Association of serum IGF-1 concentration with efficacy and safety measures in adults with GH deficiency with different GH treatment regimes: a randomized clinical trial

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Introduction

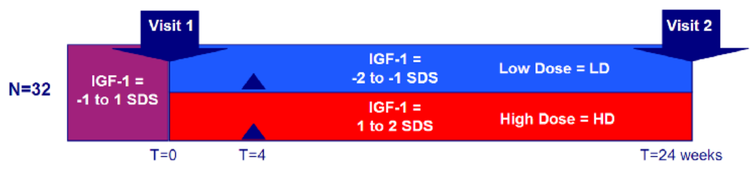
The current guidelines state that the goals of Growth Hormone (GH) therapy should be an appropriate clinical response and avoidance of side effects. The target level for IGF-1 is commonly the upper half of the reference range, although no published studies offer specific guidance in this regard.

Aim

To explore the effect of change in IGF-1 levels within the reference range on efficacy and safety measures of GH treatment in substituted GH deficient adults.

Methods

Randomisation (↓↑ GH dose):



Inclusion criteria:

Age 20–65 year, GH treatment >1 year, "stable" disease

Results

Table 1. Baseline characteristics

	LD	HD	*P value*
No. of patients	**16**	**16**	
Age, year (SD)	47.4 (10.8)	46.4 (9.3)	*0.80*
Sex, no. of females (%)	6 (37.5)	5 (31.2)	*0.71*
Onset of GHD, CO (%)	10 (62.5)	3 (18.8)	*0.01*
Cranial radiotherapy (%)	1 (6.2)	2 (12.5)	*1.00*
Pituitary surgery (%)	2 (12.5)	8 (50.0)	*0.02*
GH dose, mg/day (SD)	0.30 (0.23)	0.28 (0.18)	*0.78*
Duration GH treatment, yr (SD)	15.0 (9.3)	10.7 (6.7)	*0.15*

Figure 1. Treatment regimes

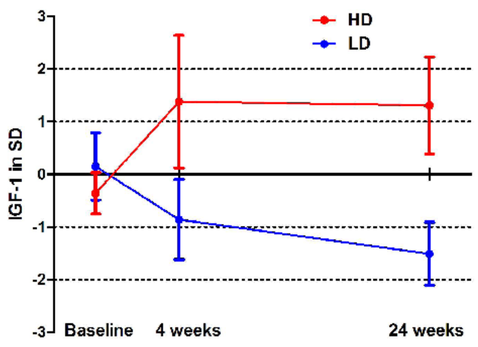


Table 2. Body composition, lipid profile, and glucose metabolism

	LD (n=15) Baseline (SD)		Change (SD)		HD (n=15) Baseline (SD)		Change (SD)		*P value*
Weight, kg	79.7	(31.9)	**0.1**	**(2.3)**	89.1	(14.3)	**-0.8**	**(5.5)**	*0.91*
BMI, kg/m²	28.2	(9.8)	**-0.0**	**(0.8)**	28.8	(4.2)	**-0.3**	**(1.7)**	*0.57*
Waist circumference, cm	97	(24)	**2**	**(5)**	105	(11)	**-3**	**(6)***	*0.07*
Waist/hip ratio	0.98	(0.07)	**-0.02**	**(0.06)**	0.97	(0.05)	**-0.02**	**(0.04)**	*0.67*
Sum of skinfolds, mm	78	(49)	**3**	**(15)**	72	(26)	**1**	**(19)**	*0.71*
Body fat, %	30.3	(10.7)	**-0.1**	**(2.4)**	30.6	(7.0)	**0.2**	**(3.2)**	*0.78*
Total cholesterol, mmol/L	5.02	(1.01)	**-0.16**	**(0.66)**	5.15	(0.98)	**-0.17**	**(0.88)**	*0.85*
HDL cholesterol, mmol/L	1.51	(0.53)	**0.03**	**(0.15)**	1.47	(0.40)	**0.03**	**(0.22)**	*0.98*
LDL cholesterol, mmol/L	3.04	(0.88)	**-0.19**	**(0.53)**	3.10	(0.94)	**-0.18**	**(0.71)**	*0.86*
Triglycerides, mmol/L	1.03	(0.38)	**0.00**	**(0.29)**	1.27	(0.59)	**0.06**	**(0.47)**	*0.18*
Fasting glucose, mmol/L	4.3	(0.7)	**0.2**	**(1.0)**	4.3	(0.9)	**0.4**	**(0.7)****	*0.54*
HbA1c, mmol/mol	38	(6)	**-0.7**	**(2.8)**	38	(3)	**0.1**	**(1.1)**	*0.32*

P value for difference between change in the LD and HD group

* P value <0.10 for change from baselne
** P value <0.05 for change from baselne

Figure 2. Physical performance

– No (difference in) change in hand grip strength (kg by dynamometer)
– No (difference in) change In physical activity (min/day by LAPAQ)
– 6 minute walk test (6-MWT):

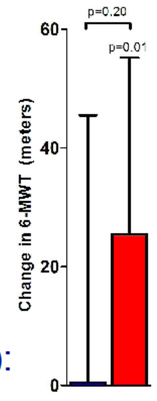


Figure 3. Quality of Life

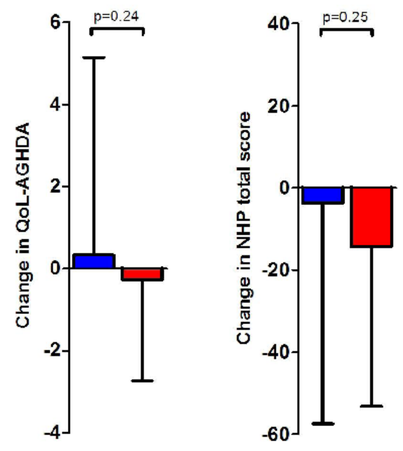
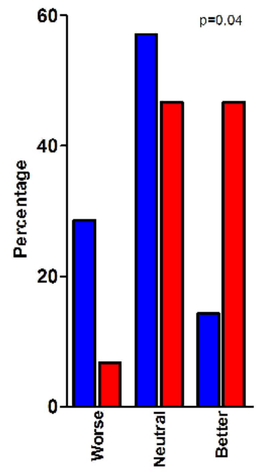


Table 3. Adverse events (AE)

	LD	HD	*P value*
Total number AEs	**25**	**25**	
Myalgia	1 (7%)	6 (40%)	*0.04*
Headache	2 (14%)	2 (13%)	*0.94*
Dizziness	3 (21%)	0	*0.06*
Arthralgia	0	3 (20%)	*0.08*
Fatigue	5 (36%)	1 (7%)	*0.05*
Sleeping problems	0	3 (20%)	*0.08*
Infections	4 (29%)	3 (20%)	*0.59*
Peripheral oedema	0	3 (20%)	*0.08*
Mood change	2 (14%)	0	*0.15*
Paresthesia	2 (14%)	1 (7%)	*0.50*
Other	6 (40%)	3 (20%)	*0.23*

Figure 4. Subjective feeling



Summary

– Decreasing IGF-1 level for six months does not lead to a significant deterioration of efficacy measures but subjects do experience more fatigue.
– Increasing IGF-1 level leads to a significant improvement of the walking distance, an overall better feeling, but also a higher fasting glucose level, and more myalgia.
– An increase in IGF-1 level may improve waist circumference.

Conclusion

Although increasing GH dose in our study to IGF-1 levels of 1 to 2 SDS improved physical performance and subjects reported an overall better feeling after six months, safety is not guaranteed with the demonstrated effect on glucose metabolism and reported adverse events.
A target level of IGF-1 in the mid-normal range seems advisable; however, more scientific evidence is warranted for use in clinical practice.

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