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Fluoride concentration in amniotic fluid and fetal cord and maternal plasma

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Summary

Fluoride concentrations were determined in plasma of 50 pregnant women, 44 samples of amniotic fluid and fetal cord blood of 29 fetuses at various stages of normal pregnancies, from an area with a relatively low water fluoride (< 0.5 ppm) content. The mean concentrations of fluoride from maternal plasma, cord plasma and amniotic fluid (\pm S.D.) were 0.033 ± 0.003 , 0.028 ± 0.005 and 0.017 ± 0.003 ppm, respectively. Maternal and fetal plasma fluoride concentrations did not differ significantly. In the older age group fetal cord plasma fluoride concentration was significantly lower than maternal plasma levels (0.012 ± 0.08 ppm vs. 0.023 ± 0.001 , respectively; $p < 0.05$). Amniotic fluid fluoride levels were significantly higher at term than in midtrimester pregnancy, 0.017 ± 0.0018 vs. 0.010 ± 0.009 ppm ($P < 0.05$), respectively. This higher concentration may imply higher fetal urinary excretion of fluoride at term due to the lower sequestration of fluoride as the process of bone calcification is more complete.

fluoride; amniotic fluid and fluoride; fluoride concentrations in pregnancy; body fluid fluoride levels

Introduction

The concentration of ionic fluoride in plasma is influenced by the quantity of ingested fluoride absorbed from the gastro-intestinal tract, its distribution in body fluid compartments, renal excretion, and fluoride turnover by calcified tissues. Under normal circumstances the fluoride concentrations in saliva [1] milk [1,2] and

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plasma [3,4] are extremely low, while urine has a much higher fluoride concentration [5]. Although there is considerable information relating the concentration of fluoride in plasma to such factors as dietary fluoride intake, aging while on a constant fluoride exposure and some disease states [4], there is little known of the relative concentration of fluoride in maternal and fetal plasma and that present in the amniotic fluid. Backer Dirks et al. [6] in an abstract reported mean fluoride concentrations of 0.19, 0.21 and 0.40 ppm at birth in sera of the mother and the neonate, and the amniotic fluid, respectively, when the drinking water contained 10–20 parts per million (ppm) fluoride. On the other hand, when the water contained 2–3 ppm fluoride, 0.10, 0.06 and 0.17 ppm fluoride, respectively, were reported in these body fluids. The plasma levels are higher than that reported in fluoridated communities where the water supply contains approx. 1 ppm fluoride [4].

In 1970 Armstrong et al. [7] found that ashed sera from maternal and umbilical blood obtained at cesarean section contained similar concentrations of fluoride and suggested that there was no placental barrier to the passage of fluoride to the fetus. Gedalia [8] reported, however, that with an adequate fluoride intake the fluoride concentration in the umbilical cord blood was consistently lower than the mother's blood level although this was not the case when the fluoride intake was low. It has been suggested that the fetal blood fluoride concentration is not increased to the same extent as maternal plasma fluoride when fluoride intake is increased [9]. Shen and Taves [10] determined the ionic fluoride concentration in maternal and cord blood with the fluoride ion electrode for the first time and obtained results consistent with their hypothesis that fluoride diffuses passively across the placenta. They found the ratio of the concentration of fluoride in sera obtained from cord blood to maternal blood to be 0.86.

The level of fluoride found in the amniotic fluid has not been well defined when the drinking water contains optimal or lower levels of fluoride and the possible physiological significance of the concentration on the development of the fetus cannot be speculated upon if the concentration is not known. The purpose of the present investigation was to determine the concentration of fluoride found in maternal and cord plasma and amniotic fluid during gestation, in patients from a geographical area where the concentration of fluoride in drinking water is low (< 0.5 ppm).

Materials and methods

From each of 50 normal pregnant patients between 16 and 40 wk of pregnancy blood was drawn in evacuated tubes containing heparin. Amniotic fluid was obtained from 44 of these patients during mid-trimester amniocentesis, for genetic diagnosis in 15 women and during elective cesarean section in 29 women. The amniotic fluids in this study were not contaminated by blood. They were centrifuged at 3000 rpm, and the cell-free supernatant was frozen. Cord blood was drawn at the cesarean sections in heparin-containing tubes. All blood samples were centrifuged and the plasma, with amniotic fluid, were stored at -40°C until fluoride was determined.

TABLE I

Effect of age on mean fluoride levels in plasma and amniotic fluid (ppm \pm S.E.)Numbers of donors are in parentheses. Values bearing the same superscript vary statistically from each other at $P < 0.05$.

Maternal age (yr)	Plasma		Amniotic fluid	Concentration ratio	
	maternal	cord		maternal plasma cord plasma	maternal plasma amniotic fluid
20-27	0.033 \pm 0.0071 (6)	0.021 \pm 0.0051 (5)	0.015 \pm 0.0013 (5)	1.17 \pm 0.251 (5)	1.87 \pm 0.415 (5)
29-33	0.033 \pm 0.0045 ^a (9)	0.029 \pm 0.0071 ^b (8)	0.017 \pm 0.0020 ^{a,c} (8)	1.19 \pm 0.230 (8)	1.78 \pm 0.294 (8)
36-39	0.023 \pm 0.0018 ^{d,e} (10)	0.012 \pm 0.0024 ^{b,d} (5)	0.010 \pm 0.0023 ^{c,e} (10)	2.97 \pm 1.027 (5)	2.83 \pm 0.628 (9)
18-39 *	0.033 \pm 0.0030 ^{d,f} (49)	0.028 \pm 0.0052 ^g (29)	0.017 \pm 0.0031 ^{f,g} (44)	1.27 \pm 0.126 (22)	2.32 \pm 0.227 (39)

* All donor samples, donors 18-39 years of age.

A stock solution of fluoride containing 10 mg fluoride per liter was prepared by dissolving 22.1 mg reagent-grade sodium fluoride in a liter of distilled water. From this stock solution more dilute standard solutions (0.01, 0.02, 0.03, 0.05, 0.10, 0.20 and 0.30 ppm F) were prepared in 50% TISAB buffer in water.

Ionic fluoride was determined in 1–2 ml plasma or amniotic fluid diluted with an equal volume of TISAB buffer (Orion Research Incorporated, Cambridge, MA) which adjusted the pH to 5.0. The millivoltage reading was measured in solutions containing known concentrations of fluoride and in the biological fluids 10 min after immersion of the electrode in the buffered solution. Millivolt readings given by the plasma or amniotic fluid specimens were converted to fluoride concentrations [3].

Means and standard error of the mean (S.E.) for different subgroups were compared by Student's *t*-test [11]. A probability value of less than 0.05 was taken as indicating significance.

Results

The effects of age on fluoride levels in maternal and cord blood are shown in Table I. The ratio of the fluoride concentrations in maternal plasma and cord plasma as well as the ratio between maternal plasma fluoride and amniotic fluid fluoride levels are calculated. To investigate the effect of the length of gestation on the relationship between the fluoride content of maternal plasma and that of the corresponding amniotic fluid specimen the donors in this series were divided into distinctly different age group ranges (Table I) and subgroups pregnant for 16–30, 36–40, and 16–40 wk (Table II).

Mean fluoride levels of 0.033 ± 0.003 , 0.017 ± 0.003 and 0.028 ± 0.005 ppm (\pm S.E.) were found in the maternal plasma, amniotic fluid and plasma from cord blood, respectively, for all patients in this study (Table I). The older patients (36–39 years of age) had significantly lower fluoride concentrations in the maternal and cord plasma as well as in the amniotic fluid than women in the two younger age groups shown in the table. The amniotic fluid had a much lower mean fluoride concentration than that found in cord or maternal plasma.

TABLE II

Mean fluoride levels in maternal plasma and amniotic fluid during gestation (ppm \pm S.E.)

Numbers of donors are in parentheses. Values bearing the same superscript are statistically different from one another with $P < 0.02$.

Weeks gestation	Maternal plasma	Amniotic fluid	Maternal plasma amniotic fluid	Cord plasma amniotic fluid
16–30	0.026 ± 0.0023^a (12)	$0.010 \pm 0.0010^{a,d}$ (12)	2.95 ± 0.442^c (12)	–
38–40	0.035 ± 0.0039^b (19)	$0.017 \pm 0.0018^{b,d}$ (16)	1.70 ± 0.190^c (15)	1.92 ± 0.355 (22)
16–40	0.031 ± 0.0025^c (31)	0.014 ± 0.0011^c (28)	2.47 ± 0.295 (27)	–

Table II relates fluoride levels in maternal plasma and amniotic fluid to the period of gestation. It is shown that in term pregnancies the fluoride concentration in maternal plasma and amniotic fluid was significantly increased, while the ratio of the mean fluoride concentration found in maternal plasma to that in amniotic fluid was significantly decreased, and was similar to the ratio calculated for the concentration in fetal cord blood plasma to that in amniotic fluid.

Discussion

Fetal urine is the major source of water, ions and other compounds for the amniotic fluid in the last two trimesters of pregnancy [12,13] Another source, quantitatively of lesser importance, is the chorionic plate of the placenta through which these compounds may transfer into the amniotic fluid from the fetal capillary bed [14,15]. Amniotic fluid is also constantly circulating through the fetal lungs which also contribute some of the fluid components [16].

The fluoride concentrations in maternal and cord plasma levels were not significantly different in patients in our series when age was not considered (Table I). This finding is in agreement with the reports of Shen and Taves [10] and Gedalia et al. [9], who did not find a difference in fluoride concentration when fluoride intake was low. In the present study the patients were also grouped according to age and only in the older age group (36–39 years of age) was there a significantly lower concentration of fluoride in cord plasma than in maternal plasma. A possible explanation for this difference is the theoretical possibility that this finding may be related to a general lower transplacental transfer in this older age group as part of a lower uterine blood flow at the placental bed. A significantly higher amniotic fluid fluoride concentration (0.017 vs. 0.010 ppm) was found in term pregnancies (Table II), manifested also by the lower mean fluoride concentration ratio of maternal plasma to amniotic fluid (1.70 vs. 2.95). The fluoride concentration in cord plasma was almost twice that in amniotic fluid. The increase in fluoride concentration in amniotic fluid is in contrast with the behavior of chloride, another halogen which has a slightly lower concentration in amniotic fluid in late pregnancy when the amniotic fluid becomes hypotonic [17]. The increase in fluoride may reflect lower uptake of fluoride in fetal calcified tissues with the decreased bone calcification at term. This lower uptake may lead to higher amniotic fluid concentration. The concentration of fluoride in amniotic fluid was lowest in amniotic fluid of older women and much lower than the concentration of maternal plasma in all groups (Table I).

These low concentrations of fluoride in amniotic fluid and the slightly lower concentration in fetal plasma compared with maternal plasma suggest that the fluoride concentration does not constitute a danger to the developing fetus of women consuming water containing less than 0.5 ppm fluoride concentration. It is likely that the amniotic fluid fluoride concentrations of persons consuming an optimal level of fluoride in water (1 ppm), based on the low plasma fluoride concentration reported by others [4], would not be high.

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