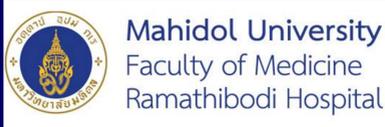


Basal Serum LH Level as a Diagnostic Test for Girls with Early Phase of Central Precocious Puberty



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Introduction

Central precocious puberty (CPP) in girls is diagnosed by having progressive breast development with accelerated growth, advanced bone age, pubertal-sized uterus and ovaries, and pubertal level of serum luteinizing hormone (LH). In early phase of CPP, basal serum LH can be overlapped with that of prepubertal girls. Therefore, gonadotropin-releasing hormone (GnRH) test is generally required to confirm the diagnosis. Previous studies showed various cut-off levels of basal and peak serum LH following GnRH analog (GnRHa) test for diagnosing CPP. However, GnRHa test is costly and labour-intensive, basal serum LH could be a more simple and practical approach. To the best of our knowledge, cut-off levels of basal serum LH to define CPP girls with different breast Tanner stages are still lacking.

Objective

To determine basal and GnRHa-stimulated peak LH levels for diagnosing girls with CPP at breast Tanner stages II and III.

Methods

Medical records of 515 girls who had breast onset before 8 years of age and underwent subcutaneous GnRHa test between the years 2007 and 2017 were reviewed. Girls who had progressive breast development and accelerated growth during a 3-6 month period of follow-up, advanced bone age and pubertal-sized uterus and ovaries were diagnosed with CPP. The girls who had no above-mentioned findings were classified as having premature thelarche (PT). In each group, patients were divided into 2 groups according to their breast Tanner stages at the time of GnRHa testing: Tanner stage II (CPPII and PTII) and Tanner stage III (CPPIII and PTIII). GnRHa test was performed by using 0.1 mg subcutaneous triptorelin and serum LH and follicle-stimulating hormone (FSH) were measured at baseline before triptorelin injection (basal level), and at 60, 90 and 120 minutes following triptorelin injection. Peak serum LH and FSH levels were defined as the maximum levels achieved during the testing. The GnRHa test results were analyzed.

Results

Table 1. Characteristics and GnRHa test results of all 515 girls with CPP and PT

Parameters	CPPII (N = 121)	PTII (N = 126)	P-value*	CPPIII (N = 211)	PTIII (N = 57)	P-value†
Age at breast onset (y)	7.6 (7.2-7.9)	7.4 (6.8-7.8)	0.031	7.6 (7.0-7.9)	7.1 (6.3-7.6)	0.004
Age at GnRHa testing (y)	7.8 (7.4-8.1)	7.5 (6.9-8.0)	0.002	7.9 (7.5-8.3)	7.3 (6.8-8.0)	<0.001
Bone age (y)	9.4 (8.3-10.0)	8.3 (7.8-8.8)	<0.001	10.0 (8.8-10.5)	8.3 (7.8-9.4)	<0.001
Z-score						
• Height	0.8 (0.2 to 1.8)	0.9 (-0.1 to 1.6)	0.401	1.2 (0.6 to 2.0)	0.7 (0.0 to 1.5)	0.003
• Weight	0.9 (0.2 to 1.8)	0.7 (-0.1 to 2.0)	0.139	1.5 (0.6 to 2.4)	1.2 (0.1 to 2.4)	0.228
• BMI	0.3 (-0.5 to 1.2)	0.1 (-0.9 to 1.2)	0.225	0.7 (-0.1 to 1.5)	0.6 (-0.1 to 1.9)	0.952
Basal LH (IU/L)	0.13 (0.09-0.30)	0.09 (0.09-0.09)	<0.001	0.24 (0.11-0.63)	0.09 (0.09-0.09)	<0.001
Peak LH (IU/L)	6.27 (4.44-9.86)	2.60 (1.99-3.68)	<0.001	9.53 (5.92-18.35)	2.57 (2.00-3.06)	<0.001
Basal FSH (IU/L)	2.39 (1.70-3.36)	1.73 (1.22-2.25)	<0.001	2.72 (1.75-3.70)	1.60 (1.15-2.49)	<0.001
Peak FSH (IU/L)	13.46 (10.67-16.72)	12.14 (8.86-14.42)	0.004	12.16 (9.77-16.56)	12.22 (8.77-14.92)	0.178

Data are presented in median (IQR); CPP, central precocious puberty; PT, premature thelarche; CPPII, CPP girls with Tanner stage II breasts; PTII, PT girls with Tanner stage II breasts; CPPIII, CPP girls with Tanner stage III breasts; PTIII, PT girls with Tanner stage III breasts; BMI, body mass index; LH, luteinizing hormone; FSH, follicle-stimulating hormone; GnRHa, gonadotropin-releasing hormone analog; *, comparing between CPPII and PTII; †, comparing between CPPIII and PTIII; ‡, comparing hormone levels between CPPII vs CPPIII and PTII vs PTIII, only basal and peak LH levels between CPPII vs CPPIII were significantly different ($p < 0.001$)

Figure 1. ROC curves of basal and peak serum LH and FSH levels for diagnosing CPP in girls with breasts Tanner stage II

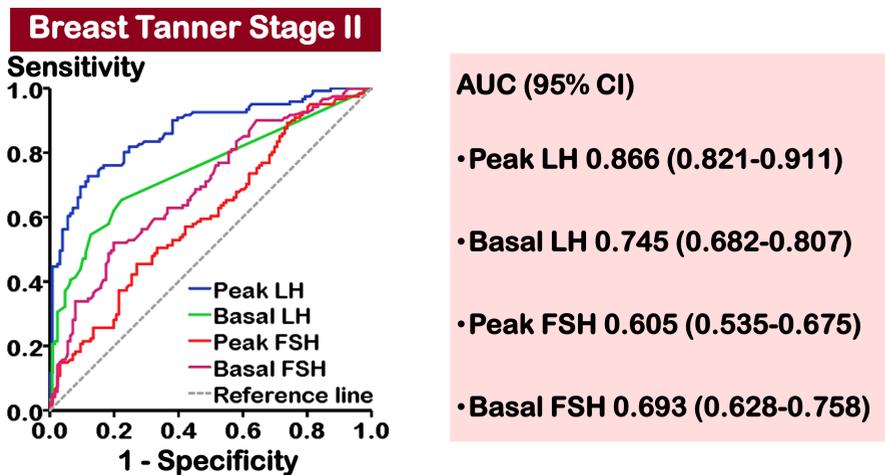
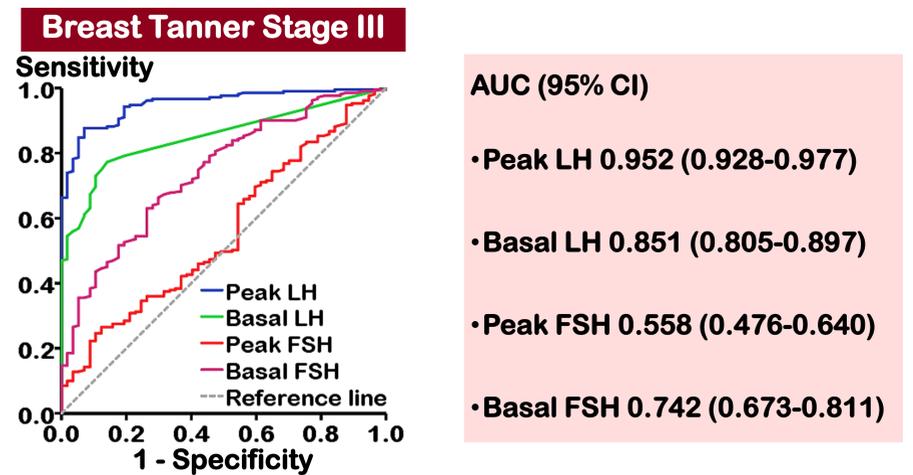


Figure 2. ROC curves of basal and peak serum LH and FSH levels for diagnosing CPP in girls with breasts Tanner stage III



ROC, receiver operating characteristic; LH, luteinizing hormone; FSH, follicle-stimulating hormone; CPP, central precocious puberty; AUC, area under the curve; CI, confidence interval

Table 2. Diagnostic accuracy of basal and peak serum LH cut-off levels for diagnosing CPP girls with breasts Tanner stages II and III

Serum LH cut-off levels (IU/L)	Breasts Tanner stage			
	II		III	
	Sensitivity	Specificity	Sensitivity	Specificity
Basal: ≥ 0.21	38	94	56	97
Peak: ≥ 5	69	90	84	95

Conclusions

- A single basal serum LH level of ≥ 0.21 IU/L
 - Useful for diagnosing girls with early phase of CPP
 - CPP could be diagnosed without GnRHa test in
 - 38% of girls with breasts Tanner stage II
 - 56% of girls with breasts Tanner stage III
- Peak serum LH ≥ 5 IU/L
 - Diagnosing CPP girls with breasts Tanner stage II: sensitivity 69% and specificity 90%
 - Diagnosing CPP girls with breasts Tanner stage III: sensitivity 84% and specificity 95%

