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EFFECT OF GROWTH HORMONE REPLACEMENT THERAPY (GRT) ON CHILDREN WITH DIFFERENT GROWTH DISORDERS IN SAURASHTRA REGION.

Paediatrics

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ABSTRACT

Objectives: To compare the growth of children treated with Growth hormone in isolated GH deficiency (IGHD), Multiple pituitary hormone deficiency (MPHD), Turner syndrome (TS), Prader willi syndrome, post tumour radiation. **Methodology:** We retrospectively reviewed the medical records of children who were on Growth Hormone Replacement Therapy (GHRT) between January 2017 till December 2022, in our tertiary care center. Growth hormone deficiency (GHD) was diagnosed when the child height was below -2 SD and or when the annual growth velocity was < -1 SD or the standing height was < −1.5 SD below the mid-parental height, in addition to a defective peak response to GH provocative testing (below 10 ng/mL) Turner syndrome (TS) was diagnosed when the X chromosome was partially or completely missing in a female. Small for gestational age (SGA) was defined as a birth weight below the 10th percentile for the gestational age, compared to a gender specific reference population. Idiopathic short stature was diagnosed, in whom with no identifiable disorder, when the height of the child was more than 2 SD below the corresponding mean height for age and sex. **Results:** Children with IGHD, MPHD, TS increased their Height SD by an average of 5.45, 2.9 ad 0.4 SD, respectively at the end of follow up period (for all groups, p: <0.001). Weight SDs did not differ significantly among all groups after GH therapy. The Height SD gain was higher in children with GHD compared to MPHD, TS, PRADER WILLI SYDROME and post tumour radiation (p:< 0.340; p: 0.021 and p: 0.070 and p:0.753, respectively). **Conclusion:** After the use of GHRT all groups had significant increase in Height SD, which was higher in IGHD compared to other groups.

KEYWORDS

Isolated Growth hormone deficiency, growth hormone replacement therapy, Turner syndrome.

INTRODUCTION

Growth hormone (GH) is responsible for most of the metabolic and growth processes inside the body. The primary role of GH is mediated by another hormone called insulin-like growth factor1 (IGF-1), which is secreted from the liver. This hormone functions principally by stimulating cell division and growth. Therefore, any disturbance that affects GH secretion will lead to growth-related abnormalities. For example, excessive secretion of GH during childhood or adulthood can lead to gigantism or acromegaly, respectively. On the other hand, reduced production of this hormone can cause growth retardation and short stature.

Exogenous growth hormone treatment had been extracted from human pituitary glands and used to treat mainly those with severe GH deficiency.

GH deficient patients are those with a peak growth hormone concentration of less than 10 ng/ml diagnosed by the growth hormone stimulation test. Since 1985, human-extracted GH was replaced byrecombinant GH therapy (RGHT), which is used to treat a wider range of conditions Growth disorders in children include Idiopathic growth hormone deficiency (IGHD), idiopathic short stature (ISS), Small for gestational age(SGA), Turner syndrome (TS), Prader Willi syndrome.

Since 1985, human-extracted GH was replaced by recombinant GH therapy (RGHT), which is used to treat a wider range of conditions. Recombinant GH is used to treat patients with GH deficiency and to improve growth and height gain. Plentiful supply of recombinant growth hormone (rhGH), acquired via recombinant DNA technology, enabled the expansion of its use beyond replacement of deficient growth hormone (GHD) including Idiopathic short stature (ISS), Small for gestational age (SGA) and Turner Syndrome.

After recombinant human growth hormone (rhGH) was introduced in the treatment of patients with growth hormone deficiency (GHD), idiopathic short stature (ISS) Turner Syndrome (TS) and Prader Willi syndrome. many studies have addressed the effect of GH treatment and changes in the height standard deviation score (SDS) after GH treatment. However, few studies comparing the effect of GH in Indian patients with different growth disorders have been designed. Therefore, this study focused on the difference in effect of GH treatment between these groups.

METHODOLOGY:

A Retrospective study was done at Shri M.P. shah medical College Jamnagar. Our study population consisted of 2 to 18 years of age who are on GHRT for various reasons for a minimum period of 1 year.

SAMPLING TECHNIQUE:

We retrospectively reviewed the medical records of children who were on growth hormone replacement therapy for various indications, between January 2017 till December 2022, in our tertiary care center with rhGH.

Statistical Methodology:

Performed by using SPSS, statistical Package. All data are expressed as mean ± SD values. ANOVA test was used to com- pare growth data among the 4 study groups. Paired t-test was used to compare HtSDS data after versus before rhGH treatment in each group and nonpaired t test to compare HtSDS.

A P-value of 0.05 or less was considered statistically significant.

RESULTS:

Total of 28 patients (male-11, female-17) aged 2-18 years who are on GHRT were taken to see effect of GH in different growth disorders like Isolated GHD(IGHD), Multiple pituitary hormone deficiency (MPHD), Turner syndrome (TS), Prader willi syndrome and Post radiation tumour.

Table – 1: Sex of Patients Vs. Indication of GHRT

INDICATION	GENDER	
	MALE	FEMALE
ISOLATED GHD	7(63%)	12(70.58%)
MPHD	2(18.18%)	3(17.64%)
TURNER SYNDROME	0	2(11.76%)
PRADER WILLI	1(9.09%)	0
POST RADIATION TUMOUR	1(9.09%)	0
TOTAL	11(100%)	17(100%)

In this study Female predilection was observed. The study population comprises 17 (60.7%) females, out of which 12 were having IGHD, 3 were having MPHD and 2 were having turner syndrome.

In this study recombinant GH dose required were 25.30 +- 3.27 in Isolated GHD, 29.3 +- 4.77 in MPHD, 51 +- 1.41 in Turner syndrome,

25 µg/kg/day in Prader willi syndrome and 31 µg/kg/day in Post radiation tumour.

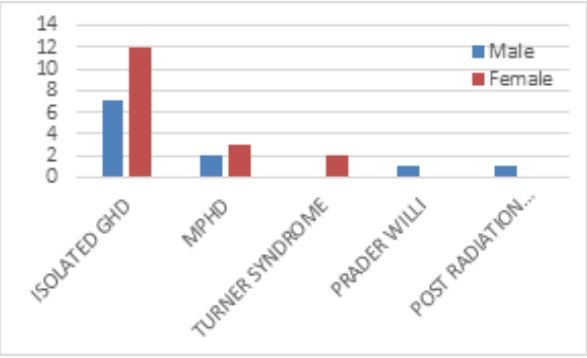

Figure 1: Sex of Patients Vs. Indication of GHRT

Table – 2: Recombinant GH Doses In Patient Of GHRT

INDICATION	NUMBERS	MEAN DOSE (µg/kg/day)	SD
ISOLATED GHD	19	25.30	±3.27
MPHD	5	29.6	±4.77
TURNER SYNDROME	2	51	±1.41
PRADER WILLI	1	25	-
POST TUMOUR	1	31	-

Table – 3: Changes in Height in 1st year in patient of GHRT

INDICATION	HEIGHT GAIN 1 YEAR	MEAN +- SD
IGHD	12.5cm/year	12.5 ± 5.45
MPHD	8.4cm/year	8.4 ± 2.79
TURNER	6cm/year	6.25 ± 0.35
PRADER WILLI	7cm/year	-
POST RADIATION	7cm/year	-

I this study observed mean height gain is **12.5 ± 5.45** in Isolated GHD, **8.4 ± 2.79 in** MPHD, **6.25 ± 0.35** in Turner syndrome, **8 cm/year** in Prader willi and **8cm/year** in Post radiation tumour.

Table 4: Various Auxological changes in patient of GHRT (ANOVA test)

		Height SD	Weight SD	BMI SD
IGHD	AGE (1)	97.74 ± 18.502	14.52 ± 6.288	14.54 ± 1.895
	AGE (F)	108.53 ± 17.812	18.21 ± 6.382	15.06 ± 1.652
MPHD	AGE (1)	92.80 ± 14.805	12.64 ± 2.886	15.09 ± 1.514
	AGE (F)	101.10 ± 13.984	15.92 ± 2.637	15.68 ± 2.490
TURNER SYNDROME	AGE (1)	121.70 ± 1.838	22.10 ± 4.101	16.23 ± 4.144
	AGE (F)	127.50 ± 2.121	29.50 ± 2.121	17.18 ± 2.036
PRADER WILLI SYNDROME	AGE (1)	96.00 ± 0.000	27.00 ± 0.000	29.00 ± 0.000
	AGE (F)	107.00 ± 0.000	33.00 ± 0.000	28.80 ± 0.000
POST RADI ATION TUMOUR	AGE (1)	115.00 ± 0.000	20.00 ± 0.000	15.27 ± 0.000
	AGE (F)	124.00 ± 0.000	22.00 ± 0.000	14.30 ± 0.000
ANOVA	P VALUE (1)	F value: 1.239, p value:0.022* (S)	F value: 2.252, p value: 0.095 (NS)	F value: 12.687, p value: 0.000* (S)
ANOVA	P VALUE (F)	F value: 1.088, p value: 0.036* (S)	F value: 3.626, p value: 0.085 (NS)	F value: 13.674, p value: 0.002* (S)

Table 4 presents the effect of GHRT therapy in the 5 study groups. The ANOVA test showed a statistically significant difference in the Height SD (P:0.036) and BMI SD (P:0.002) changes among the 5 groups. Weight SDs were not significantly different between the groups, after GHRT. (P:0.085)

Table – 5: Comparison of Growth response to GHRT in IGHD vs. TURNER SYNDROME (Paired t test) (Independent sample t test)

	delta HEIGHT (F)- (1)	Result
IGHD	10.7895 ± 5.45261	t value: 1.265,
TURNER SYNDROME	5.8000 ± 0.28284	df: 19, p value: 0.021 significant

The Height SDs improvement was significantly better in GHD children versus those with TS. And this comparison is statistically significant. (P: 0.021)

	HEIGHT (1)	HEIGHT (F)	P value
IGHD	97.74 ± 18.502	108.53 ± 17.812	t value: -8.625, df: 18, p: 0.000*
TURNER SYNDROME	121.70 ± 1.838	127.50 ± 2.121	t value: -29.000, df: 1, p: 0.022*

CONCLUSIONS

In conclusion, children with IGHD, MPHD, TS and prader willi syndrome showed significant increases in Height SD when treated with rhGH. However, their Height SD increments were significantly lower than those attained in children with IGHD.

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