Are the GH treatment doses in use within secretion rates of healthy children?

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Aim to calculate the bioavailable immunoreactive rhGH after sc injection in relation to injected GH-dose and compare the result to GH-secretory rate calculated in healthy children;
to investigate factors that influenced bioavailability (BA).

Background GH-secretion in children with normal growth rates can be used to optimize rhGH-treatment doses. For healthy children endogenous GH-secretion ranges within 0.1-11 U/24h in pre/early puberty and within 4-40 U/24h in mid-puberty[1]

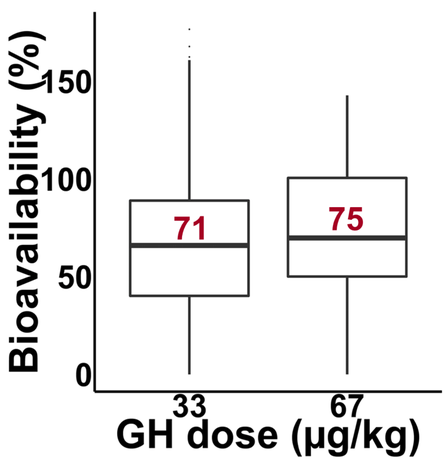
Conclusion

- The uptake of injected GH was around 70% without dose dependency, 33 - 67 µg/kg.
- A great intra- and inter-individual variation, influenced by the injection-depth.
- Bioavailable GH from GH^{33} and GH^{67} µg/kg/d corresponds to the lower range of GH secretion rates in healthy children.

Result

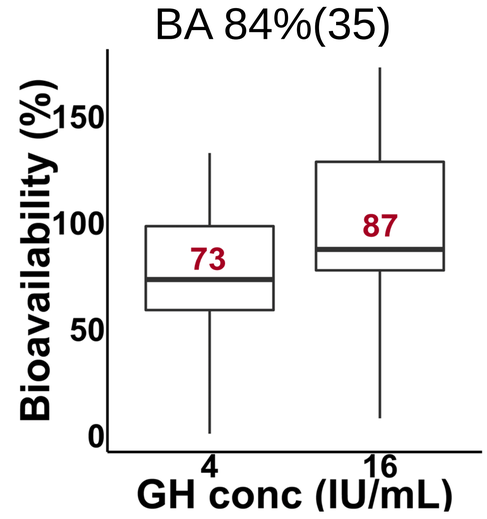
BA is presented as median and coefficient of variation,CV, and is expressed as % of the injected dose.
No dose dependency was found for GH^{33} vs GH^{67},p=0.21, **Fig1A**
A positive concentration dependency of GH 4 vs 16IU/ml, p=0.035.**Fig1B**

Fig1A Clinical-setting
BA 71%(43)



BA for GH^{33}71(34),range10-176,
forGH^{67} 75(31), range 16-143

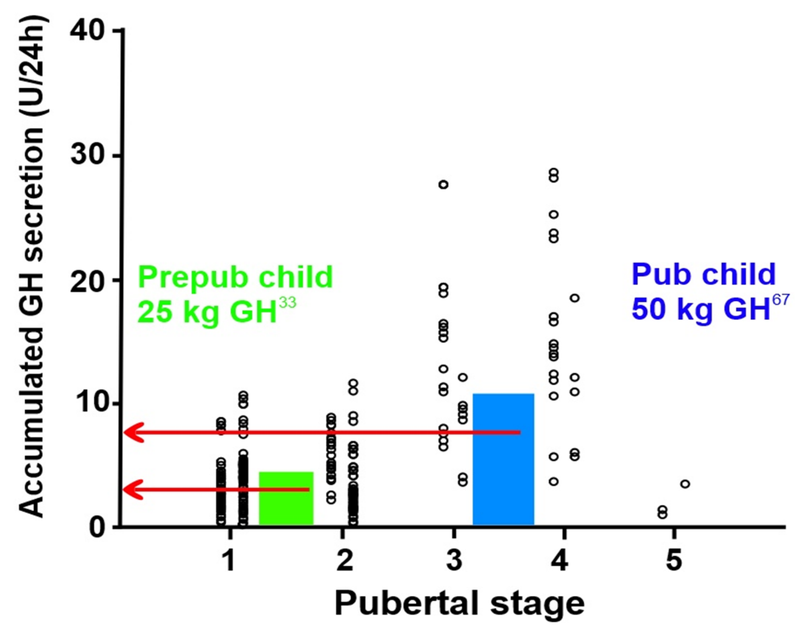
Fig 1B Experimental-setting
BA 84%(35)



BA GH4IU/ml 73(49), range1-133,
For GH16IU/ml 87(40), range 8-173

In total, 22% of the variation in BA could be explained by the variables BMI_{SDS}, GH_{peak}width and the GH-level at baseline, interpreted as proxy variables for the depth of the injection.

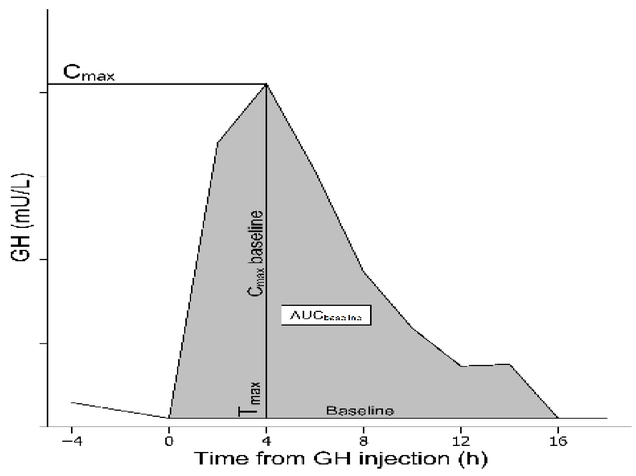
Bioavailability ≈ 70% of injected GH estimated from Clinical-setting vs GH-secretion rate (U/24h) estimated from healthv children[1]



Exogenous GH-dosing consequences:
GH^{33} in prepub 25kg child gives 825µg=2.5U/24h (70%=1.75U/24h, lower red arrow.)
GH^{67} in pub 50kg child gives 3350µg=10U/24h (70%=7U/24h, upper red arrow)
Factor 3 used to convert µg to U.

Material GH-curves from the children who were yearly followed up to 8 years after GH dose 33 (GH^{33}) or 67 (GH^{67}) µg/kg/d, given as a sc injection at 90° angle in the thigh, using a 12mm needle.
For this analysis of BA, only the GH-curves without sign of endogenous secretion and coming back to their pre-injection GH level were used.
Experimental-setting 59 GH-curves from 15 children, diagnose MPHD; GH^{33}, concentration 4 or 16IU/ml, given by a nurse at 09:00; blood samples were drawn every 30 min until 6h and thereafter every 2h until 24h after the injection.
Clinical-setting 154 GH-curves from 117 children, diagnose IGHD/ISS; GH^{33} or GH^{67}, injected by the patient/parents at 18:00; blood samples were drawn every 2h until 16h after the injection.

Methods The cumulative amount of GH in the serum was calculated with the formula[1]:
AUC_b x 0.066(k_{01}) x 0.046(V_1) x kg=uptake (mU converted to Unit) which was compared with the injected dose (U)=100% which gives the BA in %.



1.Albertsson-Wikland K et al Am J Physiol 1989;257: 809-814

Diclosure: EL, BA, SR, KAW has nothing to declare;
BK has received consultant honoraria from Pfizer.

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