J. Perinat. Med.
15 (1987) 282

Vitamin D_3 metabolites in amniotic fluid in relation with maternal and fetal sera in term pregnancies

Moshe Ron, Jaccob Menczel, Lydia Schwartz, Zvi Palti, and Gideon Kidroni

Department of Obstetrics and Gynecology, and the Research Laboratory, Department of Medicine, Hadassah University Hospital Mount Scopus, Jerusalem, Israel

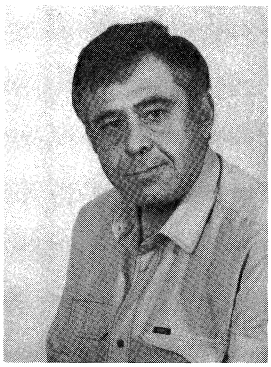
1 Introduction

Vitamin D_3 metabolites, among other important hormonal systems, regulate the feto-maternal calcium homeostasis during pregnancy [11, 22]. The three main metabolites are: 25-hydroxyvitamin D_3 ($25(OH)D_3$), which is formed in the liver by 25-hydroxylation of vitamin D_3, and is the precursor for further hydroxylation in the kidneys to 24,25-dihydroxyvitamin D_3 ($24,25(OH)_2D_3$) and to the hormonally most active form 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$).

Our present knowledge of the human maternal-fetal relationship of these metabolites is confined to studies in which these metabolites were investigated in humans by comparing post-partum maternal and cord sera levels [9, 10, 14, 15, 31]. As yet, there is not a unanimous agreement concerning the degrees and mechanisms of transplacental transfer from mother to fetus of each of the three metabolites [4, 21]. Moreover, the contribution of fetal metabolism to its own pool of the hydroxylated metabolites is still uncertain [11, 21]. A recent data shows that the fetus most probably contributes to its own $1,25(OH)_2D_3$ pool [19]. The maternal and cord sera levels of these metabolites were not yet correlated with another important compartment — the amniotic fluid. In the past, we have determined amniotic fluid levels of $25(OH)D_3$ and $24,25(OH)_2D_3$ during pregnancy [23]. However, the source of the amniotic fluid vitamin D_3 metabolites remained unclear.

In the present study levels of amniotic fluid $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ at term were compared with maternal and fetal cord serum levels. This information may be helpful in the assessment of the source of these metabolites in amniotic fluid.

Curriculum vitae



Dr. MOSHE RON *was born in Jerusalem in 1941. He finished medical school and training in Obstetrics and Gynecology at the Hadassah University Hospital, Medical Center of the Hebrew University in Jerusalem.*
In 1982 he served as a research assistant professor at the New York University Medical Center where he worked on the in vitro transplacental transfer system.
His main area of interest is perinatology. He is serving now as a senior lecturer and a staff physician in Obstetrics and Gynecology at the Hadassah University Hospital on Mount Scopus, Jerusalem, Israel.

2 Material and methods

Amniotic fluids, fetal cord and maternal blood samples were obtained from twenty-six normal pregnant white women during elective cesarean sections at 37–40 weeks of pregnancy during the period of December 1982–April 1983. None of the women received vitamin D preparations during pregnancy. Fetal and maternal sera were separated by centrifugation. The amniotic fluids obtained were not contaminated by blood. They were centrifuged at 3 000 r. p. m. and the cell free supernatant was frozen. All the samples were stored at −40 °C until further work up.

Blood samples were extracted for lipids (1.0 volume of serum + 10 volumes of ethanol) and the extracts (recoveries for $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ were 90%, 84% and 90%, respectively) were dried under nitrogen and redissolved in chloroform petroleum ether (1 : 1 by volume). Sephadex LH-20 (Pharmacia Fine Chemicals, Uppsala, Sweden) column chromatography of the lipid extracts was used to separate the vitamin D_3 metabolites. The columns (0.7 × 25 cm) were equilibrated and developed with chloroform-petroleum (b. p. 35–60 °C) 1 : 1 by volume [6]. The recovery of radioactivity from the columns was always 80%–85% or more for $25(OH)D_3$ and $24,25(OH)_2D_3$, and 60% or higher for $1,25(OH)_2D_3$.

All $1,25(OH)_2D_3$ fractions as well as several $24,25(OH)_2D_3$ fractions obtained after Sephadex LH-20 chromatography were further purified by High Pressure Liquid Chromatography (HPLC) [17]. All chromatographic systems were calibrated with authentic tritiated standard metabolites (The Radiochemical Center, Amersham, England). HPLC recoveries of $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ were 88%, 60% and 75%, respectively.

Measurements of radioactivity were carried out in a Packard Tri Carb automatic liquid scintillation spectrometer no. 3 255. Samples were dried and counted for radioactivity in 10 ml of a solution of 0.33% 2,5-diphenyl-oxazole (PPO), 0.02% 1,4- bis (2- [4-methyl-5-phenyloxazole]) benzene (dimethyl POPOP), dissolved in a 33% Triton X-100-toluene solvent (all Packard scintillation grade, Packard Instrument C., Illinois, USA). Quenching was accounted for by an external standardization and correction curves for tritium.

Established methods of competitive protein-binding assays were used to determine $25(OH)D_3$, $24,25(OH)_2D_3$ [30] and $1,25(OH)_2D_3$ concentrations [16]. (Radioactive metabolites purchased from The Radiochemical Center, Amersham, England; unlabelled metabolites – gift from F. Hoffman-La-Roche Co., Basle, Switzerland). The receptor used in the $1,25(OH)_2D_3$ assay was prepared in the buffer of EISMAN, et al. [7] with the addition of sodium molybdate [8] and kept lyophilized and refrigerated (−40 °C) until used.

To check for possible underestimations, controls were run in which known quantities of vitamin D_3 metabolites were added to serum samples. The assays of such controls resulted in good quantitative recoveries (88% for $25(OH)D_3$; 89% for $24,25(OH)_2D_3$). A student's t-test was used to assess the statistical significance of the experimental data. Where needed, a student's t-test for unequal variance was used. For correlating the various variants, least squares correlation coefficients were calculated.

3 Results

The results are presented in table I. The amniotic fluid level of $25(OH)D_3$ and $24,25(OH)_2D_3$ in this study are lower than those we have published previously and in agreement with the findings of LASEBNIK, et al. [20] (figures 1 and 2). Our data, at that time [23] were obtained by another assay method [13] which has since shown to produce higher than average results [26]. Amniotic fluid levels of $1,25(OH)_2D_3$ are shown in figure 3.

Fetal and maternal serum levels of the three vitamin D_3 metabolites were not statistically different. However, the differences between maternal serum and amniotic fluid levels of the

Table I. Levels of $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ in maternal serum, fetal cord serum and amniotic fluid at term.

Vitamin D_3 metabolites	Amniotic fluid	Fetal serum	Maternal serum
$25(OH)D_3$ ng/ml ± S. D.	0.732^b ± 0.508 (25)	13.15^a ± 8.3 (22)	18.03^a ± 10.8 (26)
$24,25(OH)_2D_3$ ng/ml ± S. D.	0.121^c ± 0.104 (26)	0.90^d ± 0.76 (22)	1.473^d ± 1.562 (26)
$1,25(OH)_2D_3$ pg/ml ± S. D.	14.3^e ± 10.0 (25)	29.2 ± 18.55 (14)	36.5^f ± 21.5 (17)

a vs b — statistically significant difference $p < 0.01$
c vs d — statistically significant difference $p < 0.01$
e vs f — statistically significant difference $p < 0.01$

Numbers in parentheses represent the number of individual analyses performed.

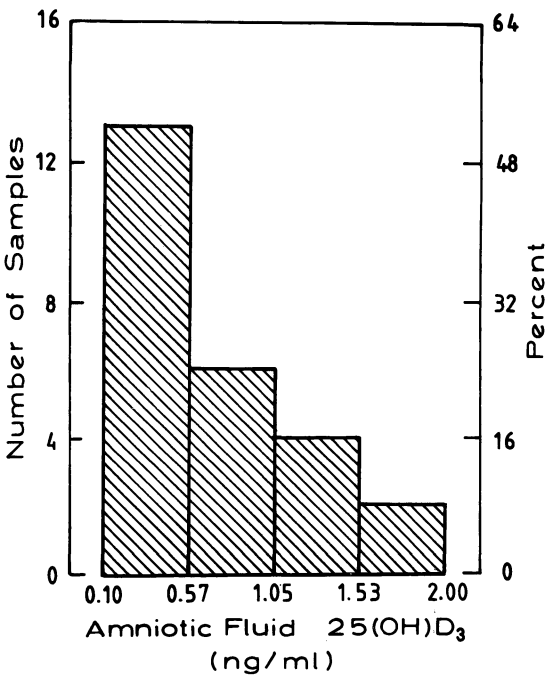


Figure 1. Histogram of amniotic fluid levels of 25 hydroxycholecalciferol.

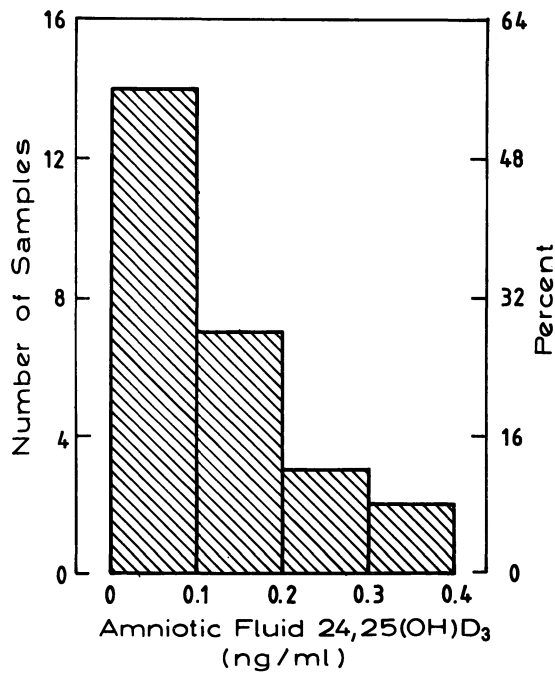


Figure 2. Histogram of amniotic fluid levels of 24,25 dihydroxycholecalciferol.

three metabolites were statistically significant ($25(OH)D_3$ — $p < 0.01$, $24,25(OH)_2D_3$ — $p < 0.01$ and $1,25(OH)_2D_3$ — $p < 0.01$).

A significant differences was found between fetal serum and amniotic fluid levels of $25(OH)D_3$ and $24,25(OH)_2D_3$ ($p < 0.01$ for both) but not between fetal serum and amniotic fluid levels of $1,25(OH)_2D_3$.

A significant correlation was found between $25(OH)D_3$ levels of maternal and fetal sera

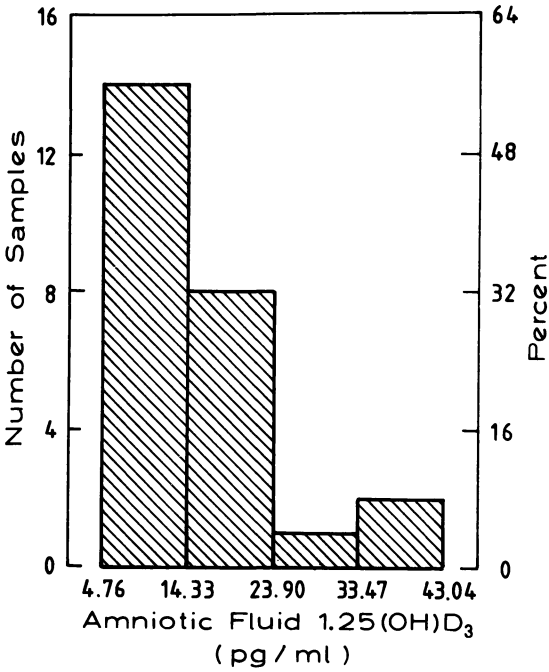


Figure 3. Histogram of amniotic fluid levels of 1,25 dihydroxycholecalciferol.

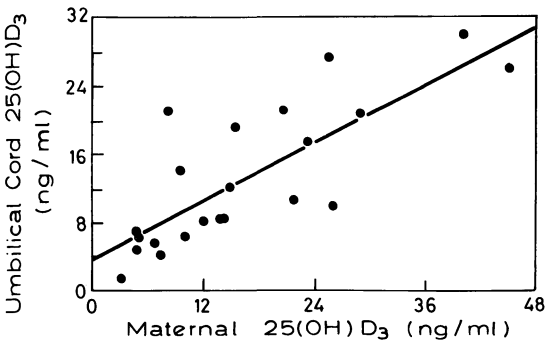


Figure 4. Correlation between maternal and fetal serum levels of 25 hydroxycholecalciferol. r = 0.791 p < 0.01.

(figure 4) (r = 0.791, p < 0.01), maternal serum and amniotic fluid (figure 5) (r = 0.697, p < 0.01) and fetal serum and amniotic fluid (figure 6) (r = 0.681, p < 0.01).

Maternal and fetal serum 24,25$(OH)_2D_3$ levels were also significantly correlated (figure 7) (r = 0.743, p < 0.01). No correlation was found between maternal and fetal sera 1,25$(OH)_2D_3$ levels, and neither for maternal serum and amniotic fluid, nor fetal serum and amniotic fluid levels for both 24,25$(OH)_2D_3$ and 1,25$(OH)_2D_3$.

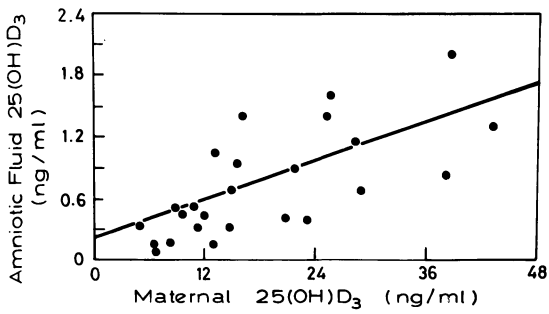


Figure 5. Correlation between maternal serum and amniotic fluid levels of 25 hydroxycholecalciferol. r = 0.697 p < 0.01.

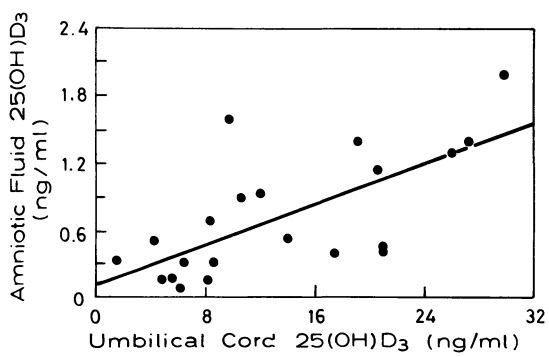


Figure 6. Correlation between fetal serum and amniotic fluid levels of 25 hydroxycholecalciferol. r = 0.681 p < 0.01.

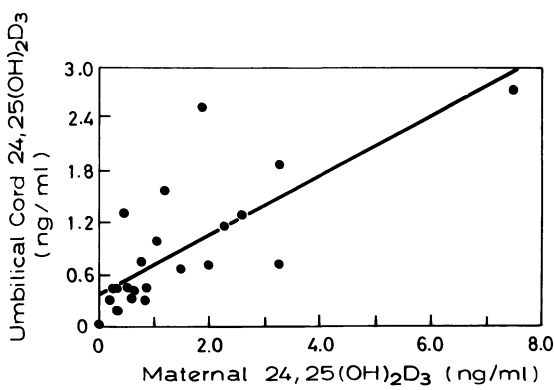


Figure 7. Correlation between maternal and fetal serum levels of 24,25 dihydroxycholecalciferol. r = 0.743 p < 0.01.

Maternal serum $1,25(OH)_2D_3$ levels were significantly higher ($p < 0.04$) at term (36.5 ± 21.5 pg/ml; $n = 17$) as compared with those from normal controls (24.9 ± 11.0 pg/ml; $n = 31$).

4 Comment

The source of amniotic fluid vitamin D_3 metabolites has yet to be established. Fetal urine is the major contributor of water, ions, steroids and other compounds to the amniotic fluid at term [3, 18]. Another source, quantitatively of lesser importance, is the chorionic plate of the placenta [1]. This route was shown to exist by the demonstration of a very rapid transfer into amniotic fluid of relatively large lipid soluble components such as meperidine (M. W. $\pm$ 300) which occurs, most probably through the fetal side of the placenta from the fetal capillary bed [28]. The amniotic fluid is also constantly circulating through the fetal lungs which contribute some of the fluid's components [5].

Data from normal adults show that urinary concentrations of $25(OH)D_3$ and $1,25(OH)_2D_3$ are low compared with their serum levels [12]. Most of these urinary vitamin D_3 metabolites are glucoronidate conjugates [12, 25]. The levels of amniotic fluid vitamin D_3 metabolites reported in this study, however, were of unconjugated forms, similar to those in blood serum, and were considerably higher than the levels expected, should urinary excretion be their main source.

The low concentrations of amniotic fluids $25(OH)D_3$ and $24,25(OH)_2D_3$ and the relatively high $1,25(OH)_2D_3$ levels compared with cord and maternal serum levels (table I) are consistent with the data of RON, et al. [24], who studied the in vitro transplacental transfer of these metabolites. These authors measured maternal to fetal transfer and demonstrated a considerably higher placental clearance of $1,25(OH)_2D_3$ compared with $25(OH)D_3$. The lower placental clearance of $25(OH)D_3$ was proportional to its stronger binding by the D-binding protein in the serum added to the perfusate, and the same may be applicable to $24,25(OH)_2D_3$.

Our finding of a good correlation between $25(OH)D_3$ levels of maternal and fetal cord sera and no correlation of $1,25(OH)_2D_3$ levels in these sera is consistent with some similar reports [2, 14, 27] and inconsistent with others [10, 29]. We found also a good correlation between the fetal and maternal serum levels of $24,25(OH)_2D_3$ ($r = 0.73$; $p < 0.01$), which differs from the data of HILLMAN, et al. [15] and WEISMAN et al. [30].

The mean cord serum levels of all three metabolites were somewhat lower than the respective maternal serum levels. Significantly lower concentrations of all three metabolites were found in the amniotic fluid as compared with the maternal serum levels. Similar differences were found between the concentration of $25(OH)D_3$ and $24,25(OH)_2D_3$ of fetal cord serum and amniotic fluid. In contrast to the above, amniotic fluid $1,25(OH)_2D_3$ levels did not differ significantly from those of the fetal cord serum levels though their concentration was about half of that of the serum. This could perhaps suggest a higher transfer clearance of $1,25(OH)_2D_3$ from fetal chorionic plate capillaries into the amniotic fluid. However, no correlation was found between $1,25(OH)_2D_3$ in amniotic fluid and fetal cord serum. There was also no correlation between fetal serum levels of $24,25(OH)_2D_3$ and amniotic fluid levels of this metabolite. The lack of correlation between the levels of these dihydroxyvitamin D_3 metabolites in fetal serum and amniotic fluid may possibly be attributed either to some fetal metabolism following ingestion of the amniotic fluid or to different sources of these metabolites to fetal serum (i. e. from maternal circulation, fetal production and decidua [32]). Although direct transfer of these metabolites from the decidua through the amniotic membrane is unlikely [1] their contribution to the amniotic fluid by the decidua [32] cannot be excluded. In comparison, $25(OH)D_3$ levels in maternal serum and fetal serum correlated well with their amniotic fluid levels ($r = 0.697$, $p < 0.01$ and $r = 0.681$, $p < 0.01$ respectively).

As the fetal liver is presumably incapable of performing the 25-hydroxylation of vitamin D_3 [11] the supply of this metabolite to the fetal serum and through the chorionic plate to the amniotic fluid is therefore most probably from only one source e. g. – maternal serum.

In conclusion: the findings in this study are consistant with the hypothesis that the main source of amniotic fluid vitamin D_3 metabolites is by a direct transfer from fetal serum through the chorionic plate of the placenta, the relative contribution of the decidua is yet to be studied.

Summary

The concentration of 25-hydroxyvitamin D_3 ($25(OH)D_3$), 24,25-dihydroxyvitamin D_3 ($24,25(OH)_2D_3$) and 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) were determined in amniotic fluid, fetal cord serum and maternal serum in 26 cases of elective cesarean sections at term. All the women had a normal pregnancy and did not get any vitamin D fortified preparations. The samples were collected during December 1982 – April 1983, at 37 – 40 weeks of pregnancy. The respective levels ($\pm$ S. D.) of $25(OH)D_3$, $24,25(OH)_2D_3$ and $1,25(OH)_2D_3$ in maternal serum were: 18.03 $\pm$ 10.8 ng/ml, 1.473 $\pm$ 1.562 ng/ml and 36 $\pm$ 21.5 pg/ml; in fetal cord serum: 13.15 $\pm$ 8.3 ng/ml, 0.9 $\pm$ 0.76 ng/ml and 29.2 $\pm$ 18.55 pg/ml and in amniotic fluid: 0.732 $\pm$ 0.508 ng/ml, 0.121 $\pm$ 0.104 ng/ml and 14.3 $\pm$ 10.0 pg/ml. The levels of the three metabolites in maternal and fetal cord serum were not statistically different. There was a statistically significant correlation between maternal and fetal serum levels of $25(OH)D_3$ and $24,25(OH)_2D_3$ ($r = 0.79$, $p < 0.01$ and $r = 0.743$, $p < 0.01$ respectively). No significant correlation was found in $1,25(OH)_2D_3$ levels between maternal and fetal cord sera. This lack of correlation may well be in agreement with the recent findings of KOUPPALA, et al. who demonstrated that the fetus contributes to its own pool of $1,25(OH)_2D_3$.
A significant difference was found between maternal serum and amniotic fluid levels of the three metabolites. A statistically significant difference was also found between fetal serum levels of $25(OH)D_3$ and $24,25(OH)_2D_3$ and amniotic fluid levels. Fetal cord serum of $1,25(OH)_2D_3$ were not statistically different from the amniotic fluid levels, even though fetal cord serum levels were higher. In in vitro studies on the transplacental transfer of vitamin D_3 metabolites, this author has shown that placental clearance of $1,25(OH)_2D_3$ from maternal to fetal circulation is about ten folds higher than that of $25(OH)D_3$, presumably due to the differences in binding of these two metabolites by the serum. Our hypothesis is that transfer of vitamin D_3 metabolites into the amniotic fluid is mainly via the fetal serum through the chorionic plate of the placenta. If this hypothesis is valid, then the expected amniotic fluid levels of the above three metabolites compared to their fetal serum levels would be as found in this work, and in consistance with our previous findings on the in vitro transplacental transfer. 25-hydroxyvitamin D_3 was the only metabolite whose levels correlated significantly both between maternal serum levels and fetal serum levels with amniotic fluid levels ($r = 0.697$, $p < 0.01$ and $r = 0.681$, $p < 0.01$ respectively). We don't have a good explanation for this finding except to assume that it may give support to the supposition of GRAY, et al. that the fetal liver does not possess the ability of 25-hydroxylation of cholecalciferol, this maternal serum serves as the only constant source of $25(OH)D_3$ enabling a steady state to be reached between the three compartments.

Keywords: Amniotic fluid, correlation, fetal cord serum, maternal serum, vitamin D_3 metabolites.

Zusammenfassung

Vitamin D_3-Metabolite im Fruchtwasser in Beziehung zur Konzentration im maternalen und fetalen Serum bei Schwangerschaften am Termin

Bei 26 primären Sectiones am Termin wurden die Konzentrationen von 25-Hydroxyvitamin D_3 ($25(OH)D_3$), 24,25-Dihydroxyvitamin D_3 ($24,25(OH)_2D_3$) und 1,25-Dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) im Fruchtwasser, Nabelschnurblut und maternalen Serum bestimmt. Alle Frauen hatten einen normalen Schwangerschaftsverlauf und keine Vitamin-D-Präparate erhalten. Die Proben wurden in der Zeit von Dezember 1982 bis April 1983 bei Geburten zwischen der 37. und 40. Schwangerschaftswoche gesammelt. Die Spiegel für $25(OH)D_3$, $24,25(OH)_2D_3$ und $1,25(OH)_2D_3$ betrugen ($\pm$ S. D.): 18.03 $\pm$ 10.8 ng/ml, 1.473 $\pm$ 1.562 ng/ml und 36.0 $\pm$ 21.5 pg/ml im maternalen Serum, im Nabelschnurblut 13.15 $\pm$ 8.3 ng/ml, 0.9 $\pm$ 0.76 ng/ml und 29.2 $\pm$ 18.55 pg/ml und im Fruchtwasser 0.732 $\pm$ 0.508 ng/ml, 0.121 $\pm$ 0.104 ng/ml und 14.3 $\pm$ 10.0 pg/ml. Bei den Konzentrationen der 3 Metabolite im mütterlichen Serum und in der Nabelschnur gab es keine statistisch signifikanten Unterschiede. Bezüglich des $25(OH)D_3$ und des $24,25(OH)_2D_3$ lag zwischen maternalem und fetalem Serum eine statistisch signifikante Korrelation vor ($r = 0.79$, $p < 0.01$ und $r = 0.743$, $p < 0.01$). Die $1,25(OH)_2D_3$-Spiegel im ma

ternalen und fetalen Serum korrelierten nicht signifikant miteinander. Dieser Befund stimmt gut mit den neueren Ergebnissen von KOUPPALA et al. überein, die zeigen konnten, daß der Fet selbst zur Veränderung seines eigenen $1,25(OH)_2D_3$-Pools beiträgt.
Bei allen 3 Metaboliten waren die Unterschiede zwischen maternalem Serum und Fruchtwasser statistisch signifikant. Beim Vergleich von Nabelschnurserum und Fruchtwasser waren die Unterschiede bezüglich des $25(OH)D_3$ und $24,25(OH)_2D_3$ statistisch signifikant, nicht aber bezüglich des $1,25(OH)_2D_3$; hier war eine Tendenz zu höheren Spiegeln in der Nabelschnur zu erkennen. Bei in vitro-Untersuchungen zum plazentaren Transfer von Vitamin D_3-Metaboliten konnte der Autor zeigen, daß die plazentare Clearance von $1,25(OH)_2D_3$ beim Übergang vom mütterlichen zum fetalen Kreislauf zehnmal höher ist als die von $25(OH)D_3$. Wahrscheinlich werden die beiden Metabolite im Serum unterschiedlich gebunden. Nach unserer Hypothese erfolgt der Transfer von Vitamin D_3-Metaboliten in das Fruchtwasser hauptsächlich über das fetale Serum durch die Chorionplatte der Plazenta. Die Fruchtwasserspiegel der 3 Metabolite lägen dann im Vergleich zur Konzentration im fetalen Serum in den Bereichen, wie wir sie auch in dieser Studie gefunden haben. Darüber hinaus wird die Hypothese durch unsere Ergebnisse bei den in vitro-Untersuchungen zum plazentaren Transfer gestützt. Nur beim $25(OH)D_3$ gab es eine signifikante Korrelation sowohl zwischen maternalem Serum und Fruchtwasser wie auch zwischen fetalem Serum und Fruchtwasser ($r = 0.697$, $p < 0.01$ und $r = 0.681$, $p < 0.01$). Diese Befunde sind nicht leicht zu erklären. Möglicherweise unterstützen sie die Auffassung von GRAY et al., die behaupten, daß die fetale Leber nicht in der Lage ist, Cholecalciferol zu hydroxylieren. Damit würde nur das maternale Serum als Quelle für das $25(OH)D_3$ in Frage kommen und so ein Steady-State zwischen allen 3 Kompartimenten erreicht werden.

Schlüsselwörter: Fetales Nabelschnurserum, Fruchtwasser, Korrelation, maternales Serum, Vitamin D_3-Metabolite.

Résumé

Métabolites de la vitamine D_3 dans le liquide amniotique, relations avec les taux sériques maternels et fœtaux lors de la grossesse à terme

On a dosé dans le liquide amniotique, le sérum fœtal au cordon, et dans le sérum maternel, lors de 26 césariennes à terme, les concentrations de 25-hydroxyvitamine D_3 ($25(OH)D_3$), 24,25-dihydroxyvitamine D_3 ($24,25(OH)_2D_3$) et de 1,25-dihydroxyvitamine D_3 ($1,25(OH)_2D_3$). Toutes les femmes avaient eu une grossesse normale et n'avaient pas reçu de supplémentation en vitamine D. Les échantillons ont été prélevés de décembre 1982 à avril 1983, à 37–40 semaines de grossesse. Les taux sériques maternels respectifs ($\pm$ DS) de $25(OH)D_3$, de $24,25(OH)_2D_3$ et de $1,25(OH)_2D_3$ étaient de: $18,03 \pm 10,8$ ng/ml; $1,473 \pm 1,562$ ng/ml et $36 \pm 21,5$ pg/ml; les taux respectifs au sang du cordon de: $13,15 \pm 8,3$ ng/ml, $0,9 \pm 0,76$ ng/ml et $29,2 \pm 18,55$ pg/ml; et les taux dans le liquide amniotique de: $0,732 \pm 0,508$ ng/ml, $0,121 \pm 0,104$ ng/ml et $14,3 \pm 10,0$ pg/ml. Les taux des trois métabolites ne sont pas statistiquement différents chez la mère et chez le fœtus au sang du cordon. Il existe une corrélation significative sur le plan statistique entre les taux maternels et fœtaux de $25(OH)D_3$ et de $24,25(OH)_2D_3$ ($r = 0,79$, $p < 0,01$ et $r = 0,743$, $p < 0,01$, respectivement). Il n'a pas été trouvé de corrélation significative en ce qui concerne les taux de $1,25(OH)_2D_3$ entre la mère et le fœtus. Cette absence de corrélation est bien en accord avec les données récentes de KOUPPALA et col. qui ont démontré que le fœtus contribue à son propre pool de $1,25(OH)_2D_3$.
On a trouvé une différence significative entre les taux des 3 métabolites au niveau du sérum maternel et du liquide amniotique. On a également trouvé une différence significative entre les taux sériques fœtaux de $25(OH)D_3$ et de $24,25(OH)_2D_3$ et les taux du liquide amniotique. Les taux fœtaux au sang du cordon de $1,25(OH)_2D_3$ ne sont pas statistiquement différents de ceux du liquide amniotique, même si les taux fœtaux au sang du cordon sont plus élevés. Dans des études in vitro sur le transfert trans-placentaire des métabolites de la vitamine D_3, cet auteur a montré que la clearance placentaire de la $1,25(OH)_2D_3$ de la circulation maternelle vers la circulation fœtale est environ 10 fois plus élevée que celle de la $25(OH)D_3$, vraisemblablement du fait des différences de liaison dans le sérum de ces deux métabolites. Notre hypothèse est que le transfert des métabolites de la vitamine D_3 vers le liquide amniotique s'effectue principalement par le sérum fœtal, à travers le chorion placentaire. Si cette hypothèse est valide, les taux attendus dans le liquide amniotique de ces trois métabolites, en comparaison des taux sériques fœtaux, devraient être ceux trouvés dans ce travail, et concordants avec nos données antérieures concernant le transfert transplacentaire in vitro. La 25-hydroxyvitamine D_3 est le seul métabolite dont les taux sont corrélés significativement pour les taux maternels et pour les taux fœtaux avec les taux du liquide amniotique ($r = 0,697$, $p < 0,01$ et $r = 0,681$, $p < 0,01$ respectivement). Nous n'avons pas de bonne explication pour ce fait sauf qu'on peut supposer qu'il peut appuyer la supposition de GRAY et col. que le foie fœtal ne dispose pas de la capacité de 25-hydroxylation du cholecalciferol, ainsi le sérum maternel servirait de seule source constante de $25(OH)D_3$ en permettant d'atteindre un équilibre stable, entre les trois compartiments.

Mots-clés: Corrélation, liquide amniotique, metabolites de la vitamine D_3, serum fœtal au cordon, sérum maternel.

Acknowledgements: This work was supported in part by the Posnack Family Foundation of Hollywood. Fort Lauderdale Florida, U.S.A.

References

[1] ABRAMOVITCH DR, KP PAYE: Pathways of water transfer between liquor amnii and the fetoplacental unit at term. Eur J Obstet Gynecol 3 (1973) 155

[2] BOUILLON R, H VAN BAELEN, P DE MOOR: 25-Hydroxyvitamin D and its binding protein in maternal and cord serum. J Clin Endocrinol 45 (1977) 679

[3] CASSADY G, M BALKE, P BAILY, B YOUNGER, J SUMMERS: Amniotic Fluid glucose in pregnancy. Am J Obstet Gynecol 127 (1977) 21

[4] DELVIN EE, FH GLORIEUX, BL SALLE, L DAVID, JP VARENNE: Control of vitamin D metabolism in preterm infants: Feto-maternal relationships. Arch Dis Child 57 (1982) 754

[5] DUENHOELTER JH, JA PRITCHARD: Fetal respiration: Quantitative measurements of amniotic fluid inspired near term by human and rhesus fetuses. Am J Obstet Gynecol 125 (1976) 306

[6] EDELSTEIN S, M CHARMAN, DEM LAWSON, E KODICEK: Competitive protein binding assay for 25-hydroxycholecalciferol. Clin Sci Mol Med 46 (1974) 231

[7] EISMAN JA, AJ HAMSTRA, BE KREAM, HF DELUCA: A sensitive precise and convenient method for determination of 1,25-dihydroxyvitamin D in human plasma. Arch Biochem Biophys 176 (1976) 235

[8] FELDMAN D, TA MCCAINE, MA HIRST, TL CHEN, KW COLSTON: Characterization of a cytoplasmic receptor-like for 1-α, 25-hydroxycholecalciferol in rat intestinal mucosa. J Biol Chem 254 (1979) 10 378

[9] FLEISCHMAN AR, FJ ROSEN, J COLES, MC SMITH, FH DELUCA: Maternal and fetal 1,25-dihydroxyvitamin D at term. J Pediatr 97 (1980) 640

[10] GERTNER JM, SM GLASSMAN, RD COUSTAN, DBP GOODMAN: Fetal-maternal vitamin D relationships at term. J Pediatr 97 (1980) 637

[11] GRAY TK, W LOWE, GE LESTER: Vitamin D and pregnancy: The maternal fetal metabolism of vitamin D. Endocr Rev 2 (1981) 264

[12] GRAY RW, AE CALIDAS, DR WILZ, J LEMAN, GA SMITH, HF DELUCA: Metabolism and excretion of ^3H-1,25$(OH)_2$ vitamin D_3 healthy adults. J Clin Endocrinol Metab 46 (1978) 756

[13] HADDAD JG, C MIN, J WALGATE, T HAHN: Competition by 24,25-dihydroxycholecalciferol in the competitive protein-binding radioassay of 25-hydroxycholecalciferol. J Clin Endocrinol Metab 43 (1976) 712

[14] HILLMAN LS, JG HADDAD: Human perinatal vitamin D metabolism: Part I. 25-Hydroxyvitamin D in maternal and cord blood. J Pediatr 84 (1974) 742

[15] HILLMAN LS, E SLATOPOLSKY, JG HADDAD: Perinatal vitamin D metabolism, IV. Maternal and cord serum 24,25-dihydroxyvitamin D concentrations. J Clin Endocrinol Metab 47 (1978) 1073

[16] JONGEN MJM, WJF VAN DER VIJGH, HJJ WILLEMS, J COEN NETERLENBOS: Analysis for 1,25-dihydroxyvitamin D in human plasma after a liquid chromatographic purification procedure with a modified competitive protein-binding assay. Clin Chem 27 (1981) 444

[17] KIDRONI G, R HAR-NIR, J MENCZEL, IW FRUTKOFF, Z PALTI, M RON: Vitamin D_3 metabolites in rat epieidymis: High 24,25-dihydroxyvitamin D_3 levels in the cauda region. Biochem Biophs Res Com 113 (1983) 982

[18] KLOPPER A: The estriol in liquor amnii. Am J Obstet Gynecol 112 (1972) 459

[19] KUOPPALA T, R TUIMALA, M PARVIAINEN, T KOSKINEN: Can the fetus regulate its calcium uptake? Br J Obstet Gynecol 91 (1984) 1192

[20] LASEBNIK R, Z EISENBERG, N LASEBNIK, Z SPIRER, Y WIESMAN: Vitamin D metabolites in amniotic fluid. J Clin Endocrinol Metab 56 (1983) 632

[21] MART JS, EG SWART, AJ HAMSTRA, HF DELUCA: Normal intrauterine development of the fetus of a woman receiving extraordinarily high doses of 1,25-dihydroxyvitamin D_3. J Clin Endocrinol Metab 51 (1980) 1138

[22] REDDY GS, AW NORMAN, MD WILLIS, D GALTZMAN, H GUYDA, S SOLOMON, DR PHILIPS, EJ BISHOP, E MAYER: Regulation of vitamin D metabolism in normal human pregnancy. J Clin Endocrinol Metab 56 (1983) 363

[23] RON M, G KIDRONI, L SCHWARTZ, D SHERER, J MENCZEL, Z PALTI: Amniotic fluid levels of 25-hydroxyvitamin D_3 and 24,25-dihydroxyvitamin D_3. Am J Obstet Gynecol 142 (1982) 113

[24] RON M, M LEVITZ, J CHUBA, J DANCIS: Transfer of 25-hydroxyvitamin D_3 and 1,25-dihydroxyvitamin D_3 across the perfused human placenta. Am J Obstet Gynecol 148 (1984) 370

[25] SATO KA, RW GRAY, J LEMAN: Urinary excretion of 25-hydroxyvitamin D in health and nephrotic syndrome. J Lab Med 99 (1982) 325

[26] SEAMARK DA, DJH TRAFFORD, HLJ MAKIN: The estimation of vitamin D and its metabolites in human plasma. J Steroid Biochem 14 (1981) 111

[27] STRIECHEN JJ, RC TSANG, TL GRATTON, A HAMSTRA, HF DELUCA: Vitamin D homeostasis in the perinatal period: 1,25-dihydroxyvitamin D in maternal cord and neonatal blood. N Engl J Med 302 (1980) 315

[28] SZETO HH, LI MANN, A BHAKTHAVATHASALAN, N LIU, CE INTURRISI: Meperidine pharmakokinetics in maternal fetal unit. J Pharmacol Exp Ther 206 (1978) 448

[29] WIELAND P, JA FISCHER, U TRECHSEL et al: Perinatal parathyroid hormone vitamin D metabolites and calcitonin in man. Am J Physiol 239 (1980) E 385

[30] WEISMAN Y, E REITER, A ROOT: Measurement of 24,25-dihydroxyvitamin D in sera neonates and children. J Pediatr 91 (1977) 904

[31] WEISMAN Y, M OCCHIPINTI, G KNOX, E REITER, A ROOT: Concentrations of 24,25-dihydroxyvitamin D and 25-hydroxyvitamin D in paired maternal-cord sera. Am J Obstet Gynecol 130 (1978) 704

[32] WEISMAN Y, A HARELL, S EDELSTEIN, M DAVID, Z SPIRER, A GOLANDER: 1,25-dihydroxyvitamin D_3 in vitro synthesis by human decidua and placenta. Nature 281 (1979) 317

Received December 10, 1985. Revised June 15, 1986. Accepted July 10, 1986.

Moshe Ron, M. D.
Dept. of OB/GYN
Hadassah University Hospital
Mount Scopus, P. O. Box 24035
Jerusalem 91240, Israel