**Growth hormone therapy in two children with Prader-Willi syndrome**

Avdjeva D 1, Tincheva R 1, Stoeva I 2

1 Department of Clinical Genetics, University Pediatric Hospital, Sofia, Bulgaria
2 National Thyroid Screening, University Pediatric Hospital, Sofia, Bulgaria

**Introduction**

The Prader Willi syndrome (PWS) is a rare endocrine-metabolic disorder that is characterised by neonatal hypotonia, hyperphagia, marked obesity, short stature, hypogonadism and behavioural problems. The Prader-Willi syndrome results from loss of an imprinted gene on the long arm of chromosome 15 within the q11-13 region, usually as a result of a deletion on the paternal chromosome or a loss or acquired abnormality of both chromosomes from the mother—maternal disomy. With an incidence of 1 in every 10,000 –15,000 births, PWS is the most common syndromal cause of marked obesity. A large number of individuals with PWS show growth hormone (GH) deficiency. Recent studies indicate beneficial effects of GH replacement therapy not only for their linear growth but also for correction of metabolic dysfunction. We present our experience with rGH therapy in two children with Prader-Willi syndrome.

**Case reports**

**Case 1**

The first patient (fig 1.2) was born from uneventful pregnancy, but the mother recalls very little intrauterine activity. A birth weight was 2750 g. and a birth length was 49 cm. A male patient was diagnosed with PWS at 8 months of age when he was referred to our genetics center because of developmental delay, muscle weakness and dysmorphic features. DNA analysis confirmed maternal disomy of chromosome 15. GH therapy was started at 3 years of age with the purpose of decreasing the fatty mass and improving muscular tone. His height was 88 cm (SDS=−0.61) and his weight was 19.5 kg (SDS=1.63). The patient received and is currently receiving Genotropin 36 0.09–0.1 IU/kg/day subcutaneously. (Fig 3)

**Case 2**

The second patient (fig 4) was born prematurely from second complicated pregnancy. Birth weight was 1700 g. and a birth length was 26 cm. She presented with neonatal hypotonia but feeding problems were not noted in the newborn period. Her developmental progress was delayed. Prader-Willi syndrome was diagnosed at 6 months of age. Genetic tests confirmed maternal disomy of chromosome 15. Chest radiographs showed severe scoliosis. GH therapy was started at 4 years of age. Her height was 102 cm (SDS=−0.45) and his weight was 19.5 kg (SDS=0.91). The rGH dose ranged from 0.89 to 0.1 IU/kg/day. (Fig 5)

**Discussion**

Diminished GH secretion is a frequent finding in children with PWS (1). That this reduction in GH represents true GH deficiency rather than suppression by obesity is supported by several observations (2,3). Data on the effect of growth hormone on body composition are encouraging with most studies showing improvement, at least in the short term. Children with PWS, who usually have deficient GH secretion, show growth-rate increases in response to rGH therapy similar to other severely GH deficient children. (3,4). The rGH therapy increases lean body mass and energy expenditure, decreases fat mass, and increases bone mineral density in children with PWS. These effects are matched by measurable functional benefits, including increases in strength and agility and ventilation drive in children, and acquisition of motor skills in infants with PWS. Changes in body composition are dose-dependent and absolute but do not regress during prolonged rGH therapy (6). In our study, the improvement of height SDS was statistically significant in Case 1 (Fig 6), which indicated that the efficacy of GH lasted for at least 6 years of treatment. Our data demonstrate that although GH therapy did not give rise to statistically significant changes in weight SDS, there was an improvement in BMI in this patient (Fig 7). These findings are in agreement with those reported by Obata et al. at (7). In Case 2 there is no an improvement of height SDS because of slow progressive scoliosis (Fig 8). Our data demonstrate that GH therapy improve a muscle tone and BMI in second patient. (Fig 9). Diabetes mellitus was the most commonly reported adverse effect, but we did not find such event at the time of this study (8).

**Conclusion**

Long-term growth hormone therapy given in sufficient dose can be expected to result in an improvement in height status and body composition in children with the Prader-Willi syndrome. The role of GH therapy in the progression of scoliosis is yet to be established. Nevertheless, we recommend careful monitoring for these patients. The management of PWS patients requires multidisciplinary approach. More long-term efficacy and safety data will be needed to determine what remains the optimal treatment in children with PWS actually improves their quality of life.

**References**