Influence of the application of the POI score on the results of GH therapy in Prader-Willi.

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BACKGROUND

International guidelines recommend monitoring serum IGF-1 concentration, ENT evaluation and polysomnography before and during GH treatment. However at present there isn't a general consensus in how to interpret these parameters for a safe management of GH therapy in PWS patients.
We have recently proposed a decision-making score, reflecting the respiratory risk, which includes polysomnography indexes, ENT findings and IGF1 blood levels (Salvatoni, 2012).
We called the score with the acronym "POI". The score is directly related to the respiratory risk and it ranges from 0 to 15.

Objective and hypotheses

The study aims to determine whether the modulation of GH therapy in children and adolescents with Prader Willi Syndrome with a specific decisional score (POI score, Salvatoni A. et al Horm.Res.In Ped. , 1012) changes and to what extent the results of the therapy.
In particular we intended to explore the following axpect:

- **Times of discontinuation of the treatment**
- **Dosage of GH**
- **IGF1 levels**
- **Linear growth**
- **Weight excess and body composition**
- **Insulin/Glucose metabolism**
- **Thyroid function**

Methods

We compared retrospectively 40 prepubertal children (21 boys), aged 4.1(3.8) year, with genetically confirmed Prader-Willi syndrome, in treatment with GH for at least 3 years. Twenty patients (group A) were treated with a GH standard dose of 0.09 U/kg/day, and treatment was discontinued according to the Italian pharmaceutical agency (AIFA) recommendations (BMI over 95th percentile and/or OSAS); in the other 20 patients (group B) the dosage of GH treatment was modulated according to the POI score. We compared in the two groups of patients the trend of the following aspects in the last two years of GH treatment: times of discontinuation of the treatment, dosage of GH, IGF1 levels, height-SDS and BMI-SDS. The sample size was sufficient to detect variation between the two groups in percentage of days in treatment/days of follow-up higher than 4.5% and in GH mean dosage higher than 0.014 U/kg/day with a Power of 80% and a statistical significance of 0.05.
The results are reported as (median (IQR). Mann-Whitney Rank test was used for statistical analysis.

Table 1

	Group A (Control)	Group B (POI)
N.	20	20
Gender (M/F)	9/11	11/9
Age at start of GH therapy (months)	10(14)	21(22)
Age at the last examination (months)	63(36)	73(40)
Genetics		
Deletion	8	2
UDP	12	9
Methylation +	0	9

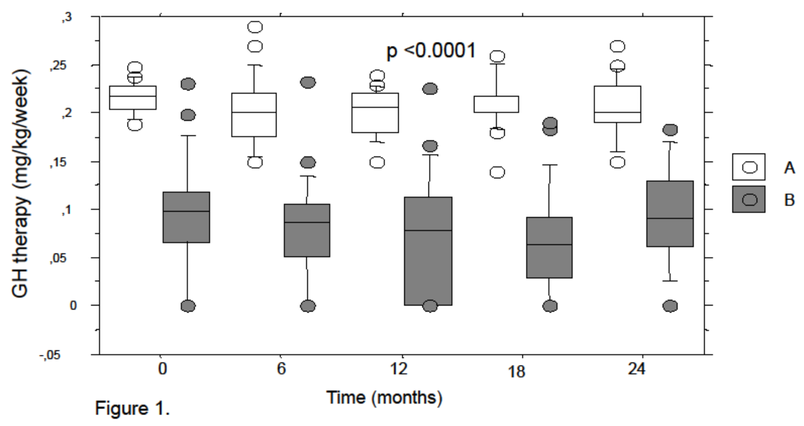
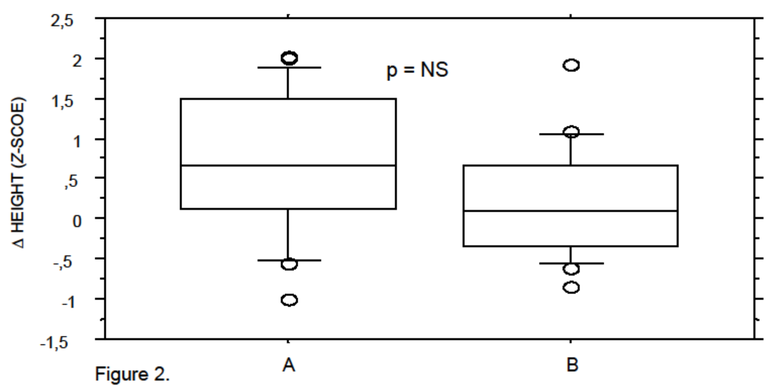


Figure 1.



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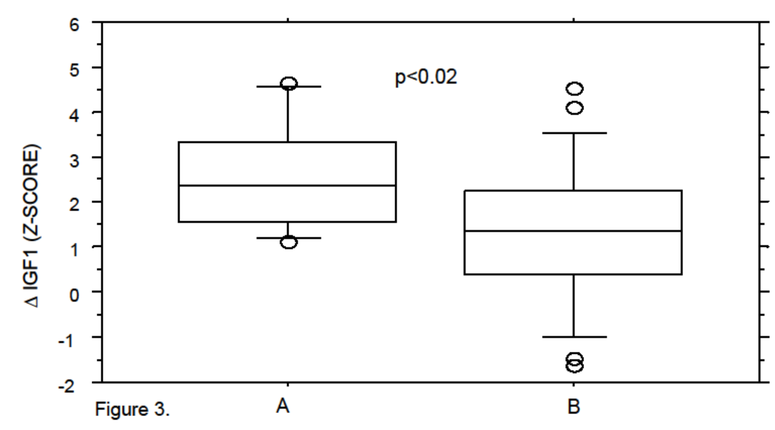

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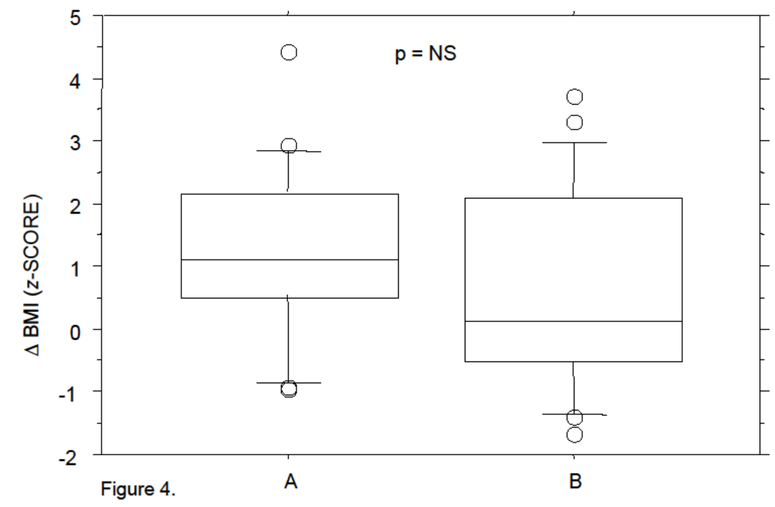

Figure 4.

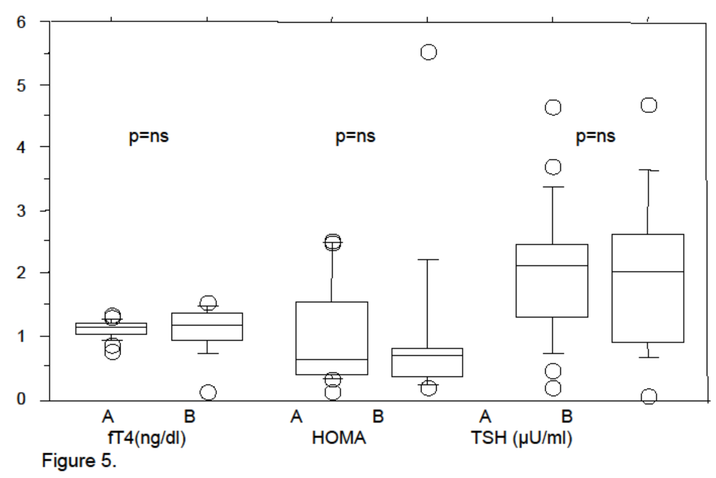

Figure 5.

POI SCORE
(Salvatoni A. et al Horm.Res.In Ped. , 1012)

Polysomnography				
Mean SpO_2	>97%	>95%	<95%	
	0	1	2	
RDI	<1	1–3	3–5	>5
	0	2	3	4
Otorhinolaryngology				
Tonsils (degree)	0–25%	25–50%	50–75%	75–100%
	0	1	2	3
Adenoids	<1/3	1/3	2/3	3/3
	0	1	2	3
IGF-1 (percentile)	<25th	25th–50th	50th–75th	>75th
	0	1	2	3

Score	Not yet on treatment	In treatment with GH
0–3	Start full dose	Maintain or increase
4–6	Start ½ dose	Maintain
7–9	Start ⅓ dose	Decrease 50%
≥10	No start	Stop therapy

RDI = Respiratory Disturbance Index.

Results

The group B resulted to be treated with significant lower dose of GH [0.08(0.06) mg/kg/week vs 0.31(0.03) mg/kg/week; p<0.0001)] (Fig.1). The two groups showed at the end the two years of treatment similar changes in BMI-SDS [Group A +1.2(1.6) vs Group B +0.1(2.6); p=ns] (Fig.4), height-SDS [Group A +0.66(1.36) vs Group B +0.10(1.01); p=ns] (Fig.2) and times of discontinuation of the treatment (one case in each group). The change in IGF1-SDS resulted significantly higher in GroupA [GroupA 2.39(1.78) vs Group B 1.36(1.82); p<0.02] (Fig.3). fT4, TSH and HOMA at the end of the study were similar in the two group of patients (Fig.5)

CONCLUSIONS

The application of specific and shared criteria, such as POI score, in the modulation of GH therapy in PWS offers the opportunity of compare in a more reliable and safe way groups of patients treated in different centers and to avoid overtreatment and or frequent discontinuation of the therapy. The use of the POI score even reducing GH doses and IGF1 levels does not significantly alter the therapeutic results.

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