Gonadotropins and Sex Hormones in Healthy Chinese Infants

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ABSTRACT

This study was conducted to investigate the infantile changing regularity of gonadotropins and sex hormones. Serum samples were obtained from 416 healthy infants (male: 215; females: 201). In male infants, peaks in serum gonadotropins and testosterone concentrations were observed at 2-4 months. In female infants, serum FSH concentrations reached peak at 2-3 months. Before 6 months, serum testosterone and LH concentrations were higher in male, while FSH was on the contrary. Peaks in serum gonadotropins and sex hormones concentrations are reached and sexual dimorphism appears in the early infancy. Defining the range of mean values and the trends for infantile gonadotropins and sex hormones could be helpful for clinical evaluation.

Keywords: *China, FSH, Gonadotropin, Infant, LH, Sex hormone.*

INTRODUCTION

Experimental evidence obtained in several species suggests that the hypothalamic-pituitary-gonadal (HPG) axis is functional during early infancy. It has been reported that transient activation of the pituitary-gonadal axis occurs; sex differences in circulating gonadotropin levels are present during the first few months of life and there is a significant difference between male and female infants(1,2). Ibanez(3) reported that prenatal growth restraint is a risk factor for postpubertal FSH hypersecretion and for reduced gonadal size. These data further emphasize the importance of fully understanding the regulatory mechanisms that govern neonatal gonadal function in the primate.

In our present study, we aimed to determine sex differences and patterns of basal luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol and testosterone in the first year of life, and the relationship between the factors (birth weight, gestational age, birth order, maternal age, labor type) with the hormonal changes.

METHODS

We recruited 416 healthy full term infants (215 males and 201 females, between 1 to 12 months). They were born appropriate for gestational age, had no perinatal asphyxia or pathological jaundice and had a normal general physical examination. Infants with chromosomal abnormality, endocrine disturbance, cerebral trauma, kidney disease, congenital cardiopathy, or other congenital malformations were excluded. Infants treated with any medication were also excluded. Recruited subjects were divided into seven groups according to chronological age. Data including birth weight, gestational age, birth order, maternal age, labor type, were collected from parents and the hospital records.

Peripheral venous blood was collected by venipuncture between 8 a.m. and 11 a.m. Serum LH,

FSH, estradiol and testosterone were measured by the nonisotopic, automated chemiluminescence immunoassay system, Immulite (DPC, USA). The detection limit was 0.1 IU/L for FSH and LH. The minimum detectable levels of estradiol and testosterone were 0.03 pmol/L and 0.001 nmol/L respectively. The intra- and inter-assay coefficients of variation were 4.8% and 7.2% for LH, 5.4% and 8.1% for FSH, 9.5% and 16% for estradiol, 7.6% and 10.3% for testosterone, respectively.

All values were expressed as median and 95% confidence intervals, as not all showed a normal distribution. Statistical differences were analyzed by Mann-Whitney test for comparison of gonadotropins and sex hormones between different genders; multiple linear regression was used to analyze the association between factors with serum concentrations of these hormones. *P* value <0.05 was considered statistically significant.

Approval of the study was granted by Zhejiang University Faculty of Medicine Ethics and Research committee and the Regional Committee for Medical Research Ethics, Zhejiang Province, PRC. Consent was obtained from parents.

RESULTS

The levels of LH, FSH, estradiol, and testosterone in infants are provided longitudinally in ***Table* I**. Serum LH and FSH reached peak (male: LH, 3.5 IU/L, FSH, 3.4 IU/L; female: LH, 0.36 IU/L, FSH, 7.1 IU/L) at 2-3 months, and declined thereafter, reaching juvenile levels by 6 months. Testosterone levels reached peak (9.15 nmol/L) at 1-3 months and were undetectable after 6 months. Serum LH and testosterone levels were generally undetectable in all female infants from 1 to 12 months. Serum estradiol levels gradually fell after birth in both male and female. LH and testosterone concentrations were higher in male than female infants during 1-5 months, whereas the concentrations of FSH were higher in female than in male infant at all ages (*P* <0.01). The estradiol concentrations were higher in female than male at 1 month only.

In our study, there were 152 healthy infants (male: 80; female: 72) aged less than 3 months that had information in detail. In the ***Table* II** it can be seen that there were no linear correlations between perinatal factors with the hormones, except birth weight that showed linear correlation with the

TABLE I LH, FSH, ESTRADIOL AND TESTOSTERONE LEVELS IN MALE AND FEMALE INFANTS

Gender	Age (month)	*n*	LH (IU/L)	FSH (IU/L)	Estradiol (pmol/L)	Testosterone (nmol/L)
Male	2	58	2.9(1.2-7.9)	2.2(0.8-5.7)	119.67(5.87-302.86)	7.63(2.91-16.57)
	3	21	3.5(0.7-6.6)	3.4(0.5-6.3)	42.95(<0.03-217.32)	8.53(3.85-19.52)
	4	19	2.4(0.1-5.4)	2.1(1.3-4.2)	4.04(<0.03-113.80)	9.15(3.85-14.11)
	5	22	1.9(<0.1-3.8)	2.1(0.3-4.6)	17.3(<0.03-146.11)	4.36(2.25-10.12)
	6	19	0.6(0.2-4.3)	0.9(<0.1-3.7)	29.3(<0.03-82.60)	2.14(1.45-5.93)
	7	22	0.8(0.1-3.3)	0.6(0.2-3.8)	16.5(<0.03-84.80)	0.40(<0.001-1.34)
	12	54	0.3(<0.1-1.5)	0.5(<0.1-1.6)	25.3(<0.03-120.1)	0.12(<0.001-1.33)
Female	2	49	0.2*(<0.1-4.7)	5.9*(0.6-48.1)	142.43**(1.84-312.04)	0.71*(<0.001-2.49)
	3	26	0.2[#](<0.1-1.0)	7.1*(1.3-19.9)	43.32(<0.03-217.32)	0.69*(<0.001-1.81)
	4	16	0.3*(<0.1-1.1)	6.5[#](3.0-12.0)	41.48(<0.03-97.65)	0.59*(<0.001-1.36)
	5	20	0.2*(<0.1-0.8)	6.1*(2.0-14.1)	48.4(<0.03-109.03)	0.33*(<0.001-1.43)
	6	23	0.2*(<0.1-0.8)	5.4*(2.0-11.4)	23.9(<0.03-113.80)	0.30*(<0.001-1.43)
	7	17	0.2[#](<0.1-2.5)	5.5*(2.7-11.3)	55.1(<0.03-102.96)	0.31(<0.001-1.74)
	12	50	0.2(<0.1-1.3)	5.7*(0.3-14.7)	3.10(<0.03-107.93)	0.14(<0.001-1.33)

*Data are presented as median and range (2.5 and 97.5 percentiles). *P=<0.001; P= <0.01; **P=0.034; comparison vs. male infant at the same age.*

WHAT THIS STUDY ADDS?

- Defining the range of mean values and the trends for infantile gonadotropins and sex hormones could be helpful for clinical evaluation.

concentrations of LH and testosterone. It is known that the difference in testosterone concentration determines the sex difference in birth weight (male>female)(4). Adjusted for gender differences, there were no linear correlation between birth weight with concentrations of LH and testosterone.

DISCUSSION

Our study showed that male infants have higher LH values than female before 5 months, whereas female infants had higher FSH values regardless of age, which indicate that LH values dominate in the male infant and FSH values dominate in the female infants.

In male infants, the plasma testosterones were found to reach peak that approaches the normal adult level for male (9.22 nmol/L) and were ten times higher than female at 1-3 months. Because testosterone is mainly synthesized in the interstitial Leydig cells, it was suggested that Leydig cell is fully functional in early male infants. Leydig cell development stimulated by elevated LH levels is responsible for the transiently elevated testosterone levels. Early stimulation of the testis with gonadotropins is important for Sertoli cell, germ cell and Leydig cell development and proliferation(5, 6). A recent study of rhesus macaques indicated that at least part of the circulating testosterone is biologically active(7,8).

In female infants, serum estradiol quickly fell to minimum level at 1-2 months and sex difference disappeared, which provides evidence that the development of the ovaries lag far behind the testes. There seems to be a definite increase in follicle maturation with age. However, the most rapid increase takes place during the first 4 months of postnatal life, concurrent with activation of the pituitary-gonadal axis. Observations indicate that infants with ovarian cysts have an elevated circulating estradiol level after birth(9). In clinical practice, if female infants show abnormally high levels of serum estradiol, there is the possibility of ovarian cyst.

To conclude the first year of life, in particular the first few months are characterized by high gonadal endocrine activity. This early hormonal activation seems to be important for sexual development and may be potentially vulnerable to endocrine interference(10). Defining the range of mean values and the trends for infantile gonadotropin and sex hormones could be helpful for clinical evaluation of intersexual states, gonadotropin deficiency or gonadal dysgenesis.

Contributors: ZZ planned the study. CJ, XH and XW collected data, performed statistical analysis and drafted the manuscript. ZZ and RY were involved in reviewing the manuscript. ZZ was involved in critically reviewing the manuscript.

TABLE II CORRELATIONS BETWEEN FSH, LH, ESTRADIOL AND TESTOSTERONE (T) AND OTHER FACTORS BEFORE 3 MONTHS

Group	*n*	Birth weight	Gestation	Birth order	Maternal age	Type of labor
FSH	152	0.840	0.155	0.163	0.141	0.153
LH	152	0.201*	0.273	0.312	0.205	0.269
E2	152	0.040	0.118	0.040	0.040	0.040
T	152	0.188**	0.216	0.219	0.188	0.193

P=0.041;P=0.039; at the same gender. Male infant: Birth weight vs. LH; r=0.023, P=0.857 vs. T ; r=0.116; P=0.352/ Female infant; Birth weight vs. LH; r=0.017, P=0.919, vs. T; r=0.029; P=0.832. There are no linear correlations between birth weight and LH, T with the same gender.*

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