Growth hormone replacement in Paediatric Insured population covered under ESI.

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Abstract

Introduction: Height is an important aspect of personality and self-esteem. People with short stature are often lured by advertisements into fake products instead of seeking medical help.
Study design: It is a retrospective study of patients presenting with the concern of short stature to the short stature clinic in Paediatric OPD.
Results: Out of 813 kids brought with the parental concern of short height to the short stature clinic, 214 (26.3%) were actually found to have short stature. Out of total 214 short stature kids, thirty three (15.4%) were started on GH for various indications. Eighteen out of 214 short kids (8.4%) had Growth hormone (GH) deficiency.
Conclusion: Awareness of the parents regarding short stature can help them to seek the necessary medical help and initiate timely intervention.
Recommendation: The height of children should be routinely plotted on an appropriate gender specific growth chart and the growth pattern analyzed over an interval of at least 6 months.
KEYWORDS: Growth hormone deficiency, short stature

Introduction:
Height of growing children is often a cause of worry to the parents especially if it is less than that of most of the peers of the same age. Also the short stature has been linked with shy personality, poor social interaction and scholastic underachievement (1). With the availability of GH in the market, parents frequently insist on its recommendation for their child even if the efficacy and safety in that particular situation is lacking. In this study we report the data of GH replacement in short stature clinics of insured population covered under ESI. ESI is an organization providing medical, sickness and maternity benefits along with many other services to its beneficiaries.

Material and Methods:
This is a retrospective study of the kids aged 5 to 15 years brought with the concern of short stature to the Short stature clinic in Paediatric OPD from Feb 2012 to August 2015. Their height was measured using wall mounted stature meter. Height was plotted on gender specific NCHS (CDC) growth chart and percentile determined. The definition of short stature used was height below the third percentile for age and sex on NCHS (CDC) growth chart. This is equivalent to < 2 S.D. The data was analyzed to calculate the percentage of kids actually having short stature.
These short kids were then worked up for causes of short stature. Their work up included assessment of diet, activity, complete blood count, mid-parental height, X ray left wrist

for bone age, thyroid function test, urine examination, renal function test and tTGA assay for coeliac disease. When GH deficiency was suspected clonidine stimulation test was done to assay GH. GH cut off of 10 ng/l was used. If GH levels were normal then Insulin like growth factor (IGF) and Insulin like Growth Factor Binding protein (IGFBP). MRI cranium was done in patients with low GH to determine the pituitary size and to identify any organic cause of GH deficiency.
Also the percentage of short stature kids requiring GH replacement were calculated and the indications for GH replacement were compiled.

Results:
Out of 813 kids brought with the parental concern of short height to the short stature clinic, 214 (26.3%) were actually found to have short stature. 18 out of 214 (8.4%) short stature kids had GH deficiency. Out of total 214 short stature kids, thirty three (15.4%) were started on GH. Male to female ratio of patients with Isolated GH deficiency was 3:1.The details of the patients started on GH are given in Table1.

Discussion:
Growth is a complex process involving psychosocial, nutritional, genetic, metabolic and endocrine factors. Hence assessment of short stature requires ruling out nutritional, genetic, metabolic factors, checking for chronic diseases and excluding other common endocrine causes before GH assay.

GH is a polypeptide comprising of 191 amino acids (2) It is secreted by anterior pituitary gland and its secretion is controlled by GH releasing hormone, somatostatin, Ghrelin (3)The effects on growth are mediated by insulin like growth factors especially IGF-1 (4). IGF binds IGFBP especially IGFBP -3. IGF and IGFBP are assayed in patients suspected of GH deficiency. GH replacement has come a long way from use of cadaveric GH in 1958 to use of recombinant GH in 1985 which has virtually eliminated the risk of Creutzfelt Jakob disease in the recipients and has also resulted in increased commercial availability.(5)

GH is a relatively safe hormone in prescribed doses (6). GH has adverse effects though occurring infrequently e.g. Type 2 Diabetes Melitus, gynecomastia, joint pains, pseudotumor cerebri and slipped capital femoral epiphysis (7) and in supra-physiologic doses can lead to cancer.(8). In our study of 33 kids on GH replacement none of the above side effects were noted.

In our study, out of 813 kids brought with the concern of short height, 214 (26.3%) were actually found to have short stature. 18 out of 214 (8.4%) short stature kids had GH deficiency. Similarly, in the study by Giovenale et al, among the 7066 short children, 650 (9.2%) had GH deficiency (9). In another study of 80,000 children in Salt Lake City Utah (10), reported 555 children with short stature and of these 33 had GH deficiency (5.9%). Their results were also comparable to our study. However, Kaplowitz et al reported an incidence of 23% GH deficiency among 60 pts referred for short stature (11). The higher incidence of GH deficiency can be explained by use of stringent definition i.e.< 3S.D. instead of <2 S.D.

In the study by Giovenale et al,(9) it was found that 0.23% of short children were found to have both coeliac disease and GH deficiency. The children diagnosed with celiac dis and not responding to gluten free diet were investigated and found to be GH deficient as well.

S. No.	Gender	Age at Start of Therapy(SoT)	Height at SoT	Weight at SoT	Dose(IU/Day) at SoT	Indication
1	F	13 Yrs	132 cm	30 Kg	3.2 IU	Turner Syndrome
2	F	10 Yrs	112.5cm	22 Kg	2 .5 IU	Idiopathic Short Stature
3	M	6 Yrs	95 cm	11 Kg	1.2 IU	Panhypopituitarism
4	M	7 Yrs	106 cm	13 Kg	1.2 IU	Idiopathic Short Stature
5	M	6 Yrs	87 cm	10 Kg	1 IU	Hypopituitarism
6	M	4 Yrs	79.5 cm	10 Kg	1 IU	Growth Hormone Deficiency
7	M	12 Yrs	124 cm	19 Kg	2 IU	Growth Hormone Deficiency
8	F	10 Yrs	116 cm	28 Kg	3 IU	Growth Hormone Deficiency
9	M	12 Yrs	127 cm	38 Kg	4 IU	Growth Hormone Deficiency
10	F	6 Yrs	91 cm	11 Kg	1 IU	Growth Hormone Deficiency
11	M	11 Yrs	130 cm	34 Kg	3 IU	Chronic Renal Insufficiency
12	F	5 Yrs	99 cm	15 Kg	2 IU	Growth Hormone Deficiency
13	M	5.10 Yrs	97 cm	10 Kg	1.5 IU	Growth Hormone Deficiency
14	F	13 Yrs	144 cm	32 Kg	3.5 IU	Idiopathic Short Stature
15	M	6 Yrs	101 cm	11 Kg	1.4 IU	Small for Gestational Age
16	M	6.6 Yrs	99 cm	13 Kg	1.5 IU	Growth Hormone Deficiency
17	M	9 Yrs	106 cm	19 Kg	2.5 IU	Achondroplasia
18	F	6.6 Yrs	105 cm	17 Kg	2 IU	Turner Syndrome
19	M	6 Yrs	98 cm	13 Kg	1.5 IU	Small for Gestational Age
20	M	10.6 Yrs	116 cm	22 Kg	3 IU	Growth Hormone Deficiency
21	F	11.9 Yrs	124 cm	20 Kg	1.4 IU	Idiopathic Short Stature
22	M	13.5 Yrs	123 cm	20 Kg	2 IU	Growth Hormone Deficiency
23	M	7.3 Yrs	81 cm	12 Kg	1.5 IU	Idiopathic Short Stature
24	M	17 Yrs	142 cm	34 Kg	3 IU	Growth Hormone Deficiency
25	M	14 Yrs	135.5cm	27 Kg	2 IU	Partial GHD
26	M	7.7 Yrs	106 cm	14 Kg	2 IU	Small for Gestational Age
27	M	8.9 Yrs	106 cm	16 Kg	2 IU	Growth Hormone Deficiency
28	F	17.3 Yrs	135.5cm	40 Kg	3 IU	Turner Syndrome
29	F	13.3 Yrs	143.5cm	40 Kg	3 IU	Isolated GHD
30	M	14.11 Yrs	117 cm	20.5 Kg	3 IU	Growth Hormone Deficiency
31	M	12.9 Yrs	115.5cm	20 Kg	3 IU	Partial GHD
32	M	3 Yrs	81 cm	10 Kg	1.2 IU	Small for Gestational Age
33	F	9.6	104 cm	21	2 IU	Turner Syndrome

		Yrs		Kg		

In our study, the male to female ratio of patients with isolated GH deficiency was 3:1. Similarly in the National Cooperative Growth Study the ratio was 2.7:1(11), whereas in the study by Kaplowitz et al the boys: girls ratio was 1.5:1 (12). Cuttler et al surveyed pediatric endocrinologists and reported that GH treatment was 1.3 times more common in boys than in girls.(13) This ratio can be due to the GH deficiency being more common in males or due to the referral bias i.e. greater concern for height in boys. In the Utah study (10) male : female ratio of GH deficient students was 2.7:1. Their results were comparable to our study. In this study the school population was studied and not the referred one. Hence the observed gender difference may not be due to referral bias.

However Grimburg et al reviewed database of children treated with GH across the world and found a male predominance of treated patients only in certain regions of the world (14) suggesting that referral bias is present only in some cultures.

When growth hormone deficiency is diagnosed as part of systemic disease, sex distribution is reflective of the sex distribution of the disease e.g. for Septo Optic Dysplasia (SOD) the male female ratio is 1.3:1(11). The referral bias towards males is not seen in such situations.

Conclusion:

GH deficiency is not an uncommon cause of short stature. Awareness of the parents to seek the necessary medical help rather than take over the counter preparations can help investigation and initiation of appropriate and timely intervention.

Recommendations:

The height of children should be routinely plotted on an appropriate gender specific growth chart and the growth pattern analyzed over an interval of at least 6 months. A height below 3rd percentile or shifting of curves should be worked up without much delay to reach a diagnosis. GH therapy should be given to only those with appropriate indications to avoid financial burden, unnecessary daily pricks and side effects.

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