

DISTURBANCES OF KIDNEY FUNCTION IN RATS WITH FLUORIDE-INDUCED HYPERGLYCEMIA AFTER ACUTE POISONING BY SODIUM FLUORIDE

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SUMMARY: Eight 14-week-old male Wistar FL strain rats were administered sodium fluoride in a single intraperitoneal dose (35 mg NaF/kg of bw). After 90 min the rats were fatally anesthetized with ether, and blood samples were taken. Compared to ten control rats, fluoride-treated rats developed hyperglycemia accompanied by a statistically significant increase in the concentration of fluoride, creatinine, and urea and a decrease in the level of protein and calcium in the blood serum. The results indicate disturbances in the filtrating function of kidneys in rats.

Keywords: Acute fluoride intoxication; Fluoride in rats; Hyperglycemia; Kidney disturbances; Serum changes.

INTRODUCTION

Acute poisoning by fluoride is most often a result of the intake of significant amounts of toxic fluoride compounds such as HF, NaF, or Na₂SiF₆. Depending on the type of fluoride compound and dose, various types of adverse responses may occur. In mammals, acute fluoride intoxication produces a clinical syndrome characterized by nausea, vomiting, diarrhea, abdominal pain, and paresthesias.¹

The purpose of this study was to induce hyperglycemia by fluoride and to examine kidney function after acute poisoning of rats (35 mg of NaF/kg of bw).^{2,3} In assessing the renal effects of fluoride, the concentration of creatinine, urea, protein, and calcium in blood serum have been examined.⁴ This study is a supplement to our previous one, in which we described the disturbance of protein metabolism in rats after acute poisoning with sodium fluoride.^{5,6}

MATERIALS AND METHODS

The experiment was carried out on 18 male Wistar FL rats (14 weeks old) obtained from the Central Animal Farm of Breeding for Experimental Animals of the Medical University of Silesia in Katowice, Poland.

The control group consisted of 10 animals and the experimental group 8 animals, all having an average body mass $202.8 \text{ g} \pm 15.02 \text{ g}$. The animals of the experimental group were administered 0.5 mL of physiological saline-sodium fluoride intraperitoneally in a single dose (35 mg NaF/kg of body mass). Rats of the control group were administered intraperitoneally 0.5 mL of physiological

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saline only. The rats were fed a standard Altromin (Germany) rat diet with an average fluoride content of 0.7 mg F⁻/kg.

Ninety minutes after being injected, the rats were fatally anesthetized with ether, and blood was taken from the left ventricle. In the blood serum, the fluoride ion concentration was determined, by an ion selective electrode.^{5,6} The concentration of urea in the serum was determined with the ALPHA-DIAGNOSTIC (Germany, catalogue No. B 6550) urea kit.⁵ The concentration of glucose was determined by the CORMAY (Poland) enzyme kit,⁶ the concentration of protein by the MERC-BIOTROL (France, catalogue No. A 01394) protein kit, creatinine by the COBAS MIRA ROCHE (Switzerland) biochemical analyzer kit, and calcium by the DIAGNOSTIC (Germany, catalogue No. C 6503-250) kit for Ca.

For statistical analysis of the results, the Student t test was applied (software package STATGRAPHIC 5.0).

RESULTS

Blood serum data from the controls and the experimental group of rats after intraperitoneal administration of a single dose of NaF in the amount of 35 mg NaF/kg of bw are shown in Tables 1 and 2. There was a 26-fold increase in the concentration of fluoride in the blood serum compared to the control group. This increase was accompanied by an 80% increase of the concentration of urea, a 47% increase of glucose, and a 19% increase of creatinine in the serum. All these changes were statistically significant. The serum concentration of protein was 14% lower, but not significantly lower, than in the control group. On the other hand, a highly significant 13% decrease in the concentration of serum calcium was observed.

Table 1. Concentration of fluoride, urea, and glucose in blood serum of rats after a single intraperitoneal injection of 35 mg NaF/kg of bw compared to the control group

Concentration in serum	Control group mean $\pm$ SD (n = 10)	Fluoride group mean $\pm$ SD (n = 8)	p-value
Fluoride μ mol/L	4.4 $\pm$ 0.2	177.0 $\pm$ 15.0	<0.001
Urea mmol/L	25.99 $\pm$ 3.39	46.87 $\pm$ 3.51	<0.001
Glucose mmol/L	3.18 $\pm$ 0.72	4.67 $\pm$ 0.77	<0.001

Table 2. Concentration of protein, creatinine, and calcium in blood serum of rats after a single intraperitoneal injection of 35 mg NaF/kg of bw compared to the control group

Concentration in serum	Control group mean $\pm$ SD (n = 10)	Fluoride group mean $\pm$ SD (n = 8)	p-value
Protein g/dL	7.62 $\pm$ 1.00	6.56 $\pm$ 0.2	>0.05 (p = 0.056)
Creatinine μ mol/L	51.27 $\pm$ 8.12	60.78 $\pm$ 7.38	<0.02
Calcium mmol/L	2.56 $\pm$ 0.17	2.23 $\pm$ 0.09	0.001<p<0.05

DISCUSSION

Fluoride hyperglycemia as found in our experiment with rats was accompanied by impairment of renal function. A statistically significant increase in the concentration of creatinine in the blood serum may have resulted from its decreased excretion which, in turn, is related to renal insufficiency. Because the concentration of creatinine in blood correlates inversely with the volume of glomerular filtration, the former is a useful marker of the filtration function of kidneys, the more so in that creatinine is excreted only via the kidneys.⁷ Impaired renal function would also explain the drastic increase of the urea in the blood serum of the treated rats. A lower rate of secretion of urea into urine resulting from renal insufficiency would cause its concentration in serum to increase. Appelton,⁸ after injection of high doses of sodium fluoride into rats found increases in the concentration of glucose, urea, and creatinine in the plasma. The increase of urea and creatinine concentration in the serum was interpreted by this author as reflecting impaired renal function.

Decreased concentration of blood serum calcium in the fluoride-treated rats may confirm renal insufficiency, although fluoride in itself is known to cause hypocalcaemia.⁸ Kidney diseases are also accompanied by a decrease in protein concentration in blood serum.⁹ Although we found no significant decrease in the concentration of protein in blood serum in our experimental animals, 37.5% of those rats were confirmed to have impaired renal function. (p for protein = 0.056. It is near the value for statistical significance. Percent [%] of rats = % values below average).

In this study, a single large intraperitoneal dose of fluoride was found to cause a much larger increase in the concentration of fluoride in serum than can be achieved by administration of fluoride via a stomach tube.^{6,10} The high concentration of fluoride in serum may also be connected with renal injury. Although the highest serum concentration of fluoride which causes acute nephrotoxic effect often exceeds 50 μ mol/L, changes in the functioning of kidneys have often been observed at lower concentrations of fluoride.¹⁰ Renal lesions caused by the pres-

ence of fluorides have already been reported by numerous authors.¹¹⁻¹⁴ Our studies have shown that in experimental fluoride-induced hyperglycemia, attention should also be paid to simultaneous occurrence of impairment of renal function. Presumably, reduced glomerular filtration takes place. Fluoride is filtrated by glomerular capillary vessels and undergoes tubular re-absorption to various degrees.¹⁵ Among halogens, renal clearance of fluorides is extremely high (35 mL/min).

CONCLUSION

In this study we found that a single dose of intraperitoneally administered NaF (35 mg/kg of bw) in rats not only induced hyperglycemia but also disturbed the function of the kidneys as manifested by reduced glomerular filtration.

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