Dramatic effect of a non-17α alkyl testosterone derivative anabolic agent on growth in a child with achondroplasia in the short term

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Background & aim: Achondroplasia is one of the most commonly known types of skeletal dysplasia, leading to short stature and severe rhizomelic dwarfism with extreme, disproportionate, short stature. Hormonal therapy with a growth hormone was associated with a significant effect on height gain in patients with achondroplasia. Currently, growth hormone is available on a limited basis for patients with growth hormone deficiency. The aim of this paper is to report the effects of a limited number of doses of nandrolone decanoate in a child with achondroplasia and very slow growth in the short term.
Materials & methods: A 4-year old girl with achondroplasia was referred owing to her parents concern and anxiety regarding her very slow growth. Growth hormone therapy was not available for the child. On referral, her weight was 13 kg and her height was 76.7 cm. Her height was 76.6 cm 6 months before, and baseline growth velocity during the previous 6 months was considered zero. She received nandolone 25 mg by intramuscular injection at days 1, 10 and 40. **Results:** The novel use of nandrolone in this child with achondroplasia resulted in a dramatic acceleration in growth without the occurrence of unwanted effects or advancement of bone age. At 2 months after the first nandrolone injection, her height was 80.5 cm. Growth velocity during the 2 months of nandrolone use increased from 0 to 1.9 cm/month. Body proportion (sitting height/total height) did not show any significant change. In this geographical location, and due to highly unusual social factors, we are unable to carry out long-term follow-up. **Conclusion:** The use of nandrolone was associated with a beneficial effect on growth without any obvious adverse effects. However, these results must be confirmed in additional trials in the future.

Achondroplasia is one of the most commonly known types of skeletal dysplasia, leading to short stature and severe rhizomelic dwarfism with extreme, disproportionate, short stature. Most patients with skeletal dysplasia show severe short stature. Surgical therapy has been attempted to correct bone deformities. Growth hormone (GH) therapy for improving severe short stature has been attempted for patients with skeletal dysplasia accompanying severe short stature caused by achondroplasia (ACH), hypochondroplasia (HCH), pseudoachondroplasia (PSACH), spondyloepiphyseal dysplasia congenita (SED) or Schmid-type metaphyseal dysplasia (MD). Hormonal therapy with GH was associated with a significant effect on height gain in patients with achondroplasia. Currently, GH is available on a limited basis for patients with GH deficiency [1–4].

Anabolic steroids prevent calcium and nitrogen loss in urine, increase protein anabolism and promote growth of bone, and thus represents a potentially worthwhile treatment option in some cases of dwarfism. The main risk of overdose is in premature epiphyseal closure; however, this can be avoided by careful, intermittent use and monitoring of skeletal maturation. Virilization is also a problem. However, methandienon and nandrolone decanoate (ND) are less virilizing than other anabolic steroids and have also been used in women effectively [5,6]. In contrast to the 17-α testosterone derivative, nandrolone esters do not cause sodium sulfobromophthalein retention. As a result, hepatic complications are infrequent with their use in ordinary doses for short periods [6,7]. The average recommended doses of ND in infants is 12.5 mg intramuscularly, and for children, 25 mg every 2–4 weeks [5,8]. Anabolic steroids lead to an improvement in growth in children with constitutional delay of growth and puberty, without advancement in bone age when used for short periods, and also improved growth of peripubertal children with chronic renal failure and children with vitamin D-resistant rickets [5,6].

Keywords: achondroplasia, growth stimulation, hormonal therapy, nandrolone

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The aim of this paper is to report the effects of a small number of doses of ND in a child with achondroplasia and very slow growth over a short period of time.

Materials & methods

A 4-year-old girl with achondroplasia was referred owing to her parents concern and anxiety regarding her very slow growth. Her parents had been informed previously by a number of physicians that there was no known therapy to improve the growth of their daughter. She was the only child of healthy parents. Apart from being affected by achondroplasia, she had never before experienced any serious illness. Her growth, as expected, was slow and her height had remained stationary during the previous 6 months. Enrolment of the child in a trial investigating the effects of ND in her condition was discussed with her parents and approved by the scientific committee in the hospital.

On referral, her weight was 13 kg and her height was 76.7 cm. These growth parameters had been almost stationary during the previous 6 months. Her height was 76.6 at 6 months prior to the study entry and baseline growth velocity during the previous 6 months was considered null. She received ND at days 1, 10 and 40. Before treatment with ND, serum potassium, calcium and liver function tests were normal. No significant change in these values was noted at 1 and 2 months after the start of ND injections. Bone age was equal to the chronological age of 4 years (four bones were present at the wrist: the hamate, capitate, triquetrum and lunatum) [9]. Bone age demonstrated no apparent advancement at 2 months after the start of ND treatment. In this geographical area and due to highly unusual social and economic circumstances, we are unable to carry out long-term follow-up examinations.

Results

The novel use of ND in this child with achondroplasia resulted in a dramatic growth acceleration without the occurrence of unwanted effects or advancement of bone age. At 2 months after the first ND injection, her height was 80.5 cm. Growth velocity during the 2 months of ND use increased from 0 to 1.9 cm/months. The short-term effect of ND on height and weight is shown in **Figure 1**. Body proportion did not show any significant change.

Discussion

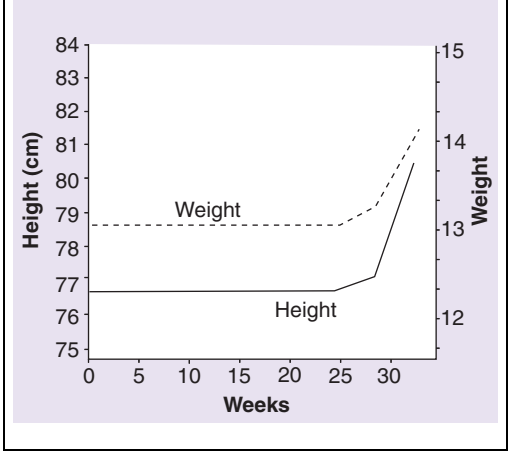
GH therapy for improving severe, short stature has been attempted for patients with skeletal dysplasia accompanying severe short stature caused by ACH, HCH, PSACH, SED or MD. GH had a significant effect on height gain. GH therapy is moderately effective for height gain. However, it is ineffective in cases of severe spinal deformities as, although bone growth is promoted, the ligaments and matrix remain too weak to support muscle tonus and the effects of gravity, resulting in worsening kyphosis and lordosis.

GH treatment for 2 months at 0.1–0.2 IU/kg/day in children with achondroplasia increased growth velocity by 1.9–3.6 cm/year (0.16–0.3 cm/month) during the first year [1]. In this study the growth stimulation in association with use of ND was much more dramatic than the effect of GH.

Reported side effects of GHs include pseudotumor cerebri, edema, slipped capital femoral epiphysis, worsening of scoliosis, gynecomastia and a recent report of increased incidence of Type 2 diabetes mellitus in children [9–12].

Oxandrolone therapy has been reported to be useful in the treatment of short stature seen in skeletal dysplasias other than achondroplasia. Oxandrolone 1.25 mg/day has been used in three patients with short stature and different forms of skeletal dysplasia. After 1 year of follow-up, it was noted that the pretreatment growth rate, which was 2.5 cm/year in the patient with SED, had increased to 6.7 cm/year after 1 year of treatment, while the pretreatment growth rate of the patient with HCH

Figure 1. The short-term effect of nandrolone decanoate on height and weight.



(chronological age: 12 [7–12 years]), which was recorded at 2 cm/year, had risen to 5.3 cm/year. The patient with multiple epiphyseal dysplasia (chronological age: 9 [5–12 years]) had a pretreatment growth rate of 1.5 cm/year, which had risen to 8 cm/year after the same period of treatment [13]. Androgen-replacement therapy has been shown to be beneficial in radiation-induced skeletal dysplasia, attenuating the growth of the spine when used to induce puberty following radiation-induced Leydig cell failure [14].

Even though non-α alkyl testosterone derivatives are not associated with hepatic damage in normal doses, they should be used with great caution in children due to their virilizing effects and the risk of premature epiphyseal closure. Thus, bone-age advancement can be avoided by intermittent use and close monitoring of skeletal maturation [5–7]. Experience with these agents in skeletal dysplasia does not exist. Management of such disorders requires careful balancing of the possible unwanted side effects associated with persistant use in serious disorders, as the benefits in such cases may outweigh the possible risks, especially when these risks can be avoided through appropriately skilled use.

Conclusion

The use of ND was associated with a beneficial effect on growth without any obvious adverse effects in the short term. However, a more lengthy study is required in order to assess the efficacy of treatment with regard to adult height prognosis and in orderto determine the optimal dosing required.

Highlights

- Hormonal therapy with growth hormone (GH) was associated with a significant effect on height gain in patients with achondroplasia (ACH).
- Oxandrolone therapy has been reported to be useful in the treatment of short stature seen in skeletal dysplasias other than ACH.
- Experience with non-17α alkyl testosterone derivative anabolic agents in ACH does not exist.
- The novel use of nandrolone in this child with ACH resulted in a dramatic growth acceleration, without the occurrence of unwanted effects or advancement of bone age in the short term.

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