Test on Kisspeptin Levels in Girls with Idiopathic Central Precocious Puberty and its Significance

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Introduction

It was generally accepted that precocious puberty (PP) refers to occurring of signs of sexual development for girls before the age of 8 or boys before 9 years old, or appearance of the menstruation for girls before the age of 10.The major manifestation of PP includes the growth spurt, together with maturity of reproduction organ and sexual characteristics being significantly earlier than the children of the same age. Of the total, the girls with idiopathic central precocious puberty (ICPP) accounts for more than 80% of those with central precocious puberty (CPP).

Problem

The pathogenesis of ICPP is unclear currently. Domestic and foreign researches confirmed that the signal pathway of Kisspeptin/ G protein-couple receptor 54(GPR54) is initiating agent of puberty growth , which probably is closely related with occurrence and development of ICPP. The early diagnosis of PP and therapeutic effect evaluation is very important for its diagnosing and treatment, but there is no research report about kisspeptin level of normal children, girls with PT and girls with ICPP ante-and-post treatment currently.

The purpose of present study aims to explore the role of kisspeptin level in initiating of puberty growth and its significance of diagnosis and therapeutic effect evaluation for girls with ICPP through comparing the kisspeptin level of girls with ICPP ante-and-post treatment, girls with PT, and normal girls of the same age, and to understand the correlation of this signal mechanism with suppression of gonadal axis in girls with ICPP at onset and post-treatment, so as to provide the new guidelines for the early diagnosis and therapeutic effect evaluation of girls with ICPP.

Objectives

CPP group: A total of 24 girls diagnosed with ICPP in our hospital from June 2012 to January 2013. The diagnosis standard of ICPP was in accordance with the diagnosis and treatment guidelines of central(true) precocious puberty for endocrinology and genetic metabolism group of pediatrics branch of Chinese medical association in 2007.

Normal control group: The girls who accepted health physical examination at the above period in our hospital. Inclusion criteria:

(1) Non-manifestation of sexual characteristics development;

(2) Height and weight were between mean ±2SD of children with the same gender and the same age;

(3) Age matched as closely as possible with ICPP group (±1 year).

PT group: Girls diagnosed with PT in our hospital at the same period. Inclusion criteria:

(1) Only premature thelarche, without occurrence of other secondary sex characteristics. No coloring of areola of breast; (2) Follow-up for 1 year. Showing the non-progressive self-limited course;

(3) Height and weight were between mean ±2SD of children with the same gender and the same age;

(4) Age matched as closely as possible with ICPP group (±1 year).

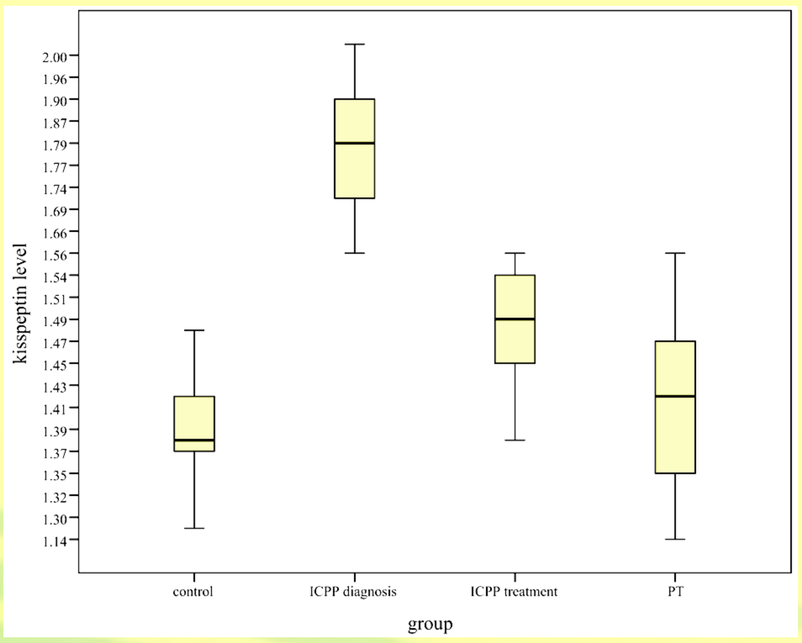
Methods

Detecting plasma Kisspetins level by ELISA

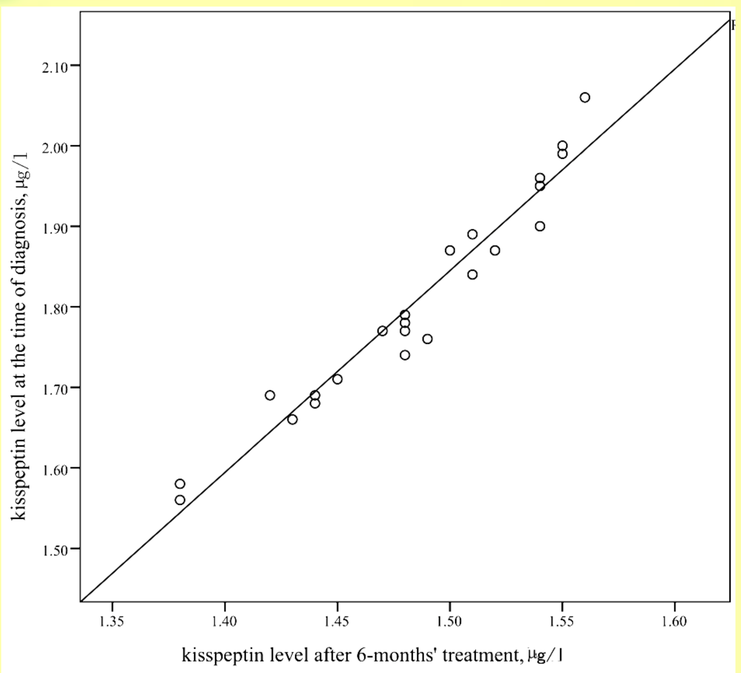
Put 1ml of blood specimen into EDTA，anticoagulant tube containing 0.6TI aprotinin (Amresco, Shanghai Hao ran Biotechnology Co., Ltd.), mixed gently and instantly, touched aprotinin with blood sufficiently to reduce degradation of protease in blood to kisspeptin, and then conserved at 4℃. Blood specimen was centrifuged for 15 minutes (l600xg, 4℃), supernatant was extracted and was conserved for detection at -80℃. All of above disposals were completed within 1 hour. After the plasma specimen was disposed by C18-SEP-COLUMN, it evaporated and dried in the freeze-drying machine, and then resolved. Kisspeptin level was detected by ELISA according to directions of the kit for Kisspeptin of PHOENIX company, USA.

Results

The kisspeptin level of ICPP group before treatment (1.80±0.13ng/ml±0.13)was higher than those of other groups with significantly statistic difference.



The kisspeptin level at the time of ICPP diagnosis and kisspeptin after treatment were positively correlated with the difference being statistically significant



Conclusions

Our experiment detected the kisspeptin levels of girls with ICPP before treatment and after 6 months of treatment, those of girls with PT and healthy controls respectively, and found kisspeptin of girls in ICPP group before treatment was significantly higher than those of other groups, which supported the viewpoint of kisspeptin probably being the activating effector of HPG axis. The significant increasing of Kiss-1 gene expression triggered pulse release of GnRH, activated HPG axis, initiated puberty development, thereby, caused the occurrence of precocious puberty .

Currently blood kisspeptin studies in children are more concentrated in kisspeptin comparison of CPP girls with PT girls or normal undeveloped girls, and there is no comparative study on plasma kisspeptin levels of ICPP girls before and after treatment in China. Our experiment detected the kisspeptin levels of girls with ICPP before treatment and after 6 months of treatment respectively, and the results showed that the kisspeptin level of ICPP group after treatment decreased significantly compared with kisspeptin before treatment. Based on such result, combined with significant decreasing of LH peak / FSH peak in the GnRH provocation test rechecked after treatment, we considered that HPG axis was suppressed and gene expression of Kiss-1 fell to phase of ante-puberty development. As for comparison of ICPP group after treatment and control group, the results between two groups were close, and kisspeptin level after ICPP treatment was slightly higher than that of the latter. However, the average age of group post-treatment was nearly 1.5 years older than control group. Further research is needed to assess whether kisspeptin could decrease to the level of control group or lower after continued treatmen