

Challenges experienced in delivering Growth Hormone therapy in children's with Prader Willi Syndrome in Birmingham Children's Hospital

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Introduction

Prader Willi Syndrome (PWS) is a rare neuro-genetic disorder inherited as a result of lack of expression in 15q11-13 gene and 70% are paternally inherited ¹. Characteristic features are dysmorphism, behavioural problems, infantile hypotonia, short stature, hypothalamic dysfunction, hyperphagia and morbid obesity ¹⁻⁵. The long-term morbidity and mortality depend on hypothalamic dysfunction and obesity. While multidisciplinary care is essential, growth hormone (GH) is a recognized treatment modality to improve body composition

Objectives

This retrospective audit was to analyse the efficacy of GH therapy on PWS patients at Birmingham Children's Hospital.

Methods

Current guidelines recommend a starting dose of 9 –12 mcg/kg/day whilst aiming to gradually increase to 35mic/kg/day within a few months, while maintaining IGF-1 level below +2SDS.

Therapeutic and sub-therapeutic doses of GH-treated groups' height, weight and body mass index (BMI) SDS were assessed and compared with independent sample T test. Data was analysed by Rstudio (ver 1.1.456) and R (ver 3.51).

Results

Out of 37 PWS patients 29 had received GH. Among GH-treated group, 21 patients had either scoliosis or obstructive sleep apnoea (OSA); only one had received a subtherapeutic starting dose.

During follow up, 18 patients had IGF1 above +2SD at some point with subsequent reduction in dose. Out of the 11 patients who had normal IGF1, 5 received less than 22mic/kg/day due to the presence of scoliosis or OSA, one had only recently started, and 5 patients were treated with GH 28 -35 mic/kg/day.

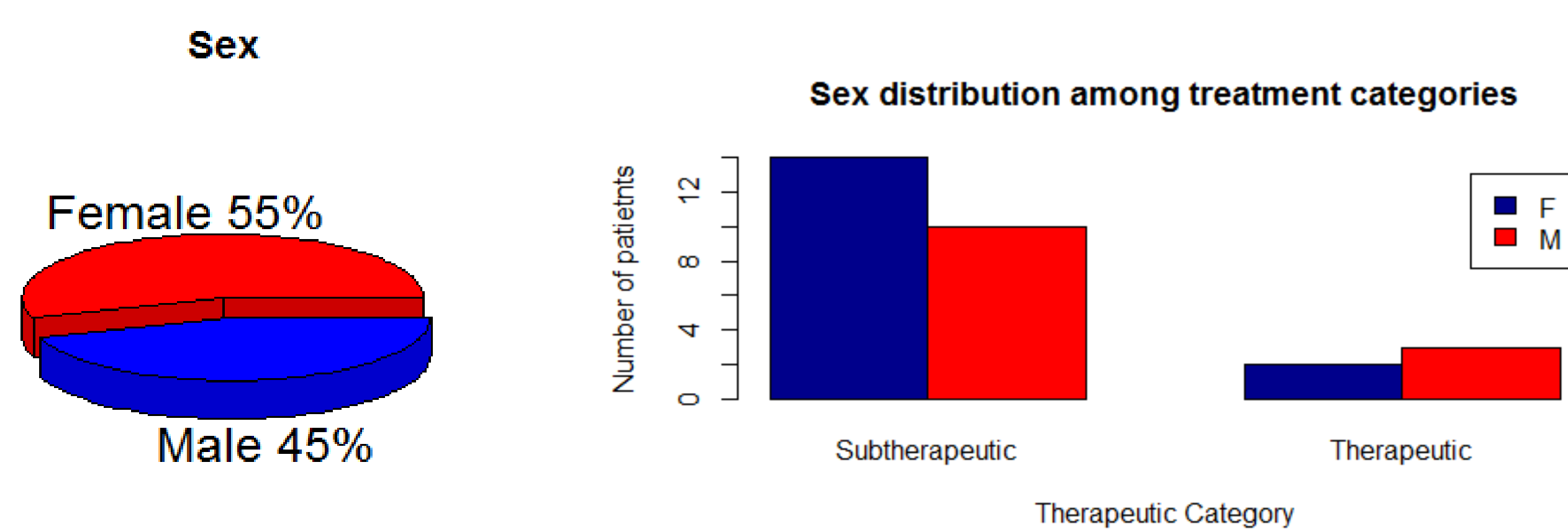


Figure 1

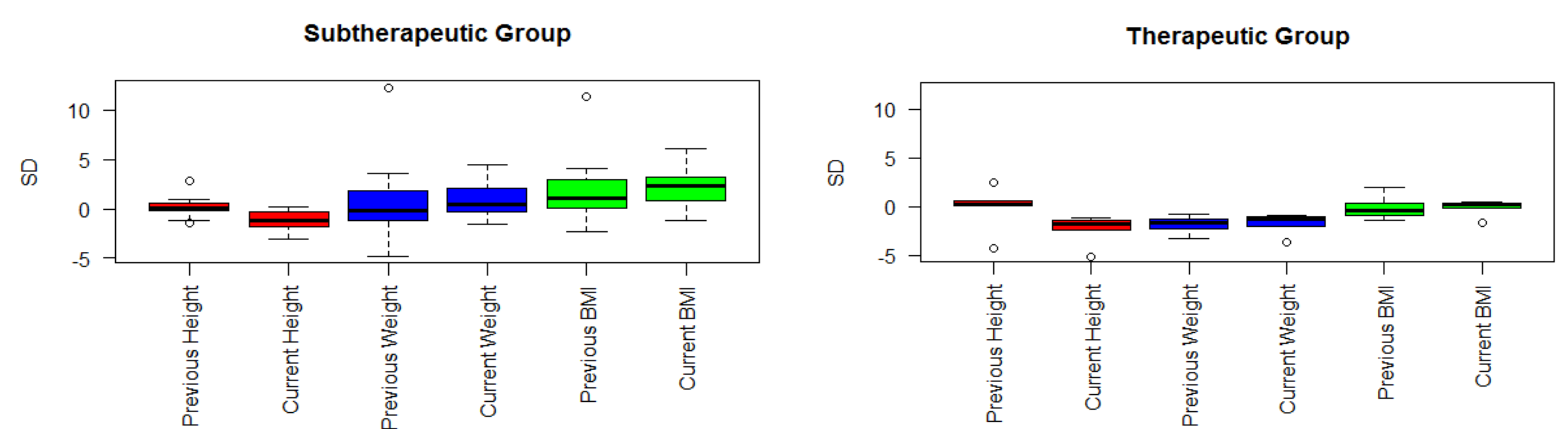


Figure 3

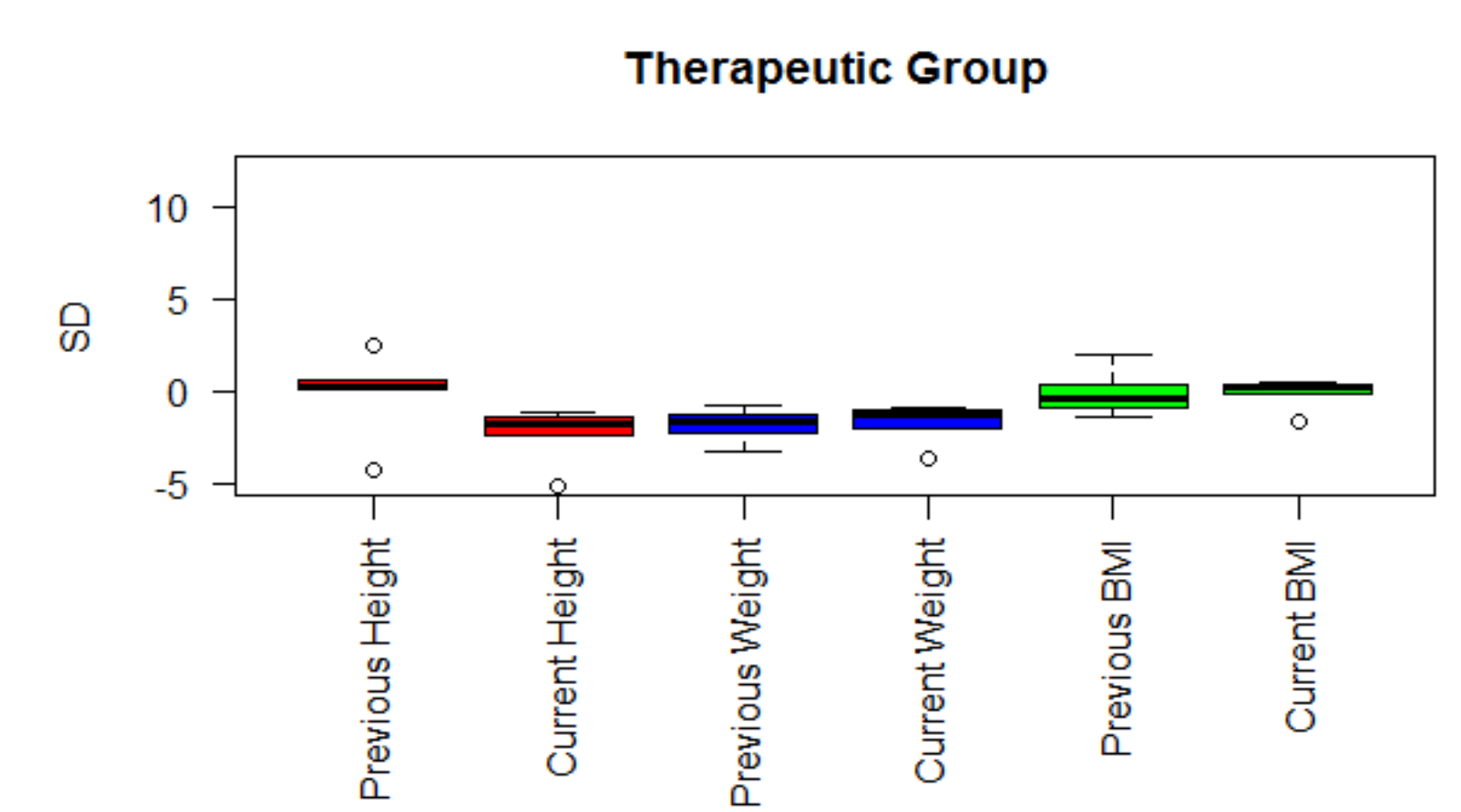


Figure 4

In both groups, height standard deviation score (SDS) had decreased (-1.33, -2.22 respectively) significantly (p values 0.014 and 0.000 respectively). In the sub-therapeutic group, weight and BMI mean SDS were increased by 0.563 and 0.490 respectively. In the therapeutic dose group, weight SDS mean was increased by 0.0413 and BMI SDS mean was decreased by 0.0534. However, BMI and weight changes were not statistically significant. Furthermore, out of the 5 patients who received recommended doses of GH, three were treated for less than 30 months and the duration may not be enough to demonstrate a significant effect.

Discussion, conclusions and recommendations

High IGF1 was a limiting factor for optimum delivery of GH in PWS patients. However, the number of patients and duration of treatment were not adequate to demonstrate significant effect of GH in the adequately-treated group.

There is evidence in other studies, that PWS patients tend to have significantly high IGF1 levels with GH therapy ⁶. Therefore, further multi-centered studies conducted for over longer periods are needed to evaluate whether GH significantly increases either the bioavailability of IGF1 or GH-related adverse effects in PWS

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