Maternal and Umbilical Cord Serum Vitamin A, E Levels and Mother-to-Child Transmission in the Non-Supplemented Vitamin A, E HIV-1 Infected Parturients with Short-Course Zidovudine Therapy

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Abstract

This study was undertaken to assess the maternal and umbilical cord serum vitamin A, E levels at delivery and mother-to-child transmission in nonsupplemented vitamin A, E HIV-1 infected parturients who received short-course zidovudine therapy. Maternal and umbilical cord serum vitamin A, E levels were quantitated by high-performance liquid chromatography in 67 HIV-1 infected parturients who received short-course zidovudine therapy. Mother-to-child transmission occurred in 13.4 per cent of HIV-1 infected parturients. There were no significant differences in the mean concentrations of vitamin A, E and vitamin E/cholesterol ratio between parturients with HIV-1 infected and non-infected infants. While maternal serum vitamin E level was adequate, nearly one-third of the parturients in the study had vitamin A deficiency. In conclusion our study has shown that there was no correlation between maternal serum vitamin A, E levels and mother-to-child HIV transmission in HIV-1 infected parturients who received short-course zidovudine therapy. However, the presence of underlying vitamin A deficiency in these parturients was common, adequate and intensive maternal-infant nutritional support should be emphasized especially in developing countries as an adjunctive measure in the reduction of mother-to-child transmission of HIV as well as the reduction in maternal and perinatal morbidity.

Key word : Serum Vitamin A, E, Mother-to-Child HIV Transmission

There is sufficient evidence indicating a higher mother-to-child HIV-1 transmission rate in the last trimester and during labour compared to the first and second trimesters. Factors influencing the transmission can be grouped into 3 main categories : viral load and maternal immune status; timing and route of delivery; and maternal nutritional status and breast-feeding(1).

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Vitamin A is an essential micronutrient for normal immune function, hematopoietic system, cellular growth, vision, and reproduction. Deficiency seems to be an important risk factor in disease progression during HIV infection[2]. Immune alterations associated with vitamin A deficiency include impaired humoral and cell-mediated immune response and pathologic alteration on the mucosal surface of the gastrointestinal and reproductive tracts including shedding of HIV-1 infected cells from the cervix and vagina[3]. The main physiological effect attributed to vitamin E is that of an antioxidant which is particularly effective in modulating immune function. Cellular antioxidants determine the latency period of HIV infection.

Studies from developing countries have demonstrated that mother-to-child transmission of HIV-1 infection is related to maternal vitamin A deficiency during pregnancy. In a study from Malawi, Africa in which HIV-seropositive mothers were stratified by their serum vitamin A levels revealed that the risk of mother-to-child transmission of HIV was more than four times lower in mothers with serum vitamin A levels > 1.40 μmol/L than in those with levels of ≤ 0.70 μmol/L[4]. While studies from the United States have revealed controversy about the association between maternal serum vitamin A level and mother-to-child HIV-1 transmission[5,6]. Maternal serum levels of vitamin A and E may be influenced by socioeconomic status and vitamin supplementation. The objective of this study was to assess the maternal and umbilical cord serum vitamin A, E levels at delivery and mother-to-child transmission in the non-supplemented vitamin A, E HIV-1 infected parturients who received short-course zidovudine therapy.

MATERIAL AND METHOD

This was a Bamrasnaradura-Ramathibodi collaborative study on perinatal HIV-1 infection. Between October, 1996 and January, 1998, eligible HIV-1 infected pregnant women attending antenatal care at Bamrasnaradura Hospital were enrolled in the study willingly. They were diagnosed during a voluntary screening for HIV and confirmed with Western blot technique. The eligible inclusion criteria were a hemoglobin value > 10 g/dL, platelet count > 100×10^9/L and urine negative for albumin and sugar. The exclusion criteria were zidovudine treatment before and during this pregnancy, allergy to zidovudine. Each woman gave written informed consent for her participation. Ferrous fumarate 200 mg daily was prescribed after entry into the study, no prenatal vitamin A, E was supplemented during the pregnancy. Maternal age, parity, weight, gestational age, duration of ruptured fetal membranes, duration of antenatal zidovudine therapy, route of delivery, fetal sex, and birth-weight were recorded at the time of delivery.

Bamrasnaradura Hospital serves a mixed population of lower and middle-socioeconomic class people in Bangkok, Thailand, and has introduced a short-course zidovudine regimen in late pregnancy and labour to prevent vertical transmission among HIV-1 infected parturients. The regimen consisted of zidovudine 300 mg capsule given orally twice daily, initiated at 36 weeks' gestation and continued until delivery; zidovudine 300 mg was given orally every 3 hours during labour. No zidovudine was given to newborns. No breast-feeding was recommended to all parturients.

All neonates were evaluated and followed prospectively at the pediatric infectious disease clinic, Bamrasnaradura Hospital. Blood tests were performed until infection status was known, at 6 months of age, for HIV genome by PCR.

Before analysis of serum vitamin A and E levels, all serum samples were stored at –70°C in aluminum foil for protection from light. Serum vitamin A (retinol) and E (α-tocopherol) were assessed at Ramathibodi Hospital using high-performance liquid chromatography[7]. Serum total cholesterol levels were assessed using enzymatic colorimetric test with lipid clearing factor (Human, Germany).

Statistical analyses were done, basal data are given as mean ± standard deviation (SD), Pearson's correlation coefficient, Student *t*-test and the analysis of variance with the software program, SPSS/PC+ were used accordingly.

RESULTS

During the study period, a total of 76 pregnant mothers were enrolled in the study. Nine cases were lost to follow-up (11.8%). Mother-to-child transmission of HIV-1 infection occurred in 9 of 67 deliveries (13.4%). There was one set of twins and there was no perinatal death in the study group. Table 1 outlines the demographic and obstetrical characteristics of the parturients with and without HIV infected infants. There were no statistically significant differences in the mean maternal age, parity, body weight, gestational age at delivery, dura-

Table 1. Demographic and obstetrical characteristics of the study population.

	Mother		
	With HIV infected Infants (n=9)	With uninfected Infants (n=58)*	Significance
Maternal age (years)	22.4 ± 3.1	25.5 ± 4.7	NS
Parity (% primiparous)	77.8	63.8	NS
Body weight (kg)	61.3 ± 5.3	63.3 ± 8.6	NS
Gestational weeks at delivery	38.7 ± 1.3	39.5 ± 1.3	NS
Duration of ruptured fetal membranes in minutes	90.0 ± 60.1	60.0 ± 29.9	NS
Duration of antenatal ZDV therapy (weeks)	2.3 ± 1.2	3.3 ± 1.5	NS
Rate of cesarean section (%)	22.2	12.1	NS
Fetal birth-weight (g)	3,172.2 ± 498.8	3,153.6 ± 389.3	NS
Fetal sex (% male)	33.3	42.4	NS

Data are presented as mean ± standard deviation, except percentage for parity, fetal sex, route of delivery, and median for duration of ruptured fetal membranes, NS = no statistical significance, P > 0.05, * = There was one set of twins

Table 2. Maternal and umbilical cord serum vitamin A, E in the study population.

	Mother		
	With HIV infected Infants (n=9)	With uninfected Infants (n=58)*	Significance
Maternal			
Vitamin A(μmol/L)	1.38 ± 0.09	1.31 ± 0.07	NS
Vitamin E(μmol/L)	24.47 ± 2.64	27.76 ± 1.49	NS
Vitamin E/cholesterol ratio	5.5 ± 0.3	5.5 ± 0.3	NS
	HIV infected Infants (n=9)	Uninfected Infants (n=59)	
Umbilical cord			
Vitamin A(μmol/L)	1.01 ± 0.12	0.96 ± 0.05	NS
Vitamin E(μmol/L)	6.13 ± 0.65	6.56 ± 0.52	NS
Vitamin E/cholesterol ratio	4.7 ± 0.5	4.5 ± 0.4	NS

Data are presented as mean ± SEM
* There was one set of twins

tion of antenatal ZDV therapy, duration of ruptured fetal membranes, rate of Cesarean section, fetal sex and birth-weight between both groups of parturients.

Table 2 shows the mean maternal and umbilical cord serum vitamin A, E concentrations and vitamin E/cholesterol ratio in both groups. There were no significant differences in the mean concentrations of both vitamins between parturients with HIV-infected and non HIV-infected infants (P > 0.05). Concentrations of vitamin A and E in the umbilical cord serum were significantly lower than the maternal levels (P < 0.05). The serum vitamin E level of cord blood was approximately one-fourth the maternal level. There was also a significant

positive correlation between serum vitamin A and E in maternal and umbilical cord concentrations ($r = 0.59312$, 95% CI 0.61988-1.24796, $P = 0.0001$; $r = 0.34567$, 95% CI 0.32904-1.67999, $P = 0.0042$, respectively).

The relative risk of mother-to-child transmission of HIV in parturients with maternal serum vitamin A $\geq$ 1.05 μmol/L and < 1.05 μmol/L was 4 of 46 (8.69%) and 5 of 21 (23.80%) respectively ($P = 0.1257$, Fisher exact test). Of the 67 parturients there were 5 (7.46%) who had maternal serum vitamin A less than 0.70 μmol/L (severe vitamin A deficiency), and 21 (31.34%) had less than 1.05 μmol/L a level that indicates vitamin A deficiency in adults, but there were only 2 (2.99%) who had serum vitamin E less than 11.61 μmol/L. Of the 68 infants born there were 16 (23.53%) who had umbilical cord serum vitamin A less than 0.70 μmol/L, and 40 (58.82%) less than 1.05 μmol/L.

DISCUSSION

Since the successful intervention for HIV-1 mother-to-child transmission with ZDV therapy (ACTG 076 trial) subsequent studies reported the effectiveness of the short course, oral antenatal and oral intermittent intrapartum ZDV dosage regimen in the reduction of mother-to-child transmission to their babies by about 50 per cent[8,9]. This regimen is more feasible and affordable for developing countries, however, nutritional deficiencies likely contribute to the higher rate of transmission especially in developing countries. In this study, maternal and umbilical cord serum vitamin A and E were assessed in the non-supplemented vitamin A and E parturients, since serum levels of both vitamins especially vitamin A may be influenced by vitamin supplementation, socio-economic status and fetal sex[10]. The socio-economic status of the study population was not assessed, but there was no difference in the proportion of fetal sex of the HIV infected and uninfected infants. Maternal serum vitamin A status was assessed by using a cut off level of 1.05 μmol/L since this was adjusted as the functional indicator of vitamin A nutritional status in pregnancy[11]. Since the serum vitamin E level is easily influenced by serum lipid concentration, the nutritional vitamin E status was assessed by the ratio of serum vitamin E to total serum cholesterol. Deficiency in vitamin E is usually considered to exist if serum α-tocopherol level is less than 11.61 μmol/L or serum vitamin E/cholesterol ratio < 2.5 in adults and < 0.6 in children[12].

In this study, there were no significant differences in the mean maternal and umbilical cord serum vitamin A, E concentrations and vitamin E/cholesterol ratio between parturients with HIV-infected and uninfected infants and the proportions of parturients who had maternal serum vitamin A less than 1.05 μmol/L in both groups were also not different, while confounding variables that might affect mother-to-child transmission of HIV i.e. gestational age at delivery, duration of ruptured fetal membranes, route of delivery (except CD4 cell count and viral load which were not available) were not different. The antiretroviral effect of zidovudine may mask the correlation between maternal vitamin A deficiency and mother-to-child transmission of HIV infection.

In normal pregnancy the maternal level of vitamin A varies during pregnancy but generally decreases progressively until term. This is believed to be for fetal storage of vitamin A. Fetal vitamin A level is usually slightly lower than the maternal level. Toward the end of gestation, adequate maternal vitamin A status and dietary intakes are important to maximize the vitamin A transferred to the fetus in preparation for parturition and lactation [10,13]. This study demonstrated interesting nutritional findings that while maternal serum vitamin E was adequate, nearly 32 per cent of the parturients in the study had vitamin A deficiency, and nearly 59 per cent of the infants born had serum vitamin A less than 1.05 μmol/L.

The result of this study also implies that (i) underlying vitamin A deficiency is common in HIV-infected parturients in developing countries, improving the vitamin A status of pregnant women with low-dose vitamin A supplementation should commence from the second trimester of pregnancy until postpartum seems to be essential as an adjunctive measure in the reduction of mother-to-child transmission of HIV as well as the reduction in maternal and perinatal morbidity, ii) since there is no doubt about the possibility of transmission of HIV through infected breast milk, prohibition of breast-feeding and the lower storage of vitamin A in infants born to HIV-infected parturients might impair the immune response and increase the risk of opportunistic infections in both HIV-infected and uninfected infants. Adequate and intensive maternal-infant nutritional support in terms of macro- and micronutrients should be emphasized especially in developing countries.

However, there are some pitfalls in this study. Serum retinol-binding protein and nutritional dietary intake were not assessed in the study. Both variables might affect the serum vitamin A levels.

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ความสัมพันธ์ระหว่างระดับวิตามินเอ อี ในซีรัมของมารดาที่ติดเชื้อเอ็ชไอวีและการถ่ายทอดเชื้อเอ็ชไอวีจากมารดาสู่ทารกในครรภ์

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การศึกษาระดับวิตามินเอ อี ในซีรัมของมารดาที่ติดเชื้อเอ็ชไอวี จำนวน 67 ราย ซึ่งได้รับยาไซโดวูดีน ชนิดรับประทาน ขนาด 300 มก. วันละ 2 ครั้ง ตั้งแต่อายุครรภ์ 36 สัปดาห์ จนเริ่มเจ็บครรภ์ และรับประทานต่อระหว่างเจ็บครรภ์ ขนาด 300 มก. ทุก 3 ชั่วโมงจนกระทั่งคลอด โดยที่ไม่ได้รับยาบำรุงเสริมที่มีวิตามินเอ อี ในระยะก่อนคลอด พบว่ามีอัตราการถ่ายทอดเชื้อเอ็ชไอวีจากมารดาสู่ทารกในครรภ์ร้อยละ 13.4 และไม่พบความสัมพันธ์ระหว่างระดับวิตามินเอ อี ในซีรัมของมารดาที่ติดเชื้อเอ็ชไอวี และการถ่ายทอดเชื้อเอ็ชไอวีจากมารดาสู่ทารกในครรภ์ อย่างไรก็ตามพบว่าประมาณหนึ่งในสามของมารดากลุ่มนี้มีภาวะขาดวิตามินเอ ในขณะที่มีระดับวิตามินอีอยู่ในเกณฑ์พอเพียง

คำสำคัญ : ระดับวิตามินเอ อี ในซีรัมของมารดา, การถ่ายทอดเชื้อเอ็ชไอวีจากมารดาสู่ทารกในครรภ์

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