Efficacy and safety profile of recombinant insulin like growth factor 1 (rh IGF1) therapy: A long term follow up study at a single tertiary centre.

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INTRODUCTION

- Recombinant human insulin like growth factor 1 (rhIGF1) therapy is the only treatment available for primary IGF1 deficiency and related disorders (figure 1).
- However, the efficacy of rhIGF1 therapy in promoting growth is controversial and therapy also needs cautious monitoring for adverse effects.

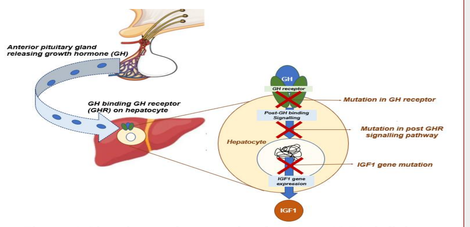


Figure-1 Showing pathogenesis of primary IGF1 deficiency

AIM

- The aim of this study was to determine the long-term efficacy and safety profile of rhIGF1 therapy.

METHOD

- Retrospective review of all patients on rhIGF1 therapy over the last 13 years (2008 -2021) at a single tertiary centre.

RESULTS

Table-1. Demographic Data

Total Patients	11
Gender	Male=8, Female=3
Median age of presentation	3.7(1.5- 13.9) years
Median age of start of rhIGF1	4.12(2- 22.9) years
Starting rhIGF1 dosage (mcg/kg/day)	80 (77-85)
Final rhIGF1 dosage (mcg/kg/day)	206 (151- 242)
Post rhIGF1 follow-up	1.3 to 12.5 years

Figure-2. Underlying Genetic mutations

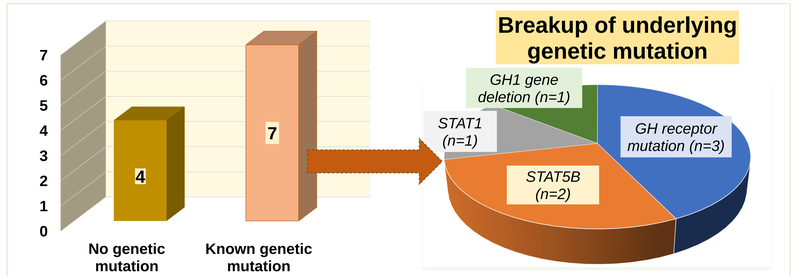


Figure-3. Pre-treatment and post-treatment mean height velocity(HV)

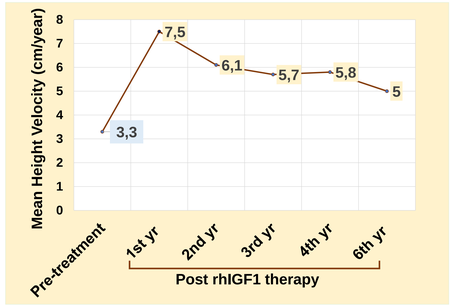
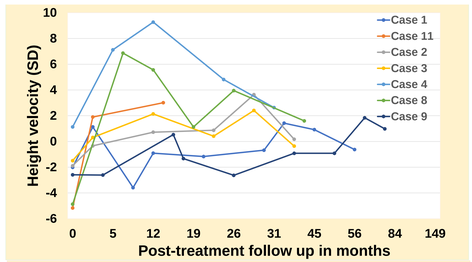


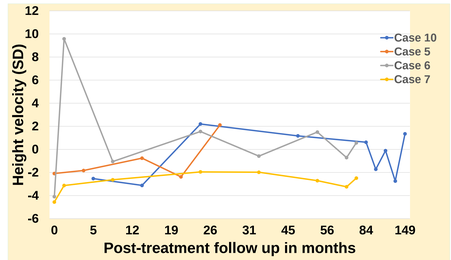
Figure-4. Post-treatment height velocity (SD) in group with known genetic mutation



Mean HV (0) = -2.41 SD, Mean HV (1 y)=3.29, ΔMean HV= 5.7SD

Case 1→ Laron; Case 2→STAT5B; Case 3→STAT5B; Case 4→STAT1; Case 8→GH1 gene deletion; Case 9→Laron; Case 11→Laron

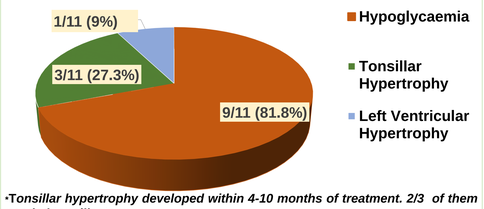
Figure-5. Post-treatment height velocity (SD) in group with no identified mutation



Mean HV (0) = -3.49 SD, Mean HV (1 y)= -1.94, ΔMean HV= 1.55SD

Case 5, 6, 7 → GH insensitivity (negative mutation), Csse10→ Laron phenotype with negative mutation.

Figure-6. Adverse effects of rhIGF1 therapy



•Tonsillar hypertrophy developed within 4-10 months of treatment. 2/3 of them needed tonsillectomy.

Table-2. Factors affecting severity of hypoglycaemia

Characteristic	Early Hypoglycaemia *After 1st dose*	Late Hypoglycaemia *2.8(2-4) months*
Number	4	5
Severity	Severe and frequent	Pre-meal
Genetic mutation	3	2
ΔMean HV (SD)	7.24 (8.18-10.43)	2.20 (1.1-3.63)
rhIGF1 dose (mcg/kg/day)	80	139 (117-157)
Tx responded	Overnight feeding	Decreasing dose (3) Post meal timing (2)

CONCLUSIONS

- Recombinant IGF1 therapy promotes growth in primary IGF1 deficiency, especially in patients with known underlying genetic mutations.
- Height velocity increment was maximal at first year post-treatment followed by a gradual decline.
- Hypoglycaemia is the most common adverse effect, followed by tonsillar hypertrophy and left ventricular hypertrophy.
- Hypoglycaemia severity may be associated with the response to rhIGF1 therapy.

REFERENCES

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