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ORIGINAL ARTICLE

Human growth hormone and Turner syndrome☆

Silvia Beatriz Sánchez Marco[a,*], Antonio de Arriba Muñoz[a], Marta Ferrer Lozano[a], José Ignacio Labarta Aizpún[a], Jesús María Garagorri Otero[b]

[a] *Unidad de Endocrinología Pediátrica, Hospital Universitario Miguel Servet, Zaragoza, Spain*
[b] *Servicio de Pediatría, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*

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KEYWORDS
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Abstract
Objective: The evaluation of clinical and analytical parameters as predictors of the final growth response in Turner syndrome patients treated with growth hormone.
Material and methods: A retrospective study was performed on 25 girls with Turner syndrome (17 treated with growth hormone), followed-up until adult height. Auxological, analytical, genetic and pharmacological parameters were collected. A descriptive and analytical study was conducted to evaluate short (12 months) and long term response to treatment with growth hormone.
Results: A favourable treatment response was shown during the first year of treatment in terms of height velocity gain in 66.6% of cases (height-gain velocity >3 cm/year). A favourable long-term treatment response was also observed in terms of adult height, which increased by 42.82 ± 21.23 cm (1.25 ± 0.76 SDS), with an adult height gain of 9.59 ± 5.39 cm (1.68 ± 1.51 SDS).
Conclusions: Predictors of good response to growth hormone treatment are: (A) initial growth hormone dose, (B) time on growth hormone treatment until starting oestrogen therapy, (C) increased IGF1 and IGFBP-3 levels in the first year of treatment, and (D) height gain velocity in the first year of treatment.

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* Corresponding author.
E-mail address: ssanchezmarco@gmail.com (S.B. Sánchez Marco).

PALABRAS CLAVE
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Talla baja;
Hormona de crecimiento

Hormona de crecimiento y síndrome de Turner

Resumen
Objetivo: Evaluación de parámetros clínicos y analíticos que actúen como predictivos de respuesta al tratamiento con hormona de crecimiento (rhGH) a largo plazo en pacientes con síndrome de Turner.
Material y métodos: Estudio retrospectivo de 25 niñas diagnosticadas de síndrome de Turner, de las cuales 17 recibieron tratamiento con rhGH y fueron controladas hasta alcanzar la talla adulta. Se determinaron diferentes variables auxológicas, analíticas, genéticas y farmacológicas a lo largo de su seguimiento en dichas consultas. Se realizó un estudio descriptivo y analítico mediante regresión lineal, con valoración de la respuesta al tratamiento a corto (12 meses) y a largo plazo.
Resultados: Se observó una respuesta favorable a corto plazo valorada en ganancia de velocidad de crecimiento en el 66,6% de los casos (velocidad de crecimiento > 3 cm/año a los 12 meses de tratamiento respecto a la previa). También se evidenció una respuesta favorable a largo plazo, valorada en una ganancia de talla total de 42,82 ± 21,23 cm (1,25 ± 0,76 SDS). Las pacientes ganaron una media de 9,59 ± 5,39 cm (1,68 ± 1,51 SDS) respecto a su pronóstico de crecimiento previo al tratamiento.
Conclusiones: El presente estudio evidencia como factores predictivos de buena respuesta al tratamiento con rhGH a largo plazo en orden de importancia: A) dosis de rhGH al inicio del tratamiento, B) tiempo de tratamiento con rhGH hasta inicio de terapia estrogénica, C) incremento en los niveles de IGF1 e IGFBP-3 durante el primer año de tratamiento y D) velocidad de crecimiento en el primer año de tratamiento.

Introduction

Turner syndrome is a chromosomal disorder that occurs in one of every 2500 live births, characterised by the complete or partial absence of a chromosome X (the complete monosomy [45,X] accounts for more than 50% of cases),[1,2] although some studies have found evidence of a high prevalence of mosaicism.[3] It is associated with a range of phenotypic characteristics, chief of which are short stature, gonadal dysgenesis, hand and foot lymphoedema, pterygium colli, cubitus valgus and cardiovascular malformations, among others.[2]

Since short stature is a common feature and the sole clinical manifestation in most cases,[1–3] several studies have evinced the efficacy of treatment with recombinant human growth hormone (rhGH), with increases in final height of ∼7–10 cm.[4–6]

Treatment with rhGH has to be initiated early when stature is more than two standard deviations (−2 SDS) below that of the general population or height velocity (HV) is below the tenth percentile for the patient's bone age. It should not be delayed past age 4 years nor initiated before age 2 years.[1,4]

Different studies have identified some predictors of adult height, such as height at initiation of treatment with rhGH, response in the first year of treatment, genetic height potential, age at initiation of treatment or mean weekly dose of rhGH.[4,6,7]

We present a study conducted in a Spanish cohort of patients with Turner syndrome with the aim of analysing the association between the response to treatment with rhGH and various factors.

Materials and methods

We conducted a retrospective study of 25 patients with a Turner syndrome diagnosis, 17 of who were treated with rhGH and followed up at the paediatric endocrinology unit of a tertiary level hospital until they reached their adult height. The patients treated with rhGH have been in followup from 1995 to present, and having reached adult height was an inclusion criterion. We also retrieved data for older cases that were not treated with rhGH on account of being diagnosed at older ages or the family refusing the treatment.

We reviewed the medical records of patients with Turner syndrome, collecting data for auxological measurements, laboratory tests, karyotyping and pharmacological treatment throughout their followup in the unit. We informed the patients of the purpose of the study and obtained their informed consent.

We assessed the short-term response to treatment with rhGH (12 months) based on changes in HV. We defined response to treatment as an increase in HV of more than three centimetres per year compared to the previous HV or an increase by three SDS at 12 months of treatment. To assess the long-term response to treatment (up to reaching adult height), we used five possible response variables: (1) an increase in height SDS compared to baseline SDS (delta HtSDS: adult height SDS− height at initiation of rhGH)[3]; (2)