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The Effectiveness of Oxandrolone in Promoting Linear Growth in Growth Hormone Deficient Children

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This two-year study consisted of a comparison of oxandrolone and growth hormone for the treatment of five children with documented growth hormone deficiency. Previously, androgens have been reported to be relatively ineffective in accelerating linear growth in growth hormone deficient children. Oxandrolone was administered for one year. Growth hormone was added in the second six months and then was given as a single agent in the third six months. Growth accelerated markedly in all patients. Only one child showed more rapid growth with the addition of growth hormone while two children actually grew more rapidly under the influence of oxandrolone alone. Growth was poor and diminished when growth hormone was given as a single agent in the third six-month period for three children but improved when oxandrolone was re-instituted in a fourth six-month treatment period. These results suggest that oxandrolone may prove to be an effective and safe substitute for growth hormone in the management of selected cases of hypopituitarism.

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OXANDROLONE has been employed increasingly in the treatment of shortness of stature of differing etiology because of its high anabolic potency and low virilizing properties.[1-7] Structurally the androgen is 17 alpha-methyl-2-oxa-5 alpha androstan-17 beta-ol-3-one. It has been suggested that androgens enhance the secretion of growth hormone and that this may be responsible for the pubertal growth spurt.[8,9] Also, there is evidence that an androgen is ineffective as an anabolic agent in hypophysectomized animals.[10] Androgens previously have been found to be less anabolic in growth hormone deficient children than in children with shortness of stature due to other causes.[11-13] The nitrogen storing effect of androgen is not dependent upon growth hormone, however, and does not involve exclusively the same metabolic mechanism inasmuch as the two hormones have been shown to manifest separate protein anabolic effects and to

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synergize when given to rats.[14] Furthermore, testosterone is capable of augmenting nitrogen storage in acromegalic subjects who are presumably already maximally stimulated by growth hormone.[15] A study was therefore designed in which oxandrolone was administered to five children with documented growth hormone deficiency, and compared to growth hormone as an agent for inducing linear growth in the same children.

Materials and Methods

Subjects:

For study five children were chosen ranging in age from 10 and 4/12 years to 12 and 6/12 years. All were dwarfed and had physical characteristics compatible with hypopituitarism. All had growth hormone deficiency proved by radioimmunoassay after arginine and insulin infusion. They had no other disorders which might cause shortness of stature. All had retardation of osseous maturation (delayed bone age). None had clinical hypoglycemia. One patient had a craniopharyngioma (postoperative) with residual diabetes insipidus and had not manifested a "catch-up" spurt of growth following surgery.

Studies:

Growth hormone deficiency was reaffirmed after arginine and insulin stimulation immediately prior to treatment. Growth hormone release was then reassessed after nine days of oxandrolone treatment and after six months of oxandrolone treatment. Oxandrolone was given (.1 mg per kilogram body weight per day) for six months and then growth hormone was added to the regimen for six months (two units three times a week). The third six-month treatment interval consisted of human growth hormone without concomitant oxandrolone and the fourth treatment period of six months consisted of the administration of oxandrolone alone. The total duration of treatment was two years. SGOT, PBI, CBC and growth hormone antibody were determined every two months and bone age was assessed every six months.

Results

Growth accelerated markedly in all cases ranging from 3¾ inches to 6½ inches with one year and 6⅛ inches to 9¾ inches with two years of treatment (Table I). The addition of HGH after six months of oxandrolone led to more rapid growth in only one child. Two children actually grew more rapidly under the influence of oxandrolone alone. In two, growth was equal during both six-month treatment periods. Reassessment of growth hormone responsiveness after oxandrolone administration showed no significant augmentation or increase in growth

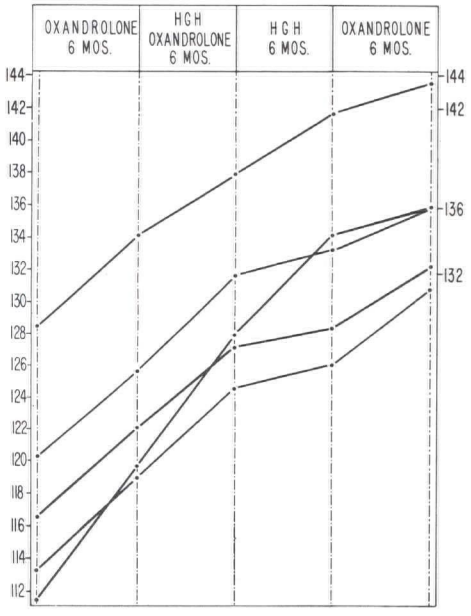

Figure 1

Graph showing growth increments for the five children for the two-year treatment period. The various treatment regimens are indicated. Each lasted six months. Height is in centimeters.

TABLE I
CLINICAL DETAILS AND GROWTH DATA FOR THE 5 CHILDREN FOR 2 YEARS

Patients		Before Treatment	6 Months Oxandrolone	6 Months Oxandrolone Growth Hormone	6 Months Growth Hormone	6 Months Oxandrolone
RR (M)	HT	45	47¼	49½	50⅛	52
10 4/12 yrs.	HT↑		2¼	2¼	⅝	1⅞
N thyroid	BA	4	4½	4½	5½	6
↓ ACTH						
SW (M)	HT	46¼	48½	50½	51	52½
11 8/12 yrs.	HT↑		2¼	2	½	1½
Craniopharyngioma	BA	7	7½	8	10	10½
Diabetes insipidus						
↓ thyroid						
LK (F)	HT	44¼	47½	50¾	53¼	54
12 6/12 yrs.	HT↑		3¼	3¼	2½	¾
N thyroid	BA	8½	10½	11½	12 **	12
N ACTH						
Familial						
CT (M)	HT	51	53¼	54¾	56¼	57⅛
12 6/12 yrs.	HT↑		2¼	1½	1½	1⅜
N thyroid	BA	6	8½	9½	10 **	12
N ACTH						
ST (M)	HT	47¾	49⅞	52¼	53	54
11 3/12 yrs.	HT↑		2⅛	2⅜	¾	1
N thyroid	BA	6	6½	7	8	9
↓ ACTH						

BA - bone age
HT - height in inches
HT↑ - height increment for 6 months
** - gonadotropins appeared

TABLE II
PEAK RESPONSES OF PLASMA GROWTH HORMONE TO ARGININE AND INSULIN STIMULATION *

Patients	Before Treatment	After 9 Days Oxandrolone	After 6 Months Oxandrolone
R.R.	A 3.3		A 2.3
	I 5.6		I 1.7
S.W.	A 1.3	A 1.3	A 1.3
	I 1.6	I 1.7	I 1.0
L.K.	A 1.2	A 1.0	
	I 1.1	I 1.0	
C.T.	A 4.1	A 5.3	A 4.0
	I 2.6	I 2.9	I 1.7
S.T.	A 6.3	A 6.7	A 9.0
	I 4.3	I 2.9	I 2.7

* A - Arginine
I - Insulin
Values expressed are for nanograms/l ml
(normal> 10 ng/l ml)

hormone levels as an explanation for the linear growth that occurred (Table II).

In the third six-month treatment period growth hormone was given without concurrent oxandrolone. Growth, although better than before any treatment, was poor compared to the first two regimens — ranging from ½ to 2½ inches. For the last six months of the two-year study, oxandrolone was again given alone without concomitant HGH and growth ranged from ¾ of an inch to 1⅞ inches. Three of the patients again manifested more growth than when receiving HGH alone and one grew equally as well (Figure 1).

One patient (RR) developed transient mild leukopenia which promptly responded to withdrawal of oxandrolone for seven days. No nausea, priapism, hirsutism, SGOT elevation, deepening of

voice or other side effects occurred due to oxandrolone. All the patients manifested increase in vigor, muscularity, weight and appetite. In none was there an unacceptable increase in osseous maturation. Bone age increased in all, but remained significantly below chronological age. None developed antibodies to human growth hormone. LK apparently responded best, growing 6½ inches in the first year and 2½ inches in the third treatment period under HGH alone. Then she grew only ¾ of an inch in the last period. She had begun excreting gonadotropins and had breast development at that time.

Discussion and Conclusion

Published data indicate that androgens generally are relatively ineffective in hypopituitarism.[11-13] In this series oxandrolone was not only effective, but it remained effective even after the children had been treated for one year with HGH. Growth occurred at a maximal rate in four children in the first six-month treatment period when oxandrolone was given as a single agent. It has been suggested that patients will grow maximally (manifest "catch-up" growth) in response to the first agent administered. However, these patients in general responded better to oxandrolone than to growth hormone except for LK who may have exhibited "diminishing returns" due to age (Table I). We have studied other GH deficient patients (unreported data) who, having grown well in response to growth hormone, sustained their growth rate with oxandrolone therapy after GH supplies were exhausted. It therefore appears that the excellent growth seen in the first treatment period is not necessarily due to the fact that there had been no prior treatment.

In view of the fact that hypopituitary patients in this small series grew well when oxandrolone was administered alone, it appears to us that this anabolic steroid may be used as a safe substitute for growth hormone in the management of some cases of dwarfism due to hypopituitarism.

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