ESPE 2021
The 59th Annual Meeting Online
22-26 September 2021

Auxological and endocrine aspects in pediatric patients with Narcolepsy Type 1. Results of long-term follow up in a Pediatric Endocrinology Center

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INTRODUCTION

Type 1 Narcolepsy (NT1) is a rare paediatric disorder characterized by excessive daytime sleepiness and cataplexy. The cause is a selective loss of hypocretin-secreting neurons, probably with an autoimmune etiology [1].

Hypocretin deficiency could affects the neuroendocrine system, causing alterations in energy balance, eating behaviour, glucose metabolism and modulation of the hypothalamic-pituitary axis. In particular, **obesity, GH deficiency** and **Central Precocious Puberty** (CPP) are endocrine complications already reported in literature for these patients [2].

AIM

The aim of this study was the **evaluation of endocrine-metabolic and auxological aspects at diagnosis and during follow-up in children affected with NT1**.

Secondary objective was to evaluate of the effect of Sodium Oxibate (SO) in the trend of the endocrine-metabolic parameters and the identification of possible prognostic factors that could identify patients at risk for endocrine complications.

METHODS

This was a Retrospective study. We have examined medical records of **98 consecutive patients** affected with NT1 referred to our center from September 2004 to February 2020.

We evaluate auxological, biochemical and radiological parameters in order to investigate endocrine-metabolic complications.

Diagnosis of CPP was made following the diagnostic algorithm developed by the Italian Paediatric Endocrinolology Society (SIEDP) [3].

The determination of BMI percentiles was used to define normal weight, overweight and obese patients [4].

We excluded patients with other forms of Narcolepsy or affected by disorders known to be associated with CPP and obesity.

RESULTS

98 patients fulfilled inclusion criteria and were recruited for the study: 53 boys e 45 girls.

Auxological parameters at diagnosis and during follow up are reported in Table 1. Median follow up was 36 ± 16 months.

*A **diagnosis of CPP was found in 21%** (21/98) and 11 subjects started treatment with GnRH analogue according to the guidelines [5].*

***Obesity was found in 33%** (33/98), while 25% (25/98) was found Overweight.*

A significative increase in baseline insulin (uIU/ml) values was found in obese subjects (15.1 ± 13.4) compared to others (12.7 ± 10.5)(p<0.05).

Others laboratoristic parameters were found in the normal range.

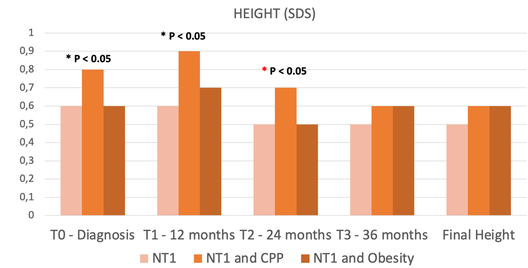
Stature (SDS) at diagnosis and during follow up is reported also in Graphic 1. Mean IGF1 levels was 297.8 ± 133.3 ug/L (SDS 0.4 ± 1.0).

*Patients treated with SO at 12 months of follow up were 46/98 (46.9%). The BMI trend is reported in Graphic 2. At 36 months of follow up, we find a significative difference in BMI SDS between SO treated vs untreated patients (0,0 ± 1,3 vs 1,3 ± 0,4) (**p<0.003**).*

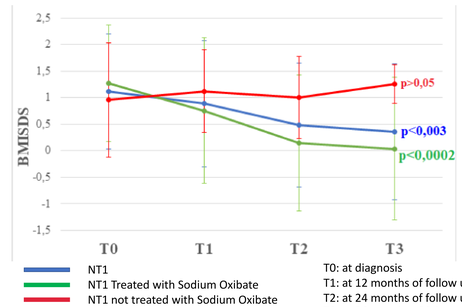
62 patients reached their final height (mean CA 15.91 ± 2.5) with SDS of 0.5 ± 1.1 in boys and 0.3 ± 1.2 in girls. Target parental height was 0.2 ± 0.8 SDS in boys and 0.3 ± 0.7 SDS in girls.

	NT1 (98)	NT1 and CPP (21/98)	NT1 and obesity (33/98)
Age at onset	8.5 ± 2.4	7.3 ± 2.1*	8.2 ± 2.5
Age at diagnosis	10.4 ± 3.2	9.1 ±2.5*	10.4 ± 3.3
Height at diagnosis (SD)	0.6 ± 1.1	0.8 ± 1.6*	0.6 ± 3.3
BMI at diagnosis (SD)	1.1 ± 1.1	1.1 ± 0.9	1.8 ± 0.6 §
Age at last visit	13.0 ± 4.2	10.6 ± 3.1*	13.22 ± 4.2
Height at last visit	0.6 ± 1.3	0.8 ± 1.7	0.7 ± 1.1
BMI at last visit	0.6 ± 1.3	0.5 ± 1.5	1.4 ± 1.6 §

Table 1 - Auxological parameters at diagnosis and at the end of follow up in NT1 patients
* p<0.05 NT1 and CPP vs NT1 and NT1 and obesity; § p<0.05 NT1 and obesity vs NT1 and CPP and NT1 alone.



Graphic 1 – Height in SDS of all patients and divided according to CPP and obesity.
* p<0.05 patients with CPP vs patients with NT1 alone or NT1 and obesity



***Graphic 2**. BMI in SDS of all patients overall and divided according to Sodium Oxibate (SO) therapy from the time of diagnosis up to 36 months.*

CONCLUSIONS

The results of our study confirm an **increased frequency of CPP and obesity** in NT1 patients compared to general population [1]. A predictor sign of CPP seems to be an **earlier age at onset of NT1.**

According to a previous study [6], we demonstrate that **treatment with SO leads to a significative improvement on BMI**, which also persist at 36 months of follow up.

To our knowledge, these are the first results regarding the final height in a large series of patients diagnosed with NT1 in pediatric age.

Our results appear in contrast with the hypothesis of a GH deficiency; in fact, we find **IGF1 levels and stature (SD) in the normal range**, as the final height where available.

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ACKNOWLEDGEMENTS

We are grateful with all the patients followed for Narcolepsy type 1 and their family members who agreed to participate in this study.

We also thanks the equipe of the Center of Sleep Disorders in Bellaria Hospital that collaborate with us in this study.

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