

PRELIMINARY RESULTS OF 1 YEAR TREATMENT WITH BIOSYNTHETIC GROWTH HORMONE IN 7 CASES OF CLASSIC GROWTH HORMONE DEFICIENCY

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ABSTRACT

Seven cases of classic growth hormone deficiency who were previously untreated, were treated with biosynthetic growth hormone. Their mean chronological age was 10.67 ± 2.93 , with height age 5.51 ± 3.53 , bone age of 6.14 ± 3.86 and with bone age lag of 48.85 %. Mean pretreatment height velocity of these cases was 2.97 ± 0.93 cm/year. Biosynthetic hGH (Norditropin and Genotropin) was administered in a dose of 12 units/m²/week at night time. After 1 year their mean height velocity had increased to 8.46 ± 2.71 cm/year. Maximum increase in height was seen during second trimester of therapy.

Key Words : Growth hormone deficiency; biosynthetic growth hormone; height velocity.

INTRODUCTION

Growth failure due to hGH deficiency is universally accepted therapeutic indication for growth hormone therapy. Till 1985, Growth hormone derived from human cadavers was used for treating children having classic growth hormone deficiency. Its use was banned world wide when Creutzfeldt Jacob disease a slow virus disease affecting the central nervous system was detected in 4 patients in UK and USA who were on human cadaveric GH therapy¹. Human GH synthesized by recombinant DNA technology has appeared as a ray of hope for treating short statured children having growth deficiency. Clinical trials world wide have proved its efficacy, when after its use pretreatment growth rate of 3-4 cm/year had changed to 8-10 cm/year during first year of treatment². Its response is most pronounced during the first year of therapy. Growth and bone age advances proportionately and successful hormone replacement can result in growth until normal height is reached⁹. The total height gain has been shown to be inversely related to Chronological age and bone age at the start of treatment and positively related to duration of therapy, stressing the importance of early diagnosis and treatment of growth hormone insufficiency¹¹.

This paper presents the results of biosynthetic growth hormone therapy in 7 children having classic growth hormone deficiency.

PATIENTS AND METHODS

During the year 1992-1994, 7 cases of classic growth hormone deficiency who had come for treatment in paediatric department Military Hospital Rawalpindi were at random selected for growth hormone therapy. These are children of serving and retired army personnels included 2 males and 5 females. They were treated with biosynthetic growth hormone for 1 year. Injections of growth hormone (Norditropin and Genotropin) were supplied by Army Medical Corps. The criteria for selection were as follows :

- * Height - 2 SD for chronological age plotted on Tanner growth chart.
- * Growth velocity checked at least during the previous year was less than 4 cm/year (Tanner standard).
- * serum growth hormone levels checked by two stimulation test were below 8 ng/ml.
- * Bone age determined by Pyele's and Gruelich's standard was more than 2 years behind chronological age.
- * No previous growth hormone was received by these children.

METHODS

Biosynthetic growth hormone was administered in a dose of 12 units/m²/week.

Frequency was three intra muscular injections per week for first three months, later on was increased to six injections per week subcutaneously for the remaining period.

While on therapy three monthly follow up including :

Measurement of height by stadiometer.

Weight.

Recording of any side effects.

Complete blood count.

Blood urea, creatinine, glucose, GTT, LFT and thyroid functions test.

Bone age was determined at 0 and 12 months.

Table 1.

Subject No	Sex	Chronological Age Yrs decimal age	Bone age	Height in yrs	Height Age cms	Body Wt in Kg	Height velocity cm/ yrs
1.	F	13.6	09.0	136	26.47	25.0	2.80
2.	F	06.2	03.5	094	47.60	14.0	3.00
3.	M	14.3	11.6	129	41.89	25.0	3.80
4.	M	08.2	02.0	08.5	73.17	09.3	4.00
5.	F	09.7	03.0	083	82.00	06.5	3.00
6.	F	13.0	10.0	136	23.00	30.6	2.40
7.	F	09.2	03.0	092	68.50	10.0	1.33

Table 2. Pre-Treatment Mean Values

Total no of patients	7
M: F	2: 5
Mean age	- 10.67 % 2.93
Mean Height age	- 5.51 % 3.53
Height age lag (%)	- 52%
Mean bone age	- 6.14 % 3.86
Bone age lag (%)	- 48.85%
Height SDS score	- 1.48 % 1.0088
Pre treatment height velocity	- 2.97 % 0.93

Table 3.

	Height	Actual	Gain
Pre-treatment	2.97 % 0.93	1.33	- 4.5
During treatment			
3 Months	7.71 % 4.33	1	- 3
6 Months	8.67 % 3.37	1.5	- 6
9 Months	8.66 % 3.61	4	- 12
12 Months	8.46 % 2.71	6	- 14
SDS	- 1.335 % 0.995		

RESULTS

Pre-Treatment Data

The youngest patient was 6.2 years and oldest was 14.3 years old, with a mean CA of 10.67 % 2.93. Characteristic clinical features of growth hormone deficiency were seen in two patients. Other details are tabulated in table 1.

During treatment of one year duration, following growth rates were recorded (Table 3). Maximum increase in height was seen during second trimester of therapy. The Mean therapy. The Mean height velocity had increased from pre-treatment value of 2.97 ± 0.93 to 8.46 ± 2.71 cms/year. After completing one year of treatment their height SDS has changed from -1.48 ± 1.0088 to -1.335 ± 0.995 and height velocity to 8.46 ± 2.71 cm/year.

Side Effects.

No significant side effects were noted during one year of follow up. None of these patients had developed hypothyroidism, hyperglycemia or derangement in renal or liverfunction test. However, two patients had shown raised values of alkaline phosphatase.

DICUSSION

The results obtained in 7 cases of classic growth hormone deficiency after 12 months of treatment with biosynthetic growth hormone of previous studies where almost identical doses of GH were used. In present study height velocity attained after 12 months was 8.46 cms/year which was comparable to that from India 8.00 cm/year France 8.1 cm/year, and

Table 4. Auxiological Parameters of Children with GH Deficiency Treated with G.H

Author f	Place of Study	No. of Patients	Doseage/ week (IU)	Freq of Inj/wk	Pre- treatment Ht. Velocity	Ht. Velocity After 12 Months
Albertson wikland et al 1988	Sweden and Finland	23	0.5/Kg	7	4.00 % 1.10	10.70 % 2.3
Vieens Clavet et al, 1988	Spain	2	0.5/Kg	6.7	3.28 % 0.60	9.76 % 2.40
Bierich JR 1988	West Germany	34	12/m	6	3.4 % 1.2	10.40 % 3.20
Job JC et al., 1988	France	32	0.6/Kg	3	3.20 % 1.30	8.10 % 1.5
Hol Com 1990	USA	218	0.48/Kg	3	3.8 % 1.8	8.90 % 2.2
Menon 1991	India	20	0.5/Kg	6.7	2.43 % 0.90	8.00 % 2.21
Present Study	Pakistan	7	12/m	6	2.97 % 0.93	8.46 % 2.71

USA 8.9 cm/year⁴. Better growth rates however have been reported in other studies, from West Germany 10.4 cm/year³ Spain 9.76 cm/year¹⁰, Sweden and Finland 10 cm/year¹. The reason for these regional variation in growth velocity is injection frequency which has been reported as an important factor. The same weekly dose when given as 6-7 injections as compared to 2-3 injections per week gives 25 % better growth stimulation^{5,6,7}. As already stated, in initial 3 months of therapy we had given three injections per week intra muscularly and then changed that to 6 injection/week by subcutaneous route for the remaining 9 months. In earlier studies clear dose-response relationship has been reported in treatment of growth hormone deficiency. Doses varying from 0.07 IU/kg/day - 0.7 IU/kg/week have been tried and after 1 year of treatment, children having bigger dose were found to have higher growth velocities^{7,11}. The dose currently recommended is 0.07 - 0.1 IU/kg/day or 15-20 IU/m²/week¹¹. Lesser dose used in this study, 12 IU/m²/week and in some previous studies was a compromise between efficacy, price and availability. A number of other variables are also reported to have correlation with the response to growth hormone during first 12 months of treatment. These include younger chronological age, younger bone age and shorter height at the beginning of therapy⁶. We also observed the same in our cases that children having less chronological age, less bone age and with more

height deficit showed a better response. However the number of cases in the present study was small as compared to other studies. we did not encounter any adverse effects in our children except that two of them had transient rise in alkaline phosphatase. Antibody testing was not carried out.

CONCLUSION

- * Our patients tolerated Biosynthetic growth hormone well. The increase in height was as anticipated i.e. approximately 9 cms/year.
- * There is a need to study more number of cases to have statistically significant results.

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