TRANSPLACENTAL PASSAGE OF FLUORIDE IN PREGNANT POLISH WOMEN ASSESSED ON THE BASIS OF FLUORIDE CONCENTRATIONS IN MATERNAL AND CORD BLOOD PLASMA

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SUMMARY: The aim of this study was to evaluate placental transfer of fluoride (F) in 30 pregnant women at the time of giving birth, who were living in Poznan, Poland, where the F concentration in the drinking water ranges from 0.4 to 0.8 mg/L. F concentrations of maternal and umbilical venous cord blood plasma were determined in samples drawn at delivery. The mean concentration of F in maternal plasma was significantly higher than in venous cord plasma (3.54 vs. 2.89 µmol/L, respectively), and both values were similar to those previously documented in pregnant women taking prenatal F supplements. The results confirm that F readily passes through the placenta and that prenatal F supplements, still recommended by some authors, are contraindicated in this population.

Keywords: Fluoride exposure; Placental F transfer; Plasma fluoride; Poznan, Poland; Pregnant women.

INTRODUCTION

Results of studies comparing F levels in maternal and umbilical cord venous blood plasma,[1-8] as well as intra-uterine studies,[9] prove that F passes through the placenta. Whether and to what extent the placenta can act as a filter and limit transmission of F to fetal circulation remain matters of debate,[1,3,4] and is therefore an important question in the discussion of prenatal F supplementation. Moreover, despite many unfavorable reports and opinions, many dental authorities still recommend prenatal F tablets for pregnant women to provide what some regard as appropriate dosages of F for the primary tooth buds. [10-14]

Our recent study of urinary fluoride levels of pregnant women in Poznan, Poland, where the F level in the drinking water is 0.4–0.8 mg/L, revealed that total F exposure of the examined population is relatively high and comparable to the level observed in areas with fluoridated water.[15] The aim of the present study was to assess F concentrations in maternal and umbilical cord venous blood plasma during delivery in the same group of pregnant women.

MATERIALS AND METHODS

The subjects of the study were 30 healthy pregnant women, 22–34 years old, who, during the pregnancy and delivery, were under medical supervision of physicians from the Department of Perinatology of the University of Medical Sciences in Poznan, Poland. These same women also participated in our recent study of urinary F levels during their pregnancies[15] and were recruited by voluntary consent in the Gynecology and Obstetrics Hospital in Poznan with approval by the Ethics Committee of the University.

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All women were hospitalized during the time of delivery. The duration of pregnancy, calculated from the date of the last menstruation, ranged from 38 to 41 weeks. Seven women delivered by caesarian section under local subarachnoid anesthesia, and the others delivered vaginally by spontaneous labor**.** All were informed of the purpose of the study and gave their consent for the blood sampling.

Seven-mL samples of venous cord blood and maternal blood were drawn at delivery into disposable polystyrene tubes containing heparin as an anticoagulant. The samples were centrifuged, and the separated plasma was stored at –20°C for 1 to 4 weeks. F analyses were conducted at pH 5.0 adjusted by TISAB III buffer with an Orion Model 96-09 F ion selective electrode in the standardized laboratory of the Department of Biochemistry and Chemistry of the Pomeranian Medical University in Szczecin. Measurements were performed using the convenient addition method[16] capable of determining F concentrations as low as 2.5 µg/L (= 0.0025 mg/L or 0.13 µM).

The data were analyzed statistically using Statistica Version 5 for Windows XP Professional Version 5.1 with significance taken as $p<0.05$.

RESULTS

Maternal and umbilical venous cord plasma F (MF and CF, respectively) and the CF MF ratio are presented in Table 1. The data were divided into two subgroups according to the value of the CF MF ratio (≥1.0 or < 1.0).

The MF concentration ranged from 2.40 to 6.80 µmol/L (mean value 3.54 µmol/L = 0.0673 mg/L), and the CF concentration ranged from 2.20 to 4.10 µmol/L (mean value 2.89 µmol/L = 0.0549 mg/L), which are significantly different.

Table 1. Maternal (MF) and cord (CF) blood plasma concentration (µmol F/L) and CF/MF ratio in two subgroups of pregnant women divided according to the CF/MF value

Group of women	No. of cases		MF	CF	CF/MF
CF/MF less than 1.0	25	Mean	3.69	2.84	0.822
		Median	3.00	2.80	0.871
		Min	2.40	2.20	0.427
		Max	6.80	3.50	0.971
		SD	1.24	0.38	0.166
CF/MF greater than or equal to 1.0	5	Mean	2.80	3.08	1.103
		Median	2.50	2.90	1.108
		Min	2.40	2.60	1.000
		Max	3.70	4.10	1.200
		SD	0.54	0.59	0.084
Total	30	Mean	3.54	2.89*	0.869
		Median	3.00	2.80	0.919
		Min	2.40	2.20	0.427
		Max	6.80	4.10	1.200
		SD	1.20	0.42	0.187

*$p<0.001$ compared with MF.

The ratio of the CF to MF concentration ranged from 0.427 to 1.20 (mean 0.869). In one case it equaled 1.0, and in four cases it exceeded 1.0.

Pearson correlation coefficients (r) and coefficients of determinations (r^2) between MF and CF, and between CF/MF ratio and maternal age are listed in Table 2. A positive correlation was found between MF and CF concentration (r = 0.45, p<0.02). There was no significant correlation between the mother's age and the CF MF ratio (p=0.41).

Table 2. Correlation between MF and CF levels and between maternal age and CF/MF ratio

	MF, CF	Maternal age, CF/MF
Pearson correlation coefficient, r	0.45*	0.16†
Coefficient of determination, r^2	0.20	0.02

*p<0.02, †p=0. 41.

DISCUSSION

Various authors, in different countries, who have measured F concentrations in the blood plasma and serum of pregnant women residing in areas with a level of F in drinking water ≤0.5 mg/L, report mean MF values of 1.46 µmol/L (0.0277 mg/L),[1] 1.79 µmol/L (0.0340 mg/L),[4] 1.37 µmol/L (0.0123 mg/L,[5] and 1.58 µmol/L (0.0300 mg/L).[7] In pregnant Polish women, Chlubek et al. found up to 4.25 µmol/L (0.0808 mg/L).[2] Despite similar content of F in the drinking water, the reported values vary widely, which might be attributed to the different total F exposures of examined populations. Today there are many other sources of F in the environment, and, as stated recently by the US National Academy of Sciences/ National Research Council, "... it is no longer feasible to estimate with reasonable accuracy the level of F exposure simply on the basis of concentration in drinking water supply."[17]

The study by Caldera et al.[1] revealed that the mean CF concentration of pregnant women taking F supplements (1.5 mg daily) residing in an area with about 0.5 mg F/L in the drinking water was 3.07 µmol/L (0.0583 mg/L), which is comparable to the value of 2.89 µmol/L (0.0549 mg/L) determined in our study group. Similarly, the intra-uterine study by Forestier et al.[9] showed that mean fetal blood serum F levels in mothers who had taken F tablets (2.212 mg NaF/day) equaled 2.6 µmol/L (0.0494 mg/L).

Results of our work indicate that CF concentrations reach, on average, 87% of those in maternal blood. Most authors have observed a similar pattern of results. The mean value of the proportion reported by other authors ranges from 60% in the study of Shimonovitz et al.[7] and the study of Gupta et al.[3], through 77% in Polish women examined by Chlubek et al.,[2] 75% in the group examined by Shen and Taves,[6] 84% in the study of Ron et al.,[5] and 91% in women examined by Montherrat-Carret et al.[4] The difference between the MF and CF levels might suggests that the placenta acts as a partial filter for F. A possible explanation of the F loss during transmission from maternal to fetal circulation has been presented by Chlubek et al.,[18] whose study revealed that F can be accumulated in the marginal parts of the placenta as a result of higher concentrations of calcium in those areas.

However, as already noted, in four cases in our study MF levels were lower than and in one case equaled CF levels. Caldera et al.,[1] who measured MF and CF levels in 91 women, obtained such results in most subjects of their study. Only a

few of the neonates had a CF level lower than the MF level. These authors note that MF and CF levels depend on the intake and the movement of F between plasma and skeleton. Instead of discussing a passive or active role of the placenta, they propose the concept of a maternal-fetal-amniotic pool that regulates maternal and fetal F plasma levels according to the F intake. Moreover, haemodynamic and haematochemical variations at the time of delivery also appear to affect CF levels, as suggested by Brambilla et al.[10] This is probably why only about 20% of the variance in CF levels in our work can be explained by variations in MF levels (Pearson correlation coefficient = 0.45 with the coefficient of determination = 0.20).

It has been suggested that higher maternal age can be related to generally lower transplacental transfer due to lower uterine blood flow at the placental bed.[2,5] Our research, however, does not confirm this view since no significant correlation was found between the mother's age and the CF/MF ratio. However, it might be connected with the wider age span of women in the studies by Ron et al.[5] and Chlubek et al.[2] (aged 18–39 and 17–38 years, respectively) compared to that of our group (aged 22–34).

It is noteworthy that results of the recent studies by Leverett et al.[19] and Fonteles et al.[20] have not supported the hypothesis that the use of fluoride supplements by pregnant women benefit their offspring. Moreover, as noted recently,[21] modern research provides little support for recommendation of either prenatal or postnatal F supplements. In spite of these controversies, prenatal fluoride supplementation has been a standard practice for years in some countries, including Poland.[10-14]

Our data indicate that in an area where the drinking water F concentration ranges from 0.4 to 0.8 mg/L, fluoride levels in maternal and cord blood plasma are comparable to those documented in patients from other areas who are taking F supplements (1.5 mg/daily). Thus, the use of additional F supplements is particularly contraindicated in this population. This practice could result in a further increase of F exposure to the fetus, which raises concerns in view of the potential negative effects of excessive amounts of F on fetal development.[22-24]

ACKNOWLEDGEMENTS

This study was supported by the Polish State Committee for Scientific Research E01922. We also wish to thank Professor Dariusz Chlubek for his expert support.

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