THE MEDICAL TREATMENT WITH PASIREOTIDE IN CUSHING'S DISEASE: AN ITALIAN MULTICENTER EXPERIENCE BASED ON "REAL WORLD EVIDENCE"

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BACKGROUND

A recent phase III clinical trial has demonstrated that 6-months treatment with the somatostatin analogue pasireotide normalizes cortisol secretion in up to 26% of patients with Cushing's disease (CD)[1]. No data are presently available on the outcome of pasireotide treatment when used in the daily clinical practice.

OBJECTIVES

The aim of the current prospective multicentre study was to evaluate the effectiveness of 6-months pasireotide treatment on cortisol secretion as well as on clinical and metabolic profiles, and tumour size, in a group of CD patients with mild to moderate disease, according to real-world evidence.

PATIENTS AND METHODS

Thirty-two CD patients started pasireotide at the dose of 600 µg bid and increased it up to 900 µg bid, or decreased it, on the basis of urinary cortisol (UC) levels during first 6 months of treatment. Hormonal, clinical and metabolic parameters were measured at 3- and at 6-months follow-up. Five (15.6%) patients discontinued treatment for side effects or unexpected accidents not related to the drug; the remaining 27 patients reached 6-months follow-up. Among these patients 14 had a very mild (UC≤1.5ULN),6 had mild (UC>1.5 and <2ULN),6 had a moderate (UC≥2 and ≤3ULN), none had severe (UC>3 and <5ULN) and 1 had a very severe (UC≥5ULN) disease. The 5 patients who discontinued the study had a very mild to moderate disease. The current study has been focused on the 31 patients with very mild to moderate disease, among whom 26 reached the 6 months follow-up

RESULTS

Responsiveness, including full control (FC, UC < ULN) and near control (NC, UC >1 and < 1.1 ULN) was registered in 21 patients. This number of responsive patients correspond to 67.7% (21/31) according to an intention to treat and to 80.8% (21/26), according to a "per protocol" methodological approach. Full control was obtained in 61.3 and 73.1% respectively (Fig.1). Three patients had mean UC within the normal range, but increased UC levels in at least one determination and alteration of hormone status confirming the persistence of CD, and were treated with pasireotide and included in the study.

A significant decrease of UC (p=0.004), as well as serum cortisol (p=0.011) and ACTH levels (p=0.002) were demonstrated in the 26 patients with very mild to moderate disease reaching the 6-months follow-up. The changes in UC levels at 6 months follow-up is showed in Fig.2.

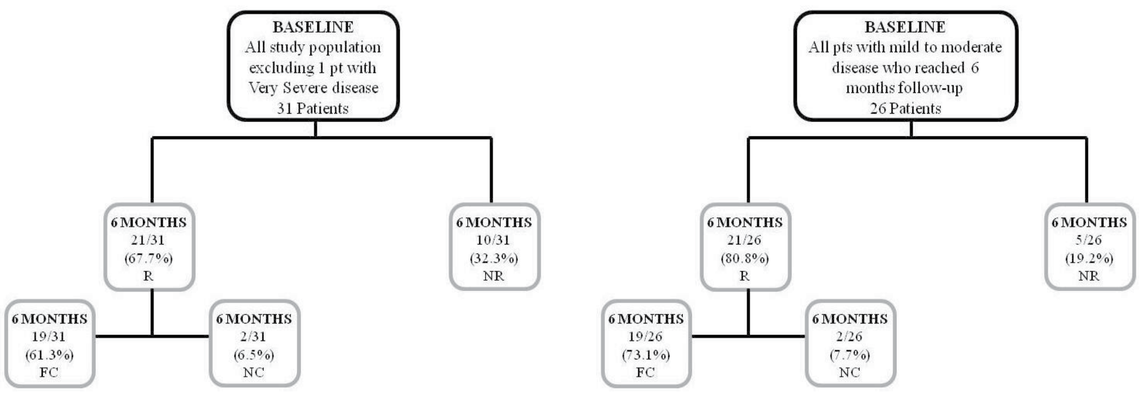

Figure 1

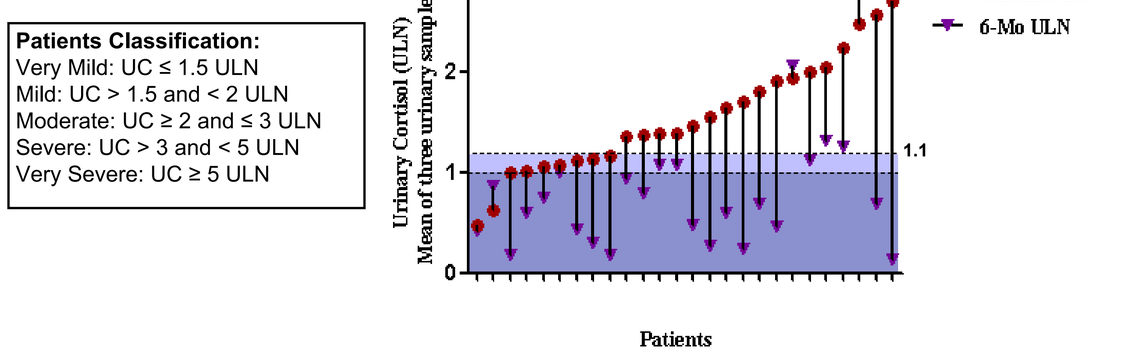

Figure 2:

A significant decrease was observed in weight (p<0.001), body mass index (BMI) (p<0.001), waist circumference (WC) (p=0.01) as well as in serum total cholesterol (0.035) and LDL cholesterol levels (p=0.011) (Fig.3).

Fasting plasma glucose (Glu) (p<0.001) and glycated haemoglobin (HbA1c) (p<0.001) levels increased significantly (Fig.4). Considering the entire cohort of 32 patients entering the study, hyperglycaemia or deterioration of diabetes was documented in 81.2% whereas gastrointestinal disturbances, mainly diarrhoea, were documented in 40.6% of patients during the period of pasireotide treatment.

Among the 18 out of 26 patients who performed pituitary MRI at baseline and at 6-months follow-up, 1 of 4 (25%) macroadenomas became microadenoma, 2 of 8 (25%) microadenomas became invisible at pituitary MRI whereas a stable picture was registered in the remaining except for 1 patient, who displayed a slight enlargement of the macroadenoma (Tab.1)

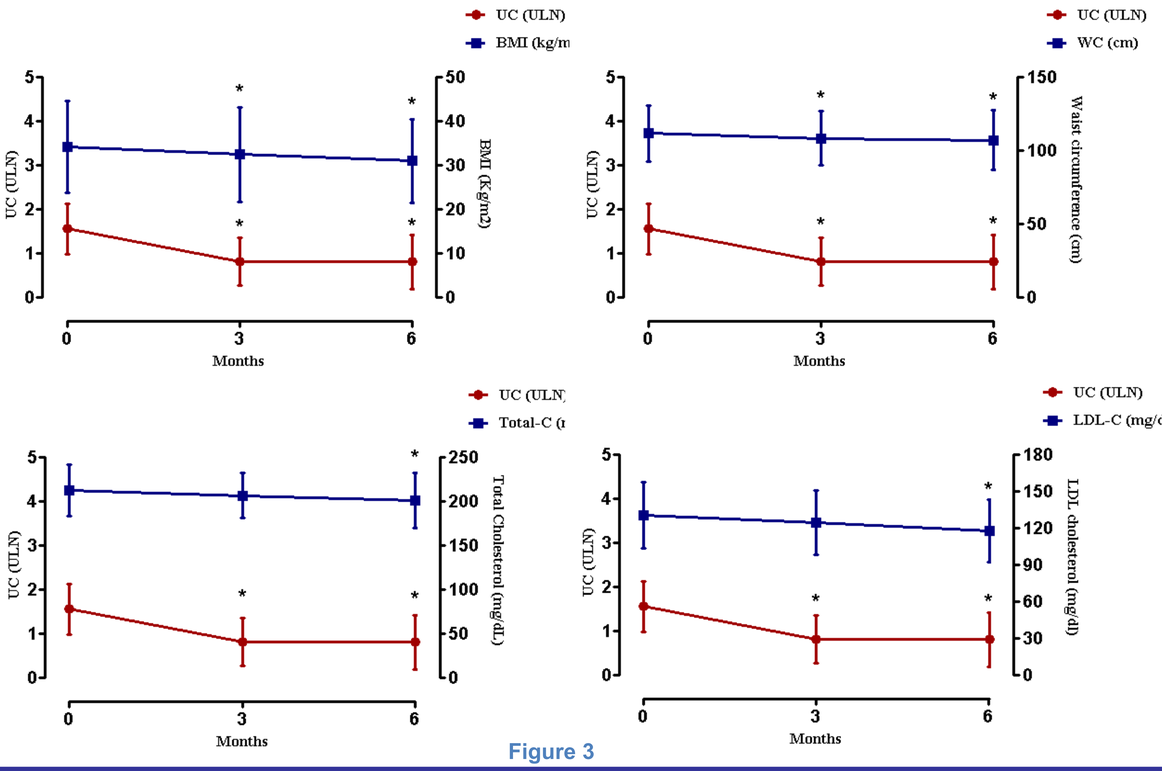

Figure 3

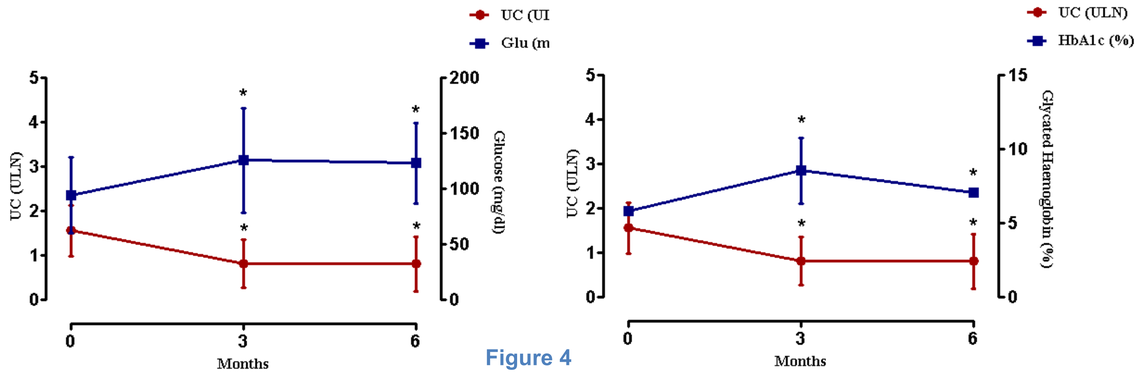

Figure 4

Changes in Tumor Size in 18 patients with available MRI among the 26 patients with mild to moderate disease who reached 6 months follow-up

	Macroadenoma	Microadenoma	Negative MRI
Baseline - no (%)	4/18 (22.2)	8/18 (44.4)	6/18 (33.3)
6 Months - no (%)	3/18 (16.7)	7/18 (38.9)	8/18 (44.4)

Table 1

CONCLUSIONS

In the real-life clinical practice, pasireotide treatment normalizes or nearly normalizes UC in at least 68% of patients with mild to moderate disease, with a full control observed in around 60% of patients. The normalization or decrease of cortisol secretion was associated with an improvement in weight, visceral adiposity and lipid profile, although associated with the occurrence or deterioration of diabetes in the majority of cases. These data confirmed the usefulness of this treatment especially in patients with milder disease.

Reference

1. Colao A, Petersenn S, Newell-Price J, et al. A 12-month phase 3 study of pasireotide in Cushing's disease. N Engl J Med. 2012;366:914–24

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