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ORIGINAL ARTICLE

Advanced bone age as an indicator facilitates the diagnosis of precocious puberty☆

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KEYWORDS
Central precocious puberty;
Bone age;
Luteinizing hormone-releasing hormone stimulation test;
Growth velocity

Abstract
Objective: Diagnosis of central precocious puberty has always been challenging in clinical practice. As an important method in the diagnosis of central precocious puberty, luteinizing hormone-releasing hormone stimulation test is complex and time-consuming. In many cases, clinical traits are inconsistent with luteinizing hormone-releasing hormone stimulation test results, therefore not reliable for diagnosis. In this study, the authors intended to find an indicator that predicts the results of the luteinizing hormone-releasing hormone stimulation test among subjects with early pubertal signs.
Methods: Cases of 382 girls with early breast development before 8 years old and luteinizing hormone-releasing hormone stimulation test before 9 years old were included and underwent follow-up tests. Patients with peak luteinizing hormone level ≥5 IU/L were considered positive in the luteinizing hormone-releasing hormone stimulation test. Anthropometric data, body mass index, bone age evaluation, blood hormones levels of luteinizing hormone, estradiol, follicle-stimulating hormone, and uterine and ovarian volumes were analyzed.
Results: Subjects with positive results in the initial test demonstrated early bone maturation, accelerated growth, and elevated basal blood luteinizing hormone, estradiol, and follicle-stimulating hormone levels, when compared with subjects with negative results in the initial test. Subjects with positive results in the follow-up test presented a more advanced bone age and more accelerated linear growth, when compared with subjects with negative results in the follow-up test.
Conclusions: According to the statistical analysis, advanced bone age is the most effective predictor of the result of luteinizing hormone-releasing hormone stimulation test.

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PALAVRAS-CHAVE
Puberdade precoce central;
Idade óssea;
Teste de estimulação do hormônio liberador do hormônio luteinizante;
Velocidade de crescimento

Idade óssea avançada como um indicador de facilitação do diagnóstico de puberdade precoce

Resumo

Objetivo: O diagnóstico da puberdade precoce central sempre foi complicado na prática clínica. Como um importante método no diagnóstico de puberdade precoce central, o teste de estimulação do hormônio liberador do hormônio luteinizante é complexo e demorado. Em muitos casos, as características clínicas são incompatíveis com os resultados do teste de estimulação do hormônio liberador do hormônio luteinizante e, assim, não são confiáveis para o diagnóstico. Neste estudo, visamos constatar um indicador que previsse os resultados do teste de estimulação do hormônio liberador do hormônio luteinizante entre indivíduos com sinais puberais precoces.

Métodos: Foram incluídos casos de 382 meninas com desenvolvimento precoce das mamas antes dos 8 anos de idade e teste de estimulação do hormônio liberador do hormônio luteinizante antes dos 9 anos e elas foram submetidas a testes de acompanhamento. Os resultados das pacientes com nível máximo de hormônio luteinizante $\geq$ 5 IU/L foram consideradas positivos no teste de estimulação do hormônio liberador do hormônio luteinizante. Foi feita uma análise dos dados antropométricos, do índice de massa corporal, da avaliação da idade óssea, dos níveis sanguíneos de hormônio luteinizante, volumes uterinos e ovarianos de estradiol (E2) e do hormônio folículo-estimulante.

Resultados: Os indivíduos com resultado positive no teste inicial demonstraram maturação precoce do osso, crescimento acelerado e níveis sanguíneos elevados de hormônio luteinizante, estradiol e hormônio folículo-estimulante, em comparação aos indivíduos com resultados negativos no teste inicial. Os indivíduos com resultados positivos no teste de acompanhamento apresentaram um maior avanço na idade óssea e crescimento linear mais acelerado, em comparação aos indivíduos com resultados negativos no teste de acompanhamento.

Conclusões: De acordo com a análise estatística, a idade óssea avançada é o indicador mais efetivo do resultado do teste de estimulação do hormônio liberador do hormônio luteinizante.

Introduction

Precocious puberty (PP) is that occurring before age 8 in girls or age 9 in boys.[1] In most cases, PP is a result of the premature activation of the hypothalamic-pituitary-gonadal (HPG) axis, which is also called central precocious puberty (CPP). CPP is usually idiopathic except when identifiable causes (*e.g.* tumors, hydrocephalus, brain lesions, or cranial trauma) are present.[2] Early bone maturation, accelerated linear growth, and pelvic ultrasonographical (USG) changes (including abnormal changes in ovarian, uterine, and adrenal volume) are usually present in PP,[3,4] in addition to other secondary sex characteristics, such as early growth of pubic hair.[5] CPP could lead to early closure of epiphysis, which eventually results in a decrease of height, among other impacts, such as psychological stress.[6] The literature reports that girls with early pubertal development present more behavior problems than their peers.[7] Thus, a detailed assessment of pubertal development for girls with suspected PP is necessary; if a diagnosis is made, proper treatment should be followed.

Premature thelarche (PT) is defined as an isolated development of breast tissue, with no other signs of sexual maturation; it is usually observed within the first 1–4 years of life. In most cases, PT is observed as a variation of normal physical development, not being considered pathological.[8,9] Children with PT present no signs of increased growth or advanced skeletal maturation, and have normal level of basal gonadotropin and E2.[10,11] With a prevalence of 4.7%, the causes of PT are largely unknown; 2–13% of cases of PT could progress to CPP,[12–14] so the clinical traits, bone age (BA), basal, and stimulated gonadotropin concentrations of the PT cases should be carefully evaluated.

The stimulated LH test is an assistive test that verifies the activity of HPG axis and distinguishes CPP cases from PT cases. For children with early progression of pubertal signs, accelerated linear growth, and early bone maturation, the CPP diagnosis is made when premature activation of HPG axis is confirmed.[15] However, the LHRH stimulation test demands a lengthy and complex sampling procedure; and sometimes, multiple tests are needed before a diagnosis of CPP can be made.[9,13] It has been reported that LH levels from two samples at 45-minute time point are required for a precise diagnosis of CPP.[9] In this study, the authors aimed to find a laboratory or clinical indicator that predicts a positive result in the LHRH stimulation test, since knowledge of such indicators could help decide the timing of the test, thus facilitating the diagnostic procedure of CPP.

In this study, the clinical and laboratory parameters of subjects with early pubertal signs were profiled and compared. Relevant parameters were correlated with the test results in initial and follow-up LHRH stimulation tests to find the most significant predictor of test results.