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Traditional Chinese medicine for idiopathic precocious puberty: A hospital-based retrospective observational study

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Summary
Objectives: To characterize the application of traditional Chinese medicine (TCM) among children with idiopathic precocious puberty (IPP).
Design and setting: This study examined data sets from patients diagnosed with IPP at Chang Gung Memorial Hospital between 2010 and 2012. The patients were allocated into three groups according their voluntary choice of treatment modalities: TCM users (received TCM treatment only), Western medicine (WM) users (received WM treatment only), and ''no treatment'' group (received no medical treatment at all).
Main outcome measures: The demographic data of children with IPP were characterized. The prescription patterns and frequencies of TCM for IPP patients were analyzed. The patients' bone maturation rates and the change of predicted height after different approaches were measured as outcomes.
Results: There were 3390 patients enrolled in the study. Zhi-Bai-Di-Huang-Wan (70.62%) was the most common herbal formula and Mai-Ya (Hordei Fructus Germinatus) (51.58%) was the most

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common single herb prescribed for IPP in all of the 2784 prescriptions. The bone maturation rates of TCM users (0.95 ± 0.20) and WM users (0.69 ± 0.05) were both decelerated but the ''no treatment'' group had an accelerated bone maturation rate of 1.33 ± 0.04. TCM and WM users also had higher predicted height after treatment (1.15 ± 1.19 cm versus 1.73 ± 0.29 cm), while the ''no treatment'' group had a decreased predicted height (−0.52 ± 0.23 cm).
Conclusions: Our study revealed a comprehensive list of TCM prescriptions for IPP patients. Future well-designed, randomized, double-blinded, and placebo-controlled clinical trials are warranted to evaluate the efficacy and safety of TCM for precocity.

Background

Puberty is an important developmental milestone for children. It is a complicated sequence of biological events leading to the progressive maturation of sexual characteristics and reproductive capacity. Precocious puberty (PP) means the early onset of puberty, such as the early development of secondary sexual characteristics, early skeletal maturation and early closure of the epiphyses, which may lead to a shorter adult height.[1] PP has a prevalence of 1 in 5000 children and a female to male ratio of more than 10:1,[2] which can result from excess sex hormone exposure, fatty tissue, environmental factors and several congenital organic diseases. A comprehensive history and physical examination, emphasizing the early detection of pathologic PP such as central nervous system abnormalities, brain tumors, adrenal pathologic problems, gonadal tumors, and genetic problems is mandatory.[2–4] Approximately 10–20% of girls and the majority of boys have underlying pathologic causes, while the others have an idiopathic etiology, belong to idiopathic precocious puberty (IPP).[5] If left untreated, discrepancies between physical and chronological ages may lead to a shorter stature. The psychosocial developmental problem is also a major concern for school-aged children.[6–8]

Currently, the use of gonadotropin-releasing hormone (GnRH) analogues is the first-line therapy for IPP.[9,10] These analogues suppress gonadotropin secretion and negatively regulate GnRH receptors, leading to a reduction of gonadal steroids to prepubertal levels.[11–13] GnRH analogues can slow down pubertal progression and bone maturation to improve adult stature.[14,15] However, side effects of GnRH analogues have been reported such as local erythema, hyperlipidemia, central obesity, temporary vaginal bleeding, and loss of bone density.[16–18] Besides, GnRH analogues are expensive and cost approximately $150 U.S. dollars every month in Taiwan.

TCM practitioners have been using oral herbs to treat many pediatric diseases for thousands of years. Nevertheless, IPP has been less described in the ancient literature, most likely because it was less common than diseases involving infection, the respiratory tract, and the gastrointestinal tract in the past. It will be very interesting to understand how TCM practitioners treat IPP and whether TCM can work on IPP. However, there is no large-scale study on TCM treatment for IPP so far. Therefore, we undertook a pragmatic approach to retrospectively review the TCM prescription patterns and the treatment outcome at a large medical institution in Taiwan from 2010 to 2012.

Methods

Data source

The data were collected from the records of outpatient clinics between January 1st, 2010, and December 31st, 2012, in the three branches of Chang Gung Memorial Hospital (CGMH) in northern Taiwan—the Taipei, Linkou, and Taoyuan branches. CGMH is not only a tertiary university-affiliated medical center but is also an institution of medical research and education. The TCM clinical service started in 1996 at CGMH. There are currently 79 TCM doctors in the Department of Traditional Chinese Medicine.

Study subjects and variables

We retrospectively reviewed the electronic records of patients with the diagnosis of PP using the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) code of 259.1 at CGMH between January 1st, 2010, and December 31st, 2012. The collected data contained the patients' gender, the date of birth, the date of encounter, diagnosis, skeletal evaluation of bone age by X-ray, WM prescription, and TCM prescription. Although PP is defined as the development of secondary sexual characteristics before 8 years of age in girls and before 9 years of age in boys,[19] we enrolled all of the patients with the diagnosed code of 259.1 who were 6–12 years old at their first visit; this approach was taken in order to not exclude the patients who had been diagnosed previously or had been diagnosed at other hospitals.

Inclusion criteria were: (1) diagnosis meets the diagnostic criteria of ICD-9-CM code of 259.1; (2) age ranges from 6 to 12 years old; (3) girls or boys. Exclusion criteria were (1) pathological precocious puberty diagnosed by hormonal, abdominal ultrasound and/or brain image studies; (2) taking long-term medicine other than GnRH analogues or TCM for more than 1 month; (3) serve diseases such as cancer, liver diseases or chronic renal failure.

Because this is a retrospective observational study, the allocation of treatment modalities was based on the patient and parent's choice. The patients were categorized into three groups: TCM users (received TCM treatment only), WM users (received WM treatment only), and ''no treatment'' group (received no medication but followed up regularly). We described their gender distributions, age at the first visit, time of visit, and duration of treatment for demographic data. In addition, we analyzed the common comorbidities