

Changes in Head Circumference with Growth Hormone Therapy in Individuals with Prader-Willi Syndrome

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Introduction: Individuals with Prader-Willi syndrome (PWS) typically have a head circumference that is smaller than expected for their family. However, as we have enrolled patients in our long-term translational research study and the Rare Disease Center Research Network (RDCRN) we have noted that growth hormone (GH) treatment causes the head circumference of young children to increase.

Methods: We retrospectively reviewed growth charts of head circumference and IGF-1 levels in individuals participating in the RDCRN study. Additionally, we obtained head circumference of the proband and family members as well as IGF-1 levels on the proband and control siblings at the time of the clinical research visit. We sought to determine trends in head circumference growth over time, both before starting GH therapy and afterwards.

Results: GH therapy increased head circumference in children with PWS. Children with IGF-1 levels within the normal range had an increase in head circumference that gave them a head circumference consistent with their family. A history of elevated IGF-1 levels and/or high IGF-1 levels for age and Tanner stage at the time of the study correlated with the head circumference inappropriately crossing percentiles on the growth chart, with the head circumference of the proband becoming larger than expected for the family. Infants with open fontanelles appear to be at the largest risk for developing a larger head circumference than expected, resulting in a triangular appearance of the skull. Children who had a history of persistently elevated IGF-1 levels had an acromegalic appearance and, often, a head circumference larger than their parents.

Conclusions: Elevated IGF-1 levels are associated with an inappropriate increase in head circumference, which is worst in young children/infants with open fontanelles when GH therapy is started. A head circumference that inappropriately crosses percentiles is a feature of acromegaly. Accordingly, this finding in such young children raises concerns as to the long-term consequences of allowing individuals with PWS to have elevated IGF-1 levels without acting on these levels to decrease the dose of GH. Many pediatricians and sub-specialists stop measuring head circumference at age 2. We recommend: 1) Measuring parental head circumference before children with PWS start GH therapy to identify a normal range of head circumference for the family; 2) Measuring head circumference at each visit, like weight and height, to track growth and identify worrisome trends in growth; 3) Monitor IGF-1 levels to keep in the normal range.