Brief Communication

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Growth Hormone Therapy in PWS with Mobile Application-Living with PWS

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Prader-Willi syndrome (PWS) is a multisystemic complex disorder characterized by hyperphagia and impaired satiety which lead to severe and early obesity. In infancy, hypotonia and poor suck are main problems, and a child goes through Failure-to-thrive. During childhood, clinical manifestations change to food seeking as well as excessive weight gain, short stature, developmental delay, cognitive disability and behavioral problems. Also, growth hormone insufficiency is frequent. Most patients receive the recombinant growth hormone (rGH) therapy that provides improvement in growth, body composition, and physical attributes. The clinical care guideline for rGH therapy in PWS had been noticed in 2013. The rGH therapy helps in body fat, lean body mass, height SDS and head circumference. Also, the rGH therapy helps motor function, psychomotor development and cognition and behavioral issues.In Samsung medical center, there are clinical care guidelines for rGH therapy in PWS and an useful application for the patients. 'Living with PWS', the name of an moblie application for PWS patients, was introduced in the lecture. The application revised to version 2. It was made more convenient to users than in version 1. It helps caregivers to schedule the rGH therapy and to monitor height and weight.

Keywords: Prader-Wiili syndrome, Growth hormone therapy, Mobile application

Introduction

Prader-Willi syndrome (PWS) is a multi-systemic complex genetic disorder characterized by hyperphagia and impaired satiety which related with hypothalamic dysfunction[1]. This characteristics is thought to be caused by the loss or failure of imprinted gene expression within chromosome 15q11-q13 as a result of the paternal copy being silenced by epigenetic factors such as DNA methylation[2]. PWS is generally characterized by short stature, weak muscle tone (hypotonia), feeding difficulties, poor growth, delayed development, intellectual disabilities, small hands and feet, growth hormone deficiency (GHD), hypogonadism, uncontrolled appetite (hyperphagia), obesity, and diabetes mellitus. A pathological increase of appetite begins from 2 to 4 years of age, and leads to chronic overeating and obesity with persistent short stature[3]. This shows severe and early obesity during childhood in PWS patients unlike in infancy.

Recombinant Human Growth Hormone Therapy (rhGH) in PWS

The prevalence of GHD in PWS was 45–80%, depending on the database and diagnostic criteria used[4,5]. GH therapy in PWS has been used frequently since its approval in the US (2000) and Europe (2001). The benefit of the rhGH therapy for children with PWS are well established and the clinical care guideline for GH therapy in PWS had been noticed in 2013[6]. GH therapy helps in Body Fat, Lean Body Mass, Height SDS and Head circumference[7]. In other study, GH therapy not only helps the linear growth and body composition of PWS patient, but also helps with motor function, psychomotor development and cognition and behavioral issues[8].

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Clinical Care Guidelines for rhGH Therapy in PWS (partially extracted)[9)]

I. After genetic confirmation of the diagnosis of PWS, rhGH treatment should be considered and, if initiated, should be continued for as long as demonstrated benefits outweigh the risks.

II. GH stimulation testing should not be required as part of the therapeutic decision-making process in infants and children with PWS.

III. Adults with PWS should have an evaluation of the GH/IGF axis before rhGH treatment.

IV. Before initiation of rhGH therapy, patients with PWS should have a genetically confirmed diagnosis and expert multidisciplinary evaluation. Diagnosing and treating comorbidities may impact on GH safety as well as on GH response.

V. Exclusion criteria for starting rhGH in patients with PWS include severe obesity (BMI>95th percentile), uncontrolled diabetes, untreated severe obstructive sleep apnea, active cancer, and active psychosis. rhGH therapy is contraindicated in children with breathing difficulties until ENT surgery and treatment of respiratory-compromising obesity has been achieved. In PWS patients, there are high incidence of both central apnea and obstructive apnea. Mostly, marked obesity or intercurrent repiratory tract infection can exacerbate obstructive apnea and could lead to sudden death. But the rhGH therapy can lead to lymphoid tissue growth due to increased IGF-I effects. It could make worsening of obstructive apnea. So, polysomnography should be performed before starting therapy.

VI. Scoliosis should not be considered a contraindication to rhGH treatment in patients with PWS.

X. IGF-I levels in patients with PWS on rhGH treatment should be maintained within the upper part of normal range (maximum 2 SDS) for healthy, age-matched normal individuals.

XI. Patients with PWS receiving rhGH must be followed carefully for potential adverse effects during GH treatment.

XII. Treatment with rhGH must be in the context of appropriate dietary, environmental, and lifestyle interventions necessary for care of all patients with PWS.

XIII. Cognitive impairment should not be a barrier to treatment with rhGH for patients with PWS.

In Our Center

There are clinical care guidelines for rhGH therapy in PWS and a useful application for the patients. We recommend that rhGH treatement started early in life (at the age of 4–6 month), beneficially and significantly altered the natural history of PWS by reducing body fat and improving muscle strength physical function, and lipid profiles without adverse effects. The starting dose should be at a low dose such as 0.25–0.3 mg/(m^2 · day) or 0.009–0.012 mg/(kg · day). The dose could be increased during the first weeks and months to reach the standard replacement rhGH dose of approximately 1.0 mg/(m^2 · day) or 0.035 mg/(kg · day) with the monitoring of clinical effects like sleep apnea, IGF-I, edema, worsening or new development of snoring, headache, and/or acromegalic clinical features. PWS patients and their parents could use the application named 'Living with PWS'. It is an moblie application for PWS patients. It help the daily use of rhGH and treatment schedule easily. In the application, we could follow up their growth by PWS growth curve and the curve shows the effectiveness of the rhGH therapy. Also, we can communitcate with the patients by the application (the "Dairy" section). The application revised to version 2. It was made more convenient to users than in version 1.

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