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ORIGINAL ARTICLE

Safety and efficacy of growth hormone treatment: GeNeSIS study in Spain☆

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Abstract
Introduction: Country-specific information on paediatric GH therapy is available from multinational studies.
Methods: A total of 1294 children in Spain enrolled in the observational Genetics and Neuroendocrinology of Short-stature International Study (GeNeSIS). Adverse events were assessed in all GH-treated patients ($n = 1267$) and effectiveness in those with GH deficiency (GHD, 78%).
Results: Mean age at time of entry to the study was 9.8 years. GH was initiated at a median (Q1–Q3) 0.22 (0.20–0.25) mg/kg/week and administered for 2.8 (1.6–4.4) years. For 262 patients with GHD and 4-year data, mean (95% CI) height velocity was 4.3 (4.1–4.6) cm/year at baseline, 9.0 (8.7–9.4) cm/year at 1-year, and 5.5 (5.2–5.8) cm/year at 4-years. Height standard deviation score (SDS) was −2.48 (−2.58 to −2.38) at baseline and −1.18 (−1.28 to −1.08) at 4 years. Final height SDS minus target height SDS ($n = 241$) was −0.09 (−0.20 to 0.02). In 1143 GH-treated patients with ≥1 year follow-up, 93 (8.1%) reported treatment-emergent adverse events. Serious events were reported for 7 children, with 2 considered GH-related.
Conclusion: These data confirm the benefit of GH replacement therapy on height gain for the patients in Spain. The safety profile was consistent with that already known for GH therapy.

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Seguridad y efectividad del tratamiento con hormona de crecimiento: estudio GeNeSIS en España

Resumen
Introducción: La información específica de cada país sobre el tratamiento pediátrico con hormona de crecimiento (GH) proviene de estudios multinacionales.
Métodos: En España, 1.294 niños participaron en el estudio internacional y observacional sobre genética y neuroendocrinología de la talla baja (GeNeSIS). En los pacientes tratados con GH (n = 1.267) se evaluaron los acontecimientos adversos. En aquellos con deficiencia de GH (DGH, 78%) también se evaluó la efectividad.
Resultados: La media de edad al inicio del estudio fue 9,8 años. La mediana (Q1-Q3) de duración del tratamiento fue 2,8 (1,6-4,4) años y la dosis inicial de GH 0,22 (0,20-0,25) mg/kg/semana. En 262 pacientes con DGH con datos a 4 años, la velocidad media (IC 95%) de crecimiento fue 4,3 (4,1 a 4,6) cm/año al inicio; 9,0 (8,7 a 9,4) cm/año tras un año y 5,5 (5,2 a 5,8) cm/año a los 4 años. La puntuación de desviación estándar (SDS) de talla fue —2,48 (—2,58 a —2,38) al inicio y −1,18 (−1,28 a −1,08) a los 4 años. La SDS de talla final menos la SDS de talla diana (n = 241) fue −0,09 (−0,20 a 0,02). De 1.143 pacientes tratados con GH con seguimiento ≥1 año, 93 (8,1%) comunicaron acontecimientos adversos surgidos durante el tratamiento. En 7 niños se comunicaron acontecimientos adversos graves, que en 2 casos se consideraron posiblemente relacionados con GH.
Conclusión: La terapia de sustitución con GH fue efectiva para el aumento de talla en los pacientes españoles. El perfil de seguridad fue acorde con el ya conocido para el fármaco.

Introduction

The main goal of treatment with growth hormone (GH) in children and adolescents is to promote normal growth. Since the introduction of recombinant human GH in 1985, final height outcomes have improved in thousands of children with growth-related disorders. The main indication for treatment with GH continues to be GH deficiency (GHD) in children[1] or adults.[2] However, its use has evolved with time and new indications have been approved. The newly approved indications in the paediatric age group outside of GHD include Turner syndrome, short stature in children born small for gestational age (SGA), Prader-Willi syndrome, chronic renal failure and short stature due to short-stature homeobox-containing gene (SHOX) haploinsufficiency.[1,3–10]

Many studies have demonstrated that adverse events related to GH therapy are rare, especially at the currently recommended doses,[6,7,11–15] although cases of intracranial hypertension, scoliosis and slipped femoral capital epiphysis have been reported in a small number of patients.[1,14–16] There has been concern about a possible association of GH therapy with glucose metabolism disorders and the development of neoplasms in patients with risk factors.[12,14,17–19]

The long-term outcomes and safety of GH therapy have been documented in large international registries, such as the Kabi International Growth Study (KIGS), the National Cooperative Growth Study (NCGS), and the Genetics and Neuroendocrinology of Short Stature International Study (GeNeSIS). It is also important that data specific for each country are gathered to assess the effectiveness and safety of clinical practise and treatment regimens in comparison to the overall data. The aim of this study was to assess the safety and effectiveness of GH therapy in Spanish paediatric patients based on data from GeNeSIS.

Methods

Study and population characteristics

GeNeSIS was an open-label, multinational, prospective observational research programme the purpose of which was to assess the long-term safety and effectiveness of GH therapy (Humatrope®, Eli Lilly and Company, Indianapolis, USA) in children with short stature. Patients were diagnosed and managed according to standard paediatric endocrine practice. The programme was conducted in accordance with the ethical guidelines of the Declaration of Helsinki, received institutional board approval, and met all applicable regulatory requirements in the participating countries. The parents or legal guardians of each patient provided written consent for data collection, processing and publication prior to enrolment.

The study included patients undergoing or that were going to start treatment with GH for growth promotion. Patients with a previous history of neoplasm or a SHOX deficiency disorder were only included if they had never received GH therapy before. Patients with closed epiphyses were not eligible for entry, although those whose epiphyses closed during the study were allowed to continue participating in the study. In Spain, 56 centres with paediatric endocrinology units participated in the study.