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ORIGINAL ARTICLE

ASSOCIATION BETWEEN SEX HORMONES IN HUMAN BREAST MILK AND INFANT GROWTH AND DEVELOPMENT

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Background– Although the influence of gonadotropins and steroid sex hormones on human growth and development are very well established, little is known concerning the role of these hormones in breast milk.

Methods– In the present study, the concentrations of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol and progesterone in the blood and milk of 19 lactating mothers were measured by radioimmunoassay 1 and 6 months after delivery. Weight, height, head circumference and development of the infants were simultaneously clinically examined at 1 and 6 months.

Results– Serum levels of LH, FSH and estradiol were 3–fold higher in the samples collected 6 months after delivery as compared to the first month, whereas progesterone levels were lower (55%) at six months than at one month. A positive correlation was found between the levels of all hormones in serum and in breast milk. The levels of FSH, LH and estradiol in the milk correlated directly with growth and developmental indices, whereas milk progesterone levels were negatively correlated with infant growth and development.

Conclusion– The results suggest that the levels of FSH, LH and estradiol in human breast milk play an important role in the growth and development of infants. For progesterone, the opposite is true.

Keywords • estradiol • gonadotropins • growth • hormones • infant development • milk, human

Introduction

The major action of steroid sex hormones is on the development, growth and regulation of the reproductive system.[1] The presence of these hormones in human breast milk, entering either by passive diffusion or via an active concentration mechanism from the blood, can be of great concern to infants.[2–4] It has been reported that human milk contains 6 to 7 times more luteinizing hormone-releasing hormone (LHRH) than the corresponding plasma values.[5] These observations have led to the speculation that the levels of pituitary gonadotropins and gonadal steroids might be proportionately high in milk.

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Because gonadal steroids can be either tropic or damaging to the nervous system, and can exert important influences on infant's development and behavior,[6] this study was undertaken to measure the follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol and progesterone concentrations in the blood and milk of lactating mothers, and to investigate any relation between the levels of these hormones and the infants' growth and development.

Patients and Methods

After obtaining informed consent from pregnant women who were admitted to Shahid Beheshti Hospital, Isfahan, Iran, 23 healthy lactating mothers (mean age ± SD, 26.7 ± 5.1 yr) were randomly selected from those records of patients

Table 1. Correlation between gonadal hormone concentrations in blood and breast milk at 1 and 6 months postpartum

Hormone	1 month		6 months	
	Serum	Milk	Serum	Milk
FSH (IU/L)	2.59 ± 0.92	0.33 ± 0.02 r = 0.79	7.01 ± 2.39	1.84 ± 0.66 r = 0.94
LH (IU/L)	3.16 ± 1.02	0.68 ± 0.02 r = 0.59	10.55 ± 1.99	0.88 ± 0.16 r = 0.82
Estradiol (pmol/L)	167.6 ± 27.5	133.3 ± 19.8 r = 0.87	264.1 ± 66.8	163.6 ± 32.6 r = 0.94
Progesterone (μmol/dL)	0.47 ± 0.13	0.25 ± 0.12 r = 0.54	0.21 ± 0.13	0.16 ± 0.09 r = 0.84

Data presented as mean ± SD. FSH = follicle-stimulating hormone; LH = luteinizing hormone.

experiencing normal term (40 ± 2 weeks of pregnancy) and natural delivery. Blood and milk samples were obtained at 1 and 6 months after delivery (2–4 ml). All of the infants were receiving breast milk as their only source of nourishment. Neither mothers nor their infants were receiving any medications. Of the 23 cases who were enrolled in the study, four were excluded because they had either received therapeutic agents or were lost to follow-up during the 6-month study period. The newborns were examined 1 and 6 months after birth according to the criteria developed by Gesell and Amatruda[7] and evaluated by Mussen et al.[8] Briefly, eye movement and response, sound and face recognition, attention on features, holding things by hand, neck and feet movements, the capacity to follow a moving target and making sounds were scored.

Using clinical diagnostic kits (Spectria, Orion Dianostica, Finland), the levels of FSH, LH, estradiol and progesterone were measured by radioimmunoassay (RIA) of 50 μL samples of serum or milk. Antibodies (250 μL) were added to each tube and incubated for 3 hours at room temperature. For progesterone and estradiol, 50 and 100 μL of each sample was then transferred to coated 1-mL capacity tubes, and 500 μL ^{125}I-labelled progesterone (170 – 200 KBq) or estradiol was added and incubated for 3 hours at room temperature. The assey mixture was decanted and the tube was washed with 1 mL of washing solution. The tubes were then counted in a gamma counter for one minute and the concentrations of the hormones were calculated automatically using standard curves (radioactive count/min against hormone concentration on log–log graph design.

Derivation of Pearson correlation coefficients, Leven's test for examining the equality of variances, *t* test for comparing the means and two-tailed test of significance were performed using SPSS statistical software.

Results

The quantity of gonadotropins (LH and FSH), estradiol and progesterone in maternal blood and breast milk samples, collected 1 and 6 months after delivery, are presented in Table 1. Serum levels of LH and FSH in samples collected 6 months after delivery were approximately three-fold higher than samples taken after the first month. A higher estradiol level (~ 60%) was also observed in 6-month serum samples compared 1-month samples. Conversely, progesterone levels in the serum samples were lower at 6 months (55%).

The Pearson correlation coefficients of the hormone levels in milk samples and corresponding serum samples are also shown in Table 1. There was a positive relationship between the levels of all four hormones in serum and milk. For the first month, the highest correlation coefficient was that of estradiol (r = 0.87); the figure reached 0.94 at 6 months postpartum. Similar relations were found for FSH, LH and progesterone.

Table 2 summarizes the growth and development indices (height, weight and head circumference) of the infants at 1 and 6 months of age. Referring to Table 2, no significant differences were found between the growth indices of boys and girls. However, the growth indices increased significantly at 6 month of age in both sexes as compared to first month. These results are consistent with the data reported in the literature.[9]

The association between the concentrations of the milk hormones and growth and developmental indices of the infants are shown in Tables 3 and 4. After the first month of life, there was a weak association between milk hormone levels and growth indices (Table 3). By the sixth month, however, the correlation coefficients between these

Table 2. Growth and development of the infants.

	1 month		6 months	
	Boys	**Girls**	**Boys**	**Girls**
Developmental score	8.59 ± 0.94	8.84 ± 0.90	8.56 ± 0.91	8.75 ± 0.86
Height (cm)	58.11 ± 2.07	56.31 ± 2.62	72.70 ± 1.78*	68.50 ± 2.16*
Weight (g)	4,341 ± 634.1	3,913.8 ± 604.4	8,317.1 ± 169.5*	7,010.8 ± 815.1*
Head circumference (cm)	37.11 ± 1.06	36.92 ± 1.14	43.64 ± 1.16*	43.15 ± 1.18*

Data are presented as mean ± SD. *Statistically significant differences between 1 and 6 months ($p < 0.005$).

parameters had become statistically significant. Estradiol and FSH were directly correlated with the developmental score (r = 0.69 and 0.64, respectively), whereas progesterone concentrations were inversely related (Table 4). Similar relations were found between these three hormones and the weight of the infants. In addition, a positive correlation was observed between the milk LH concentration and the weight of the infants (r = 0.7). Moreover, the milk concentrations of the hormones were weakly related to the height and head circumferences of the infants at 6 months of age (Table 3).

Discussion

The range of FSH, LH, estradiol and progesterone concentrations in the serum samples of this were study consistent with previous reports.[10] We found an association between milk gonadal hormones and infant growth. It appears that as the estradiol levels increases, the development of infants would promote, whereas the increase in progesterone levels has the opposite effect. Estradiol is reported to promote synaptogenesis in the brain[6]; thus, one role of estradiol in infant development might be in promoting neuron interconnection in the brain. In addition, estrogens increase mRNA synthesis in target tissues, which can result in a more generalized increase in synthesis of proteins.[11] This is consistent with the positive correlation of the breast milk estradiol and weight gain of the infants during the first 6 months of nursing (Table 3).

Progesterone can be considered to have the opposite effect of estradiol because it actually antagonizes the action of estradiol in certain tissues.[11] Moreover, elevated postpartum progesterone may inhibit lactogenesis and contribute to poor production of mother's milk.[12] Further investigations in this field are needed to assess the physiologic significance of sex hormones in human milk at different temporal stages of lactation.

In conclusion, the data reported here lend credence to the possibility that certain hormones in human breast milk play a very prominent role in the growth and development of the infants.

Table 3. Correlation between milk gonadal hormones and developmental and growth indices of infants receiving breast milk only at 1 month postpartum (n = 19)

	Estradiol	Progesterone	FSH	LH
Developmental score	0.49*	–0.21*	0.08	0.03
Weight	0.21	–0.18	–0.02	–0.34
Height	0.03	–0.19	0.19	0.12
Head circumference	0.00	–0.22	0.02	0.05

*r values higher than 0.50 or lower than –0.50 and with a p value less than 0.05 were considered statistically significant. FSH = follicle-stimulating hormone; LH = luteinizing hormone.

Table 4. Correlation between milk gonadal hormones and developmental and growth indices of infants receiving breast milk only at 6 months postpartum (n = 19)

	Estradiol	Progesterone	FSH	LH
Developmental score	0.69*	–0.68*	0.64*	0.48
Weight	0.62	–0.54*	–0.57*	–0.71*
Height	0.13	–0.28	0.12	0.22
Head circumference	0.36	–0.27	0.36	0.31

*r values higher than 0.50 or lower than –0.50 and with a p value less than 0.05 were considered statistically significant. FSH = follicle-stimulating hormone; LH = luteinizing hormone.

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