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Comparing the cumulative dose of growth hormone therapy using body weight-based dosing vs body surface area-based dosing in children with Turner syndrome—data from the ANSWER study

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Objective

This analysis compares cumulative growth hormone (GH) doses when adjusting GH dosage based on body weight (BW; actual dosing) vs body surface area (BSA; theoretical dosing calculated from average BSA and dose) in children with Turner syndrome (TS), using data from the American Norditropin Studies: Web-Enabled Research (ANSWER) Program.

Introduction

- Previously, only a single study compared BSA- vs weight-based GH dosing in girls with TS[1]
  - This analysis suggested that BSA-based dosing may decrease cumulative GH doses and treatment costs compared with weight-based dosing while providing at least equal adult-height gains
- The ANSWER Program is a long-term, US-based, non-interventional study designed to collect information on the effectiveness and safety of Norditropin® GH
  - This dataset may be useful in comparing BW-based and theoretical BSA-based dosing in different patient populations
- From June 2002 to September 2016, 20,204 pediatric patients were enrolled in ANSWER by their treating physicians, including 1003 patients with TS
  - Patient information was entered by participating physicians using a Web-based tool

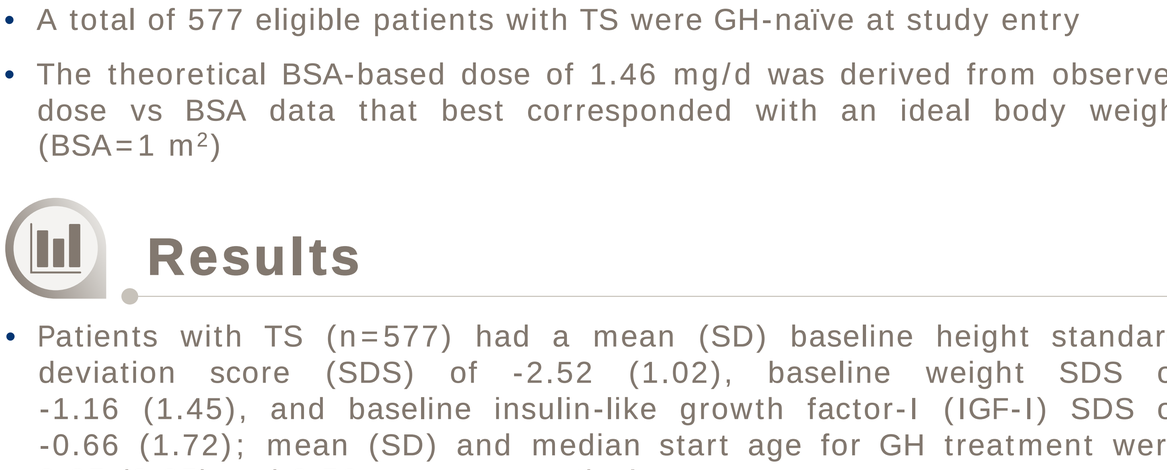
Methods

- A total of 577 eligible patients with TS were GH-naïve at study entry
- The theoretical BSA-based dose of 1.46 mg/d was derived from observed dose vs BSA data that best corresponded with an ideal body weight (BSA=1 m^2)

Results

- Patients with TS (n=577) had a mean (SD) baseline height standard deviation score (SDS) of -2.52 (1.02), baseline weight SDS of -1.16 (1.45), and baseline insulin-like growth factor-I (IGF-I) SDS of -0.66 (1.72); mean (SD) and median start age for GH treatment were 9.25 (3.95) and 9.56 years, respectively
- At baseline, 338 patients (59%) were aged <10 years and 239 (41%) were ≥10 years; spontaneous puberty (Tanner stage ≥2) was reported for 23 patients
- After starting GH treatment, mean IGF-I SDS increased from baseline (-0.66) to year 1 (+1.11), and then remained stable during subsequent years of treatment follow-up **(Figure 1)**

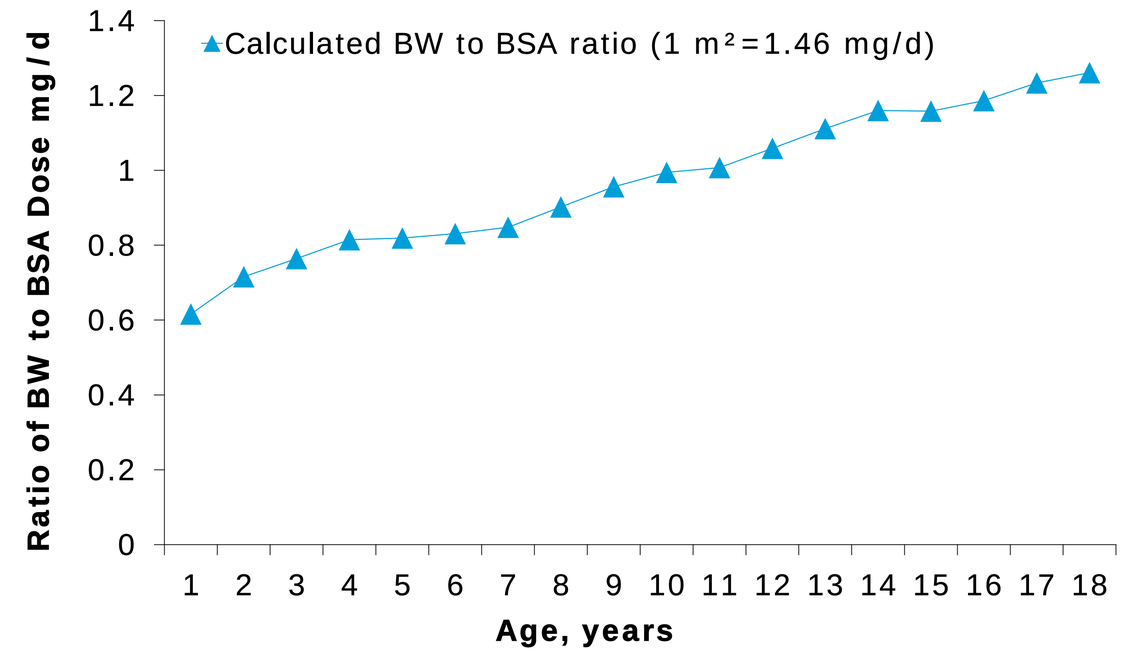
Figure 1 ♦ TS patients' IGF-I SDS by years of treatment



IGF-I SDS, insulin-like growth factor-I standard deviation score; TS, Turner syndrome.
Error bars indicate +/- SE.

- The ratio of BW-based to theoretical BSA-based GH dose (1.46 mg/d) was <1 before age 10 years and >1 after age 10 years **(Figure 2)**

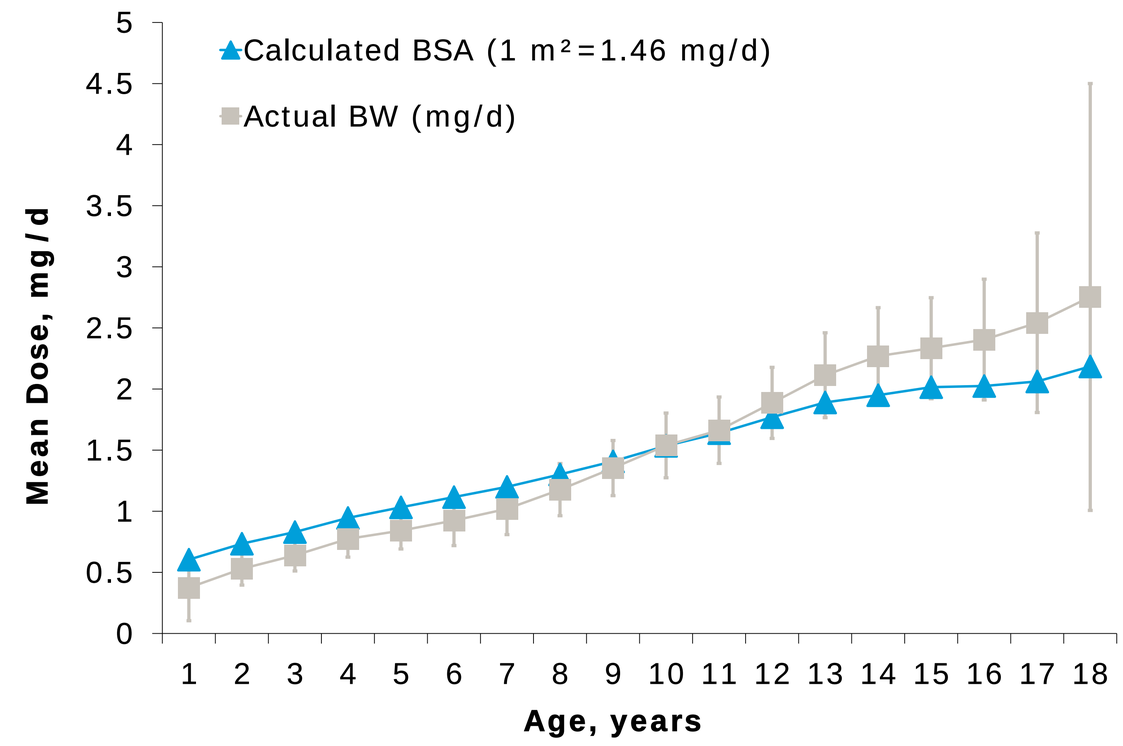
Figure 2 ♦ Ratio of BW to BSA dose in mg/d by age



BSA, body surface area; BW, body weight.

- Compared with BSA-based dosing, mean GH dose with BW-based dosing was lower before age 10 years, but higher after age 10 years **(Figure 3)**

Figure 3 ♦ TS patients' mean dose by age: actual by BW or hypothetical by BSA



BSA, body surface area; BW, body weight; TS, Turner syndrome.
Error bars indicate +/- SE.

Conclusions

- GH dosing based on a hybrid method in which the GH dose is BW-based before age 10 years and BSA-based after age 10 years may result in a lower cumulative dose than BW-based GH dosing alone.
- Conclusions regarding the effectiveness of BSA-based dosing could not be derived from these retrospective data, as all BSA-based doses were theoretical.
  - Demonstrating the effectiveness of a hybrid dosing method may support a rationale for optimized and individualized GH dosing and could have the potential to lower the cost of therapy.
- Further research is warranted to explore the benefits of a hybrid dosing method and whether this approach results in height outcomes similar to those of BW-based dosing.

Reference

1. Schrier L, et al. *Horm Res Paediatr.* 2014;81(5):319-330.

CONFLICT OF INTEREST DISCLOSURE

PB has served as a consultant for and has received research funds from Novo Nordisk Inc. and Ipsen and has served as a consultant for Novartis; MEG had a research contract and was a consultant for Versartis, has served as a consultant for Ipsen, Novo Nordisk Inc., Pfizer, and Sandoz, and has been a member of a data safety monitoring board for Ascendis; JR has served as a consultant for Novo Nordisk Inc. and OPKO; NH and VO are employees of Novo Nordisk Inc.

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