependence between fluoride concentrations and the foregoing free radical parameters occurs, respective correlation coefficients were calculated.

RESULTS AND DISCUSSION

Fluoride concentrations increased in all organs and tissues in a dose and exposure-time dependent manner.[1] Also, the concentration of TBARS and carbonyl groups in kidney, liver, brain, testes, and plasma increased in the same manner.[2,3] On the other hand, the activity of glutathione peroxidase (GPx) and

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concentration of reduced glutathione (GSH) decreased in a dose and exposure-time dependent manner.[2,3]

Glutathione peroxidase (GPx) removes H_2O_2 by coupling its reduction to H_2O with oxidation of reduced glutathione, GSH. It is the most important enzyme for extraperoxisomal inactivation of H_2O_2, especially in the liver. GPX enzymes are widely distributed in animal tissues and are specific for GSH as a hydrogen donor.

Correlation coefficients between fluoride concentrations and investigated free radical parameters are presented in the following table.

Table. Correlations between fluoride concentrations and investigated free radical parameters

Parameter	Tissue	Number of mean values	Correlation coefficient	p-value
F^-/GPx	kidney	51	–0.802	<0.001
	liver	45	–0.791	<0.001
	brain	44	–0.662	<0.001
	testes	53	–0.696	<0.001
	blood	46	–0.654	<0.001
F^-/GSH	kidney	55	–0.826	<0.001
	liver	51	–0.720	<0.001
	brain	45	–0.826	<0.001
	testes	52	–0.628	<0.001
	blood	46	–0.700	<0.001
F^-/TBARS	kidney	57	0.846	<0.001
	liver	51	0.796	<0.001
	brain	50	0.694	<0.001
	testes	59	0.662	<0.001
	blood	39	0.702	<0.001
F^-/carbonyl groups	kidney	57	0.777	<0.001
	liver	46	0.796	<0.001
	brain	44	0.688	<0.001
	testes	56	0.878	<0.001
	blood	41	0.332*	0.316

*Non-significant

No information about correlations between fluoride concentrations and free radical parameters in soft tissues were found in the literature. In this study the

existence of significant negative correlation coefficients was demonstrated between fluoride concentrations in liver, kidney, brain, testes, and blood (serum, plasma) and the activity of glutathione peroxidase (r = –0.802 to –0.654) as well as the concentration of GSH (r = –0.826 to –0.628). On the other hand positive correlations were found between concentrations of fluoride and TBARS (r = 0.846 to 0.662) as well as between concentrations of fluoride and carbonyl groups (r = 0.878 to 0.688) in the investigated tissues. Only in serum/plasma was there no correlation (r = 0.332) between fluoride levels and carbonyl concentrations.

These results indicate that fluoride intensifies lipid peroxidation and protein oxidation and reduces the antioxidant potential in the living cells. Fluoride effects on structure and functions of tissues and organs also suggest production of free radicals that have adverse influences on the defense mechanisms of living cells.[6,14-16]

Authors investigating the influence of fluoride on the specific parameters considered here have sometimes reported different, even contradictory results.[17,18] Some authors have found a decrease in parameters characterizing the antioxidant defenses in the body and an increase in free-radical mediated tissue impairments (like lipid peroxidation, oxidation of proteins, oxidative DNA damage).[7,8,19-21,22-24]

Other investigators,[25-27] however, have reported that fluoride does not impair antioxidant systems. Such differences in results are possible due to many factors, like differences in animal species, dose, mode and time of exposure, kind of tissues examined, as well as methods used for biochemical assay.[28,29]

The results of our studies support the positive findings of various authors[7,8,11,12,30] and indicate the involvement of free radical mediated mechanisms in fluoride toxicity.

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