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### INTRODUCTION

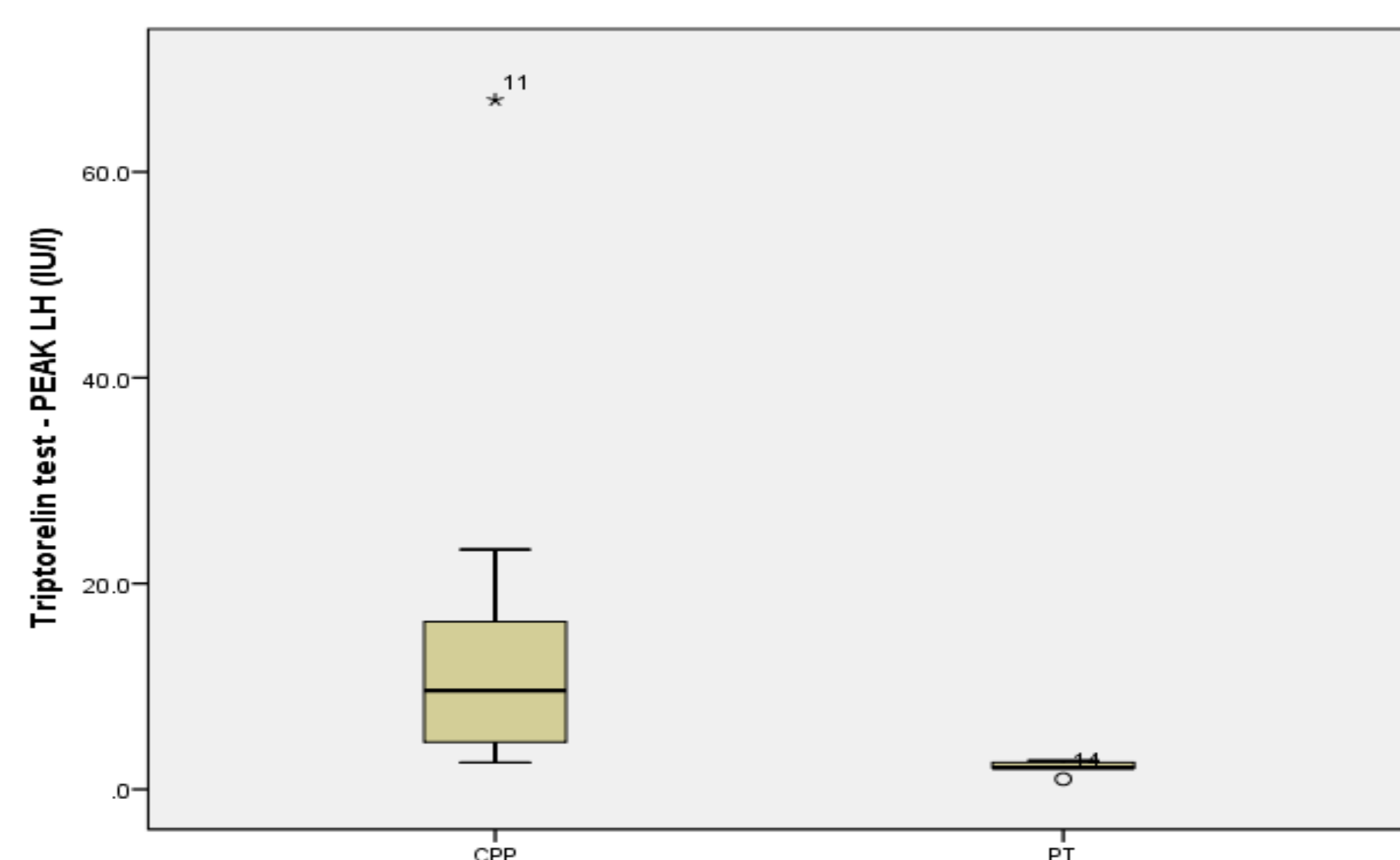
GnRH test is standard in confirming the diagnosis of central precocious puberty (CPP). However, GnRH (Relefact) is not always readily available in Serbia and several other countries.

Two studies so far have assessed the use of triptorelin test in diagnosing CPP, with different sampling protocols, and in only one of these studies the triptorelin test findings were compared to the GnRH test findings.

### OBJECTIVES

- to evaluate the diagnostic accuracy of the triptorelin test compared to the GnRH test in girls with suspected CPP.

- finding the optimal timing for blood sampling during triptorelin test.



### METHOD

Enrollment of 50-100 girls with premature breast development is planned. Study was officially approved by the Hospital Ethics Committee.

Baseline investigations: basal levels of FSH, LH, estradiol (E2), TSH, fT4, bone age (BA), abdominal and pelvic ultrasound. Both triptorelin and GnRH tests were performed in all enrolled girls within two weeks, in a randomized order:

#### Triptorelin (Diphereline) test procedure:

- Basal samples: FSH, LH, E2 (08 AM)
- Administration of 100 µg per m<sup>2</sup> of triptorelin s.c.
- Sampling: FSH and LH after 30, 60, 90, 120 and 180 min.
- Sampling after 24h: FSH, LH and E2



#### GnRH (Relefact) test procedure:

- Basal samples: FSH, LH, E2 (08 AM)
- Administration of 100 µg per m<sup>2</sup> of GnRH i.v.
- Sampling: FSH and LH after 30, 45 and 60 min.



The diagnosis of CPP was made according to the GnRH test findings (LH peak  $\geq 3.3$  IU/l). If the clinical signs of CPP (accelerated height, bone age, etc.) are noted within a year of test in subjects with negative GnRH test results (PT – premature thelarche group), GnRH test will be repeated, and these patients will be reassigned to the CPP group or PT group according to the results.

### RESULTS

Subject enrollment has started; both triptorelin and GnRH test results are currently available for 14 girls:

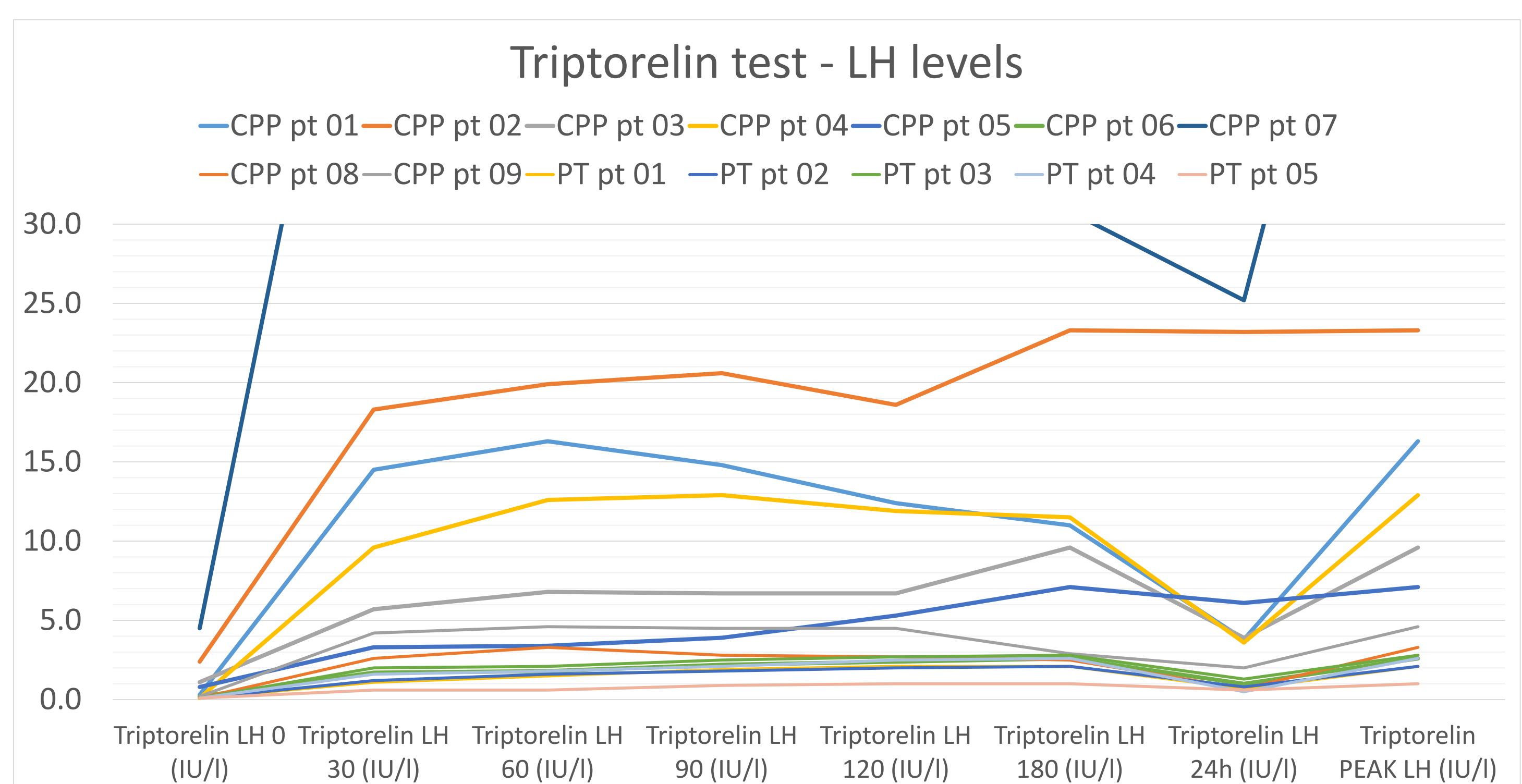
#### CPP group (n=9):

- Age at thelarche  $5.2 \pm 3.4$
- Tanner: B 2-4, P 1-3
- BA advanc.  $1.7 \pm 1.2$  yr \*
- Height SDS  $1.6 \pm 0.9$
- BMI SDS  $0.8 \pm 0.9$
- Basal LH 0.3 IU/l (0.1-2.9) \*\*
- Peak LH (GnRH) 11.3 IU/l (3.5-29)
- Peak LH (tript)  $16.3 \pm 20.1$  IU/l \*\*
- 24h E2 (tript)  $782 \pm 457$  IU/l \*\*

#### PT group (n=5):

- Age at thelarche  $4.7 \pm 3.0$
- Tanner: B 2-3, P 1-2
- BA advanc.  $-0.1 \pm 1.1$  years \*
- Height SDS  $0.9 \pm 1.0$
- BMI SDS  $1.2 \pm 1.0$
- Basal LH 0.1 IU/l (0.1-0.1) \*\*
- Peak LH (GnRH) 2.4 IU/l (2.2-2.9)
- Peak LH (tript)  $2.1 \pm 0.7$  IU/l \*\*
- 24h E2 (tript)  $109 \pm 75$  IU/l \*\*

\*  $p < 0.05$ ; \*\*  $p < 0.01$



- LH peak cutoff of  $\geq 3.0$  IU/l during triptorelin test showed 100% specificity and 89% sensitivity in detecting CPP.

- Using this cutoff resulted in missing one girl with CPP (LH peak during GnRH test 6.1 IU/l), which had non-progressive form of CPP with mild bone age advancement (+0.75 years).

- Lowering triptorelin LH peak cutoff to 2.6 IU/l would increase the sensitivity to 100%, reducing specificity to 60%.

### CONCLUSION

Triptorelin test with LH peak cutoff  $\geq 3.0$  IU/l can be used as alternative test for diagnosing CPP. GnRH test should be performed in girls with triptorelin test LH peak  $< 3.0$  IU/l if they show advancement of bone age or other signs of pubertal progression during follow-up.

### REFERENCES

1. Freire AV, Escobar ME, Gryngarten MG, Arcari AJ, Ballerini MG, Bergada I, and Ropelato MG. 2013 High diagnostic accuracy of subcutaneous Triptorelin test compared with GnRH test for diagnosing central precocious puberty in girls. *Clinical Endocrinology* 78, 398–404.
2. Poomthavorn P, Khlairit P, Mahachoklertwattana P. 2009 Subcutaneous Gonadotropin-Releasing Hormone Agonist (Triptorelin) Test for Diagnosing Precocious Puberty. *Horm Res* 2009;72:114–119.
3. Wu FCW, Butler GE, Kelnar CJH, Sellar RE. Patterns of pulsatile luteinizing hormone secretion before and during the onset of puberty in boys: a study using an immunoradiometric assay. *J Clin Endocrinol Metab* 1990;70:629-637.
4. Yen SSC, VandenBerg G, Rebar R, Ehara Y. Variations in pituitary response to synthetic LRF during different phases of the menstrual cycle. *J Clin Endocrinol Metab* 1972;35:931-7.
5. Carel JC, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics* 2009; 123:e752.
6. Kim HK, Kee SJ, Seo JY, Yang EM, Chae HJ, Kim CJ. Gonadotropin-releasing Hormone Stimulation Test for Precocious Puberty. *Korean J Lab Med*. 2011 Oct;31(4):244-249.

