

Concentrations of vitamins A and E in amniotic fluid, extraembryonic coelomic fluid, and maternal serum in the first trimester of pregnancy

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Abstract

Paired samples of amniotic fluid and coelomic fluid were obtained by transvaginal ultrasound guided amniocentesis from 15 women with an ultrasonographically normal pregnancy between 8 and 12 weeks' gestation. Vitamins A and E were measured in the two pregnancy fluids and in maternal serum by high performance liquid chromatography with detection by ultraviolet absorption and fluorimetry respectively. Concentrations of vitamins A and E were higher in maternal serum than in coelomic fluid and were generally undetectable in amniotic fluid. All differences in concentration were significant. The vitamin E/cholesterol ratio was similar in maternal serum and coelomic fluid. No correlation was shown between the vitamin concentrations in the three fluids. These findings suggest that the coelomic cavity plays a part in the maternofetal exchange of these vitamins.

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In early human pregnancy the homeostatic mechanisms involved in embryonic and fetal nutrition are largely unknown. Before 12 weeks' gestation, the main route of maternofetal vitamin exchange may be across the coelomic cavity and secondary yolk sac.¹ Haematrophic nutrition (transfer by the placenta) may only begin after the establishment of a true intervillous circulation at 13-14 weeks' gestation.²

Vitamin A is essential for the maintenance of life, growth, and general health. Vitamin E appears to be the principal lipid soluble, chain breaking antioxidant and is important for the prevention of lipid peroxidation in biological membranes. The aim of this study was to determine the concentrations of these two fat soluble vitamins in fluid from the amniotic and coelomic cavities in early pregnancy.

Subjects and methods

The study was approved by the ethics committee at St Bartholomew's Hospital, London. Fifteen women consented to transvaginal ultrasound guided amniocentesis before surgical termination of pregnancy at 9-12 weeks' gestation. All women had accurate menstrual data and had not taken vitamin supplements periconceptionally. A maternal

venous blood sample was taken before induction of anaesthesia.

Transvaginal ultrasonography was performed using an Aloka SSD 620 (Aloka, Tokyo, Japan) instrument with a 5 MHz curvilinear vaginal probe. A normal singleton pregnancy was seen in each case and gestational age was confirmed by measurement of the crown-rump length. A gestational age of 11 weeks included crown-rump length measurements of 11 weeks plus 0 days to 11 weeks plus 6 days. Extraembryonic coelomic fluid and amniotic fluid samples were collected by puncturing the respective fluid cavities with an 18 gauge needle (Casmed, London). All samples were stored at -20°C before analysis.

Vitamin A (retinol) was measured by high performance liquid chromatography (HPLC) with ultraviolet detection as described by Filteau *et al.*³ The interassay and intra-assay coefficients of variation were 12.6% and 5.8% respectively and the minimum detection limit was of the order of 2 pmol. Vitamin E (α tocopherol) was measured by HPLC with fluorimetric detection.⁴ The interassay and intra-assay coefficients of variation were both less than 5%. The detection limit was of the order of 2 pmol. For the two assays the extracts from the coelomic and amniotic fluids were concentrated 30-fold in an attempt to obtain measurable peaks. Cholesterol concentrations were measured enzymatically using a commercial kit supplied by Sigma Chemical. Increased volumes ($\times 20$) were taken from the coelomic and amniotic fluids compared with the serum samples.

The significance of differences between groups was calculated using Wilcoxon's paired rank test.

Results

Tables 1 and 2 give the concentrations of vitamins A and E in amniotic fluid, coelomic fluid, and maternal serum. Vitamins A and E could not be detected in 10/15 (66%) and 13/15 (87%) of the amniotic fluid samples

Table 1 Vitamin A concentrations in 15 matched samples of amniotic fluid, extraembryonic coelomic fluid, and maternal serum at 9-12 weeks' gestation

| Vitamin A ($\mu\text{mol/l}$) | Amniotic fluid | Coelomic fluid | Maternal serum |
|---------------------------------|----------------|----------------|----------------|
| Median | 0 | 0.08 | 1.85 |
| Minimum | 0 | 0.04 | 1.10 |
| Maximum | 0.06 | 0.37 | 2.55 |
| Interquartile range | 0 | 0.07-0.12 | 1.33-2.13 |

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Table 2 Vitamin E concentrations in 15 matched samples of amniotic fluid, extraembryonic coelomic fluid, and maternal serum at 9–12 weeks' gestation

| Vitamin E ($\mu\text{mol/l}$) | Amniotic fluid | Coelomic fluid | Maternal serum |
|---------------------------------|----------------|----------------|----------------|
| Median | 0 | 0.26 | 17.01 |
| Minimum | 0 | 0.10 | 3.56 |
| Maximum | 0.03 | 0.55 | 56.70 |
| Interquartile range | 0 | 0.23–0.41 | 12.64–23.98 |

respectively. Median concentrations of vitamins A and E were higher by factors of 23 and 65 respectively in maternal serum compared with coelomic fluid ($p < 0.001$ for the two vitamins). Vitamin E/cholesterol ratios were similar in maternal serum and coelomic fluid (table 3). There was no correlation between vitamin A concentrations, vitamin E concentrations, or vitamin E/cholesterol ratios in the three fluids.

Discussion

This study shows that in the late first trimester, vitamins A and E are present in coelomic fluid, whereas in general they could not be detected in amniotic fluid. The interpretation of these findings is uncertain because the exact source and function of human extraembryonic coelomic fluid is unknown. The coelomic cavity appears to play a part in maternofetal fluid and nutrient exchanges¹ and coelomic fluid may be a transudate produced and secreted by the trophoblast, chorion, and decidualised endometrium from maternal serum.⁵ Nutrients present in coelomic fluid can reach the developing fetus via the secondary yolk sac and vitelline circulation. Animal studies have shown that endometrial

Table 3 Vitamin E/cholesterol ratios in 15 matched samples of extraembryonic coelomic fluid and maternal serum at 9–12 weeks' gestation

| Vitamin E/cholesterol ratio ($\mu\text{mol}/\text{mmol}$) | Coelomic fluid | Maternal serum |
|---|----------------|----------------|
| Median | 4.32 | 4.46 |
| Minimum | 1.62 | 1.07 |
| Maximum | 9.18 | 9.09 |
| Interquartile range | 3.78–6.75 | 3.82–6.04 |

and decidual secretions contain retinol and retinol binding protein.⁶

Vitamins A and E are fat soluble and as a result are transported in aqueous environments such as coelomic fluid and serum bound to protein. Vitamin A is bound to retinol binding protein, and vitamin E, like cholesterol, is carried by lipoproteins. The fact that the vitamin E/cholesterol ratio is similar in maternal serum and the coelomic fluid suggests that the reduced vitamin E concentrations in the latter result from a reduced transport capacity. Presumably concentrations of the retinol binding protein are also lower in coelomic fluid than in serum. The concentrations of the vitamins found in the coelomic and amniotic fluids agree with our previous observation that total protein and albumin concentrations are much lower in amniotic than coelomic fluid.⁵ Hypervitaminosis A can cause embryofetotoxic and teratogenic effects including abortion, cataract, urogenital malformations, cleft palate, anencephaly, and corticosteroidosis. There are no reported harmful effects of vitamin E on the human fetus.

The present findings are compatible with the hypothesis that the coelomic cavity plays a part in the maternofetal exchange of vitamins A and E. The exact mechanisms controlling maternofetal exchange in early pregnancy remain uncertain, however.

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