RECOMBINANT HUMAN GROWTH HORMONE THERAPY ALLOWS TO REACH A NORMAL FINAL ADULT HEIGHT IN COELIAC CHILDREN WITH GROWTH HORMONE DEFICIENCY DUE TO HYPOPHYSITIS

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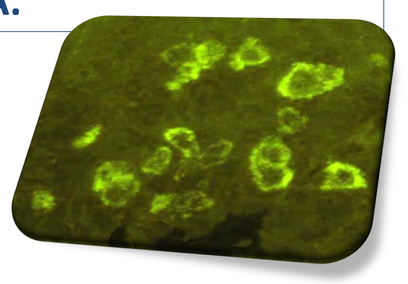
Introduction

Coeliac Disease (CD) can be associated with impaired growth in children after a prolonged period of Gluten-Free Diet (GFD). A small percentage of CD patients does not show catch-up growth during GFD because of growth hormone (GH) secretion deficiency (GHD) that could be associated with antipituitary autoantibodies (APA).

Objective and Hypothesis

This study aims to evaluate the efficacy of recombinant human GH (rhGH) therapy on final adult height in children with CD and GHD associated with APA.



Methods

From a cohort of 130 patients with CD we identified 6 patients with persistent growth impairment after at least one year from the GFD initiation, due to GHD.

Diagnosis of GHD was performed following to the Italian Agency for drugs (AIFA) guidelines [http://www.iss.it/binary/rnoc/cont/ALLEGATO_1_nota39_18_11_2010.pdf]:
a) height < -3 SDS or b) height < -2 SDS associated with annual growth velocity < -1SDS for chronological age and gender (6-months follow-up) or c) annual growth velocity < -2 SDS or < -1.5 SDS after two consecutive years also without short stature
b) GH response <10 µg/L to two different stimulation test performed in different days

APA and/or antihypothalamus autoantibodies (AHA) resulted positive at high titers in four out of six CD-GHD patients.
They all started rhGH therapy at the recommended weekly dose of 0.233 ± 0.007 mg/kg subcutaneously for a mean period of 3.21 ± 1.88 years.
Non-parametric statistical analysis was performed by STATISTICA™ software (StatSoft Inc., Tulsa, OK, USA).

Results

Patients showed a significant height SDS gain from the onset of rhGH therapy (T1) to the stop (T2) (-2.09 ± 0.35 vs. -1.00 ± 0.43, respectively; p = 0.0277) and the final adult height SDS, evaluated after one year from the rhGH interruption (T3), was within the target height (-0.81 ± 0.69 vs. -0.57 ± 0.61, respectively; p = 0.248) (Fig. 1).
Results did not changed analyzing data according to APA and/or AHA status (positive vs. negative): final adult height was consistent with the TH and achieved independently from the autoantibodies positivization.

Auxological data/Patient	I	II	III	IV	V	VI
Gender	M	M	M	F	M	F
Age (years)						
T1	8.60	11.0	14.4	12.5	14.6	11.6
T2	11.58	14.1	16.8	14.9	16.5	14.1
Bone age (years)						
T1	5.5	10.0	12.0	10.5	13.0	10.5
T2	9.0	13.5	14.5	12.0	15.0	13.5
TH SDS	-0.44	0.32	-0.23	0.46	-1.01	-0.85
Height SDS						
T1	-2.08	-1.43	-2.23	-2.10	-2.24	-2.46
T2	-1.45	-0.9	-0.73	-0.33	-1.45	-1.39
T3	-0.9	-0.86	0.06	0.12	-1.39	-1.52
Height SDS correct per TH						
T1	-1.64	-1.75	-2.00	-2.56	-1.23	-1.61
T2	-1.01	-0.92	-0.50	-0.79	-0.44	-0.54
T3	-0.46	-1.18	0.17	-0.34	-0.38	-0.67
BMI SDS						
T1	-0.32	-1.21	-1.07	-1.58	-0.69	-1.02
T2	-0.49	-1.17	-2.28	-1.99	-0.53	-1.37
T3	-0.81	-1.20	-2.36	-1.85	-0.43	-1.83

Tab. 1 Clinical characteristics of CD patients at GHD diagnosis (T1), at the end of rhGH treatment (T2) and after 12 months from the treatment suspension (T3)

Laboratory data/Patients	I	II	III	IV	V	VI
GH (ng/ml) peak to stimulation test						
Arginin	7.20	7.30	4.00	9.40	8.10	5.00
L-Dopa	7.00	7.60	2.70	8.90	5.90	10.8
Antibodies status						
APA T1	1:32	1:64	A	1:64	A	A
AHA T1	A	A	A	1:32	1:16	A
TSH (mUI/L)						
T1	1.5	2.7	4.2	2.9	3.2	3.6*
T2	2.23	4.49	3.04	1.88	2.45*	4.73*
FT4 (ng/dL)						
T1	0.99	1.28	1.00	0.99	1.04	1.21*
T2	1.10	1.21	11.3	8.8	13.1*	11.8*
IGF-1 SDS for age and gender						
T1	-2.00	-2.00	-3.00	-2.50	-1.00	-2.00
T2	-0.50	-0.80	- 1.00	-0.90	1.20	0.10
Pituitary/hypothalamus MRI T1	N	N	N	N	Cystic pineal	N

*L-thyroxine therapy

Tab.2 Endocrinological, autoimmune and neuroradiological characteristics of CD patients at T1 and T2

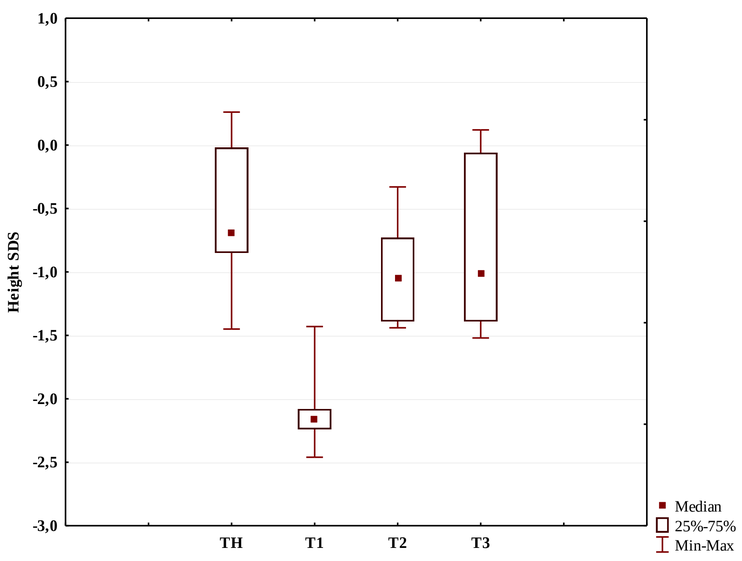


Fig. 2 Height SDS changes in study population
(TH vs. T1 p = 0.0277; T1 vs. T2 p = 0.0277; T2 vs. T3 p = 0.1729; TH vs. T3 p = 0.248)

Conclusions

In patients with CD and GHD the association of GFD and rhGH treatment seems to allow an adequate catch-up growth and the achievement of height within target height and presence of LYH seems not to influence the efficacy of the treatment.

References

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Authors have nothing to disclose