

THE EFFECT OF DOSE ON MATERNAL – FOETAL TRANSFER OF
FLUORIDE IN RABBITS

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Received July 16, 1990.

Placental transfer of fluoride was investigated by fluoride determination in the bones and teeth of newborn rabbits whose mothers had been treated with fluoride during pregnancy. The mothers were given doses of 0, 0.10, 0.52 and 1.05 mmol fluoride per kg body weight as sodium fluoride, from the 16th day after conception to the end of pregnancy. All the doses produced a significant increase of fluoride level in the bones and teeth of newborn rabbits, indicating that the placenta was no barrier for the passage of fluoride.

Key terms: fluoride in bones, fluoride in teeth, pregnancy, rabbit placenta, sodium fluoride.

Placental transfer of fluoride is still a matter of controversy. Some authors describe the role of the placenta as that of a barrier preventing excessive amounts of fluoride from reaching the developing foetus. Others believe that the function of the placenta is to make sure that the foetus receives its due share of fluoride. Observations on the human foetus (1) have shown that increase in the skeletal fluoride level is proportional to that of calcification, if drinking water contains 0.5–0.6 ppm F⁻. *Knouff and co-workers* (2) investigated placental transfer of fluoride in pregnant dogs treated with different levels of fluoride in drinking water. Fluoride was not detected in the foetus of the mother that had received 2.3 ppm F⁻ during the last eight weeks of gestation, but was measurable in the foetus of the mother whose drinking water had contained 11.3 ppm F⁻ throughout pregnancy. The authors concluded that maternal tissues had the capacity to retain certain amounts of fluoride. However, according to *Hobbs and co-workers* (3) elevated maternal ingestion of F⁻ produced no significant effect on the placental transfer of fluoride. *Bell and co-workers* (4) showed that the placenta formed a barrier for the free passage of F¹⁸, while *Maplesden and co-workers* (5) stated that fluoride

in the foetus increased with high dietary fluoride (50–300 ppm F^-) intake in rats and rabbits. They also proved that the placental passage of F^- was greater in the rabbit than in the rat. More recently, the effectiveness of prenatal fluoride intake has been investigated in respect to caries prevention (6–8).

The aim of this work was to study the placental transfer of fluoride in pregnant rabbits in conditions of chronic intoxication with different doses of fluoride by determining fluoride level in the skeleton of newborn rabbits.

MATERIALS AND METHODS

Four groups of eight female rabbits each (*Oryctolagus cuniculus* – Belgian hare, 1.5 years old, weighing 2.5–3 kg before conception) were administered aqueous solutions of sodium fluoride which gave daily fluoride dose levels of 0, 0.10, 0.52 or 1.05 mmol per kg body weight. Treatment was by intubation, daily, from the 16th day after conception up to the end of pregnancy. Fluorides were not administered during the first phase of pregnancy for fear of inducing negative effects on foetal development. Gestation lasted 30–33 days. Fluoride levels in the animal diet were low: 45 μmol per kg oats and 56 μmol per kg hay; drinking water contained 5.26 μmol F^-/L .

Fluoride levels were determined in femoral bones and in the teeth of pups killed immediately after birth (each female rabbit, 4–6 newborns). Fluoride analyses in all samples were carried out with an ion-selective electrode (9) after fluoride microdiffusion as proposed by Soldatović and Nedeljković (10). Student's t-test was used for statistical analysis. The means and standard deviations were calculated for each group.

RESULTS

Experimental results are shown in Figure 1. All fluoride doses administered to pregnant rabbits (0.10, 0.52 and 1.05 mmol F^-/kg) induced a significant increase in the fluoride content in the bones and teeth of the newborn ($P < 0.001$). The increase was dose dependent, i.e. the amount of fluoride in the newborn depended on the dose given to pregnant mothers. High concentrations were found in the skeletons of newborn rabbits whose mothers were treated with a dose of 1.05 mmol F^-/kg body weight. Compared with control values, fluoride concentrations after treatment were 59 times higher in the bones and 56 times in the teeth.

DISCUSSION

The optimal fluoride level for reducing dental caries is 52.6 $\mu\text{mol}/\text{L}$ (mg/L) in drinking water. However, fluoride levels exceeding 78.9 $\mu\text{mol}/\text{L}$ (1.5 mg/L) can cause various disturbances in the body, because of the effect on enzyme reactions and especially because of the negative effect of fluorosis on skeletal mineralization, which

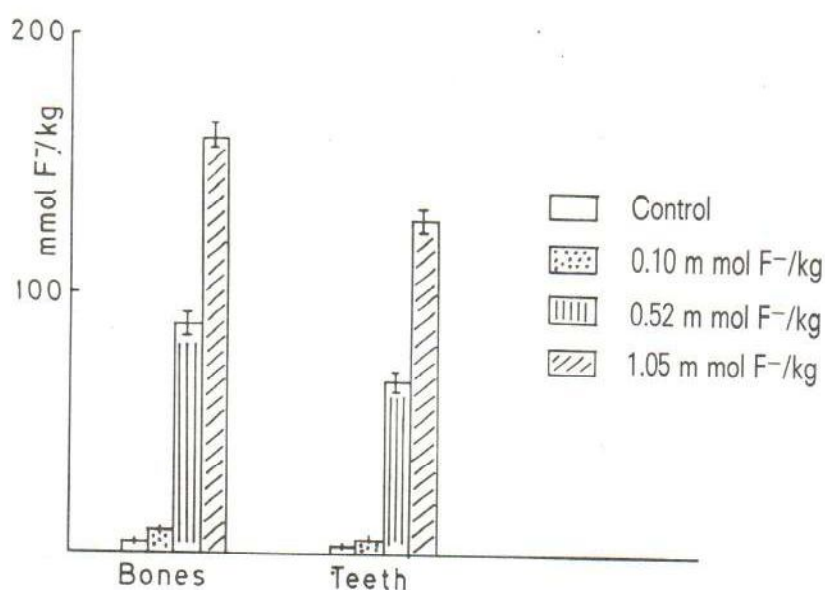


Figure 1. Fluoride levels in the bones and teeth of newborn rabbits whose mothers had been exposed to various levels of fluoride during pregnancy

begins in the uterine phase. One of the most sensitive biological reactive processes of the body to fluoride intoxication takes place in the teeth. The effectiveness of prenatal fluoride administration as a caries-preventive method in the newborn, or the appearance of intoxication, depend upon the placental transfer of fluoride. The existing data on placental fluoride transfer (2 - 5, 11) are inconsistent, probably because of the species differences and differences in the levels of dose administered.

Based on autoradiographic investigations of F^{18} distribution in mice and rats *Ericson and Ullberg* (12) consider the placenta to form a partial barrier to fluoride. *Miller and Phillips* (13) investigated the effect of age on the level and metabolism of fluoride in the bones of rats on fluoride supplemented diet and found that young rats deposited and retained greater amounts of dietary fluoride than the adult. The same conclusion can be drawn from our previous investigations carried out in rabbits (14) as well as from the results of this work. There have been studies on humans showing that there is no placental barrier to fluoride (6, 7). Investigations carried out on guinea pigs showed an increase in the mean enamel fluoride concentrations which was in correlation with maternal plasma fluoride levels (8).

In this experiment we investigated the effect of dose on placental transfer of fluoride in rabbits. We observed a significant, although non-linear, dose-dependent increase of fluoride in the bones and teeth of all newborn rabbits. Our results show that the rabbit placenta is a poor barrier for the passage of fluoride, for all fluoride doses administered.

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Sažetak

UTICAJ DOZE NA PROLAZ FLUORIDA KROZ PLACENTU U KUNIĆA

Prolaz fluorida kroz placentu ispitivan je određivanjem koncentracije fluorida u kostima i zubima mladunaca gravidnih ženki kunića tretiranih fluoridima. Primenjene su doze 0, 0,10, 0,52 i 1,05 mmol F^{-} /kg telesne mase u obliku vodenog rastvora natrijum-fluorida, od 16. dana posle začeća do kraja graviditeta. Pri svim ispitivanim dozama dolazi do porasta koncentracije fluorida u kostima i zubima mladunaca, što pokazuje da placenta ne predstavlja barijeru za prolaz fluorida.

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Ključne reči: fluorid u kostima, fluorid u zubima, graviditet, placenta u kunića, natrijum-fluorid.