Secondary Hyperparathyroidism Is Not Always an Obstacle to Improved Growth during Recombinant Human Growth Hormone Treatment

S. Picca
I. Perruzza
M. Cappa
G. Rizzoni

Dear Sir,

It is known that secondary hyperparathyroidism (HPT) is only a contributory cause of growth retardation in renal children [1] unless bone deformities occur altering skeletal morphology [2]. Nonetheless, the prevention of excessive parathyroid hormone (PTH) secretion by calcitriol administration has been generally considered essential to achieve linear growth [3]. Since recombinant human growth hormone (rhGH) treatment has been available for stunted children, no significant increase in PTH serum levels during rhGH treatment has been demonstrated [4, 5]. Recently, the induction of secondary HPT associated with poor response to rhGH treatment has been reported [6].

In order to verify if HPT could negatively affect response to rhGH treatment, we have retrospectively analyzed serum PTH levels together with growth rate during rhGH treatment in our children on chronic hemodialysis.

Eleven children (7 boys, 4 girls), aged 6.7-14.2 years, were selected for rhGH treatment on the basis of the following criteria: chronological age > 3 years, height < 2 standard deviation score (SDS) for chronological age and/or height velocity < 2 5th centile during the year before the start of treatment, no evidence of systemic disease, malnutrition or radiological signs of osteodystrophy. All patients were prepubertal at the start of treatment.

Dosage of rhGH was 4 IU/m² of body surface area/day (± 10%). Intact PTH was measured by radioisotopic assay (Nichols Institute Diagnostics).

Treatment duration ranged from 9 to 36 months: 1 patient was treated for 9 months, 1 for 12, 5 for 24, 3 for 36 and 1 for 48

Dear Sir,

It is known that secondary hyperparathyroidism (HPT) is only a contributory cause of growth retardation in renal children [1] unless bone deformities occur altering skeletal morphology [2]. Nonetheless, the prevention of excessive parathyroid hormone (PTH) secretion by calcitriol administration has been generally considered essential to achieve linear growth [3]. Since recombinant human growth hormone (rhGH) treatment has been available for stunted children, no significant increase in PTH serum levels during rhGH treatment has been demonstrated [4, 5]. Recently, the induction of secondary HPT associated with poor response to rhGH treatment has been reported [6].

In order to verify if HPT could negatively affect response to rhGH treatment, we have retrospectively analyzed serum PTH levels together with growth rate during rhGH treatment in our children on chronic hemodialysis.

Eleven children (7 boys, 4 girls), aged 6.7-14.2 years, were selected for rhGH treatment on the basis of the following criteria: chronological age > 3 years, height < 2 standard deviation score (SDS) for chronological age and/or height velocity < 2 5th centile during the year before the start of treatment, no evidence of systemic disease, malnutrition or radiological signs of osteodystrophy. All patients were prepubertal at the start of treatment.

Dosage of rhGH was 4 IU/m² of body surface area/day (± 10%). Intact PTH was measured by radioisotopic assay (Nichols Institute Diagnostics).

Treatment duration ranged from 9 to 36 months: 1 patient was treated for 9 months, 1 for 12, 5 for 24, 3 for 36 and 1 for 48

PUBERTAL

\[-0.5 \quad 0 \quad 0.5\]

DELTA H-SDS

\[-0.5 \quad 0\]
DELTA H-SDS

0.5

Fig. 1. Δ-HSDS and mean PTH levels in hemodialyzed children under rhGH treatment. Each point represents Δ-HSDS of 1 year plotted with mean PTH level of the same year. a Values of pubertal children; b Values of prepubertal children.

Two pubertal children showed catch-up growth, increasing both height velocity (HV) (from 0.4 to 6.6 cm/year and from 1.3 to 6.4 cm/year, respectively) and height standard deviation score (HSDS) (from -2.4 to -2.15 and from -4.85 to -2.95, respectively). In the same period they developed severe HPT (842 and 850 pg/ml, intact PTH mean yearly level, respectively) with radiological signs of osteodystrophy, without showing bone deformities. Also 2 prepubertal children showed a good response to rhGH (HV from 3.3 to 5.3 and from 4.2 to 6.6 cm/year; HSDS from -2.39 to -2.26 and from -4.07 to -3.7, respectively), while mean yearly PTH level was 136 and 241 pg/ml. In the second prepubertal child, radiological signs of osteodystrophy and a parathyroid adenoma were found.

Linear regression between growth during rhGH treatment, expressed as difference in height standard deviation score (Δ-HSDS) / year and mean PTH of the corresponding year (fig. 1 A), showed a positive and statistically significant correlation for pubertal children, while it did not for prepubertal ones (fig. 1B).

Our results are in contrast with those reported by Langman et al. [6]; in their study a mean intact level of 182 pm/ml is defined ‘elevated’ and thought to be responsible of poor response to rhGH treatment. In our study both some pubertal and prepubertal children could increase growth under rhGH treatment in the presence of HPT. Children showing pubertal spurt had highest PTH levels. The present results show that during rhGH treatment, HPT, per se, is not an obstacle to improved growth. It remains to be elucidated if the pubertal spurt is somehow responsible of HPT: there is no evidence that during puberty PTH levels increase significantly [7] and it has not been demonstrated that rhGH stimulates PTH secretion [4, 5]. More data are needed to clarify the role of PTH during rhGH treatment.

References


Nephron 1997;75:239-240
Picca/Perruzza/Cappa/Rizzoni