CARDIOVASCULAR PROFILE IMPROVEMENT DURING NATALIZUMAB TREATMENT

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Introduction

Cardiovascular comorbidities have been associated with the risk of multiple sclerosis (MS) progression[1]. Different studies have associated dyslipidemia with clinical and neuroradiological measures of disease progression, and, similarly, high levels of disability are more common in MS patients with obesity. Indeed, cholesterol and triglycerides can enhance the inflammatory process through determining endothelial dysfunction, with induction of adhesion molecules and recruitment of monocytes.
In keep with this, there is a growing body of evidence suggesting that an improvement in the cardiovascular profile can affect positively MS-related outcomes[2] and Natalizumab has been associated with a more anti-atherogenic lipid profile[3].
Therefore, the present study aims to evaluate cardiovascular comorbidities (blood pressure, obesity, uricemia, diabetes, cholesterol and triglycerides) in a longitudinal cohort of relapsing-remitting (RR) MS patients treated with Natalizumab.
Associations between variations of cardiovascular risk factors and disease evolution were also explored.

Methods

The present observational prospective cohort study has been conducted at the MS Clinical Care and Research Centre of the Federico II University Hospital of Naples, Italy, between January 2015 and June 2016. The inclusion criteria for the examined population were: diagnosis of RRMS and use of Natalizumab prescribed in accordance with the local regulatory indications for clinical practice.
The cardiovascular risk factors (Body Mass Index, Systolic blood pressure, Uric acid, LDL, HDL and total cholesterol, and triglycerides) were recorded at the first avaible visit and at the last one, and their variation was calculated. Relapses occurring during the study period were recorded and disability was scored with the Expanded Disability Status Scale (EDSS) by certified clinicians (**Table 1**).

Results

Seventy-one patients were included in the present study and were followed-up during a 12.9±6.2 month period. At multilevel mixed-effects linear regression models, the population presented with a significant reduction of total cholesterol (Coeff=-7.340; 95%CI=-13.152--1.527)(**fig.1 D**), and a non-significant reduction of LDL cholesterol (Coeff=-1.872; 95%CI=-8.481-0.736), and of triglycerides (Coeff=-8.815; 95%CI=-34.011-5.380)(**fig.1 E and G**). Uric acid levels increased during the study period (Coeff=0.159; 95%CI=0.212-0.340)(**fig.1 C**).

Conclusions

The present longitudinal cohort study found a reduction of lipids and an increase of uric acid levels in RRMS patients during 12-month treatment with Natalizumab.
The reduction of circulating lipids has been previously described during Interferon beta treatment[4], and has been associated with improved MS outcomes. In our population, we found a reduction of total and LDL cholesterol, which is known for its positive impact on the cardiovascular profile due to antioxidant and anti-inflammatory properties.
The increase of uric acid levels after 12-month Natalizumab treatment can be considered a sign of improved oxidative balance, rather then a worsening of the cardiovascular profile. Of note, uric acid levels are generally reduced in MS and are negatively associated with relapse occurrence and disability progression.
In conclusion, our findings suggest that Natalizumab treatment has a beneficial effect on the lipid profile and on the oxidative balance. Possible associations with disease outcomes deserve to be investigated in larger cohorts with longer follow-ups.

TABLE 1. Demographic, clinical and cardiovascular features.
Table shows demographic, clinical and cardiovascular features of the population at baseline and follow-up. Data are presented as mean±standard deviation, number (percentage), or median (minimum and maximum value), as appropriate. P-values are shown from adjusted multilevel mixed-effects linear regression models (*: p<0.05).

	Baseline *(n=71)*	***Follow-up*** *(n=71)*	*p-values*
Age, *years*	35.7±10.7		
Gender, *female (%)*	50 (70.4%)		
Disease duration, *years*	8.8±14.4		
Duration of Natalizumab treatment at study entry, *months*	11.7±14.1		
Study duration, *months*		12.9±6.2	
Patients with relapse, *number (%)*		8 (11.3%)	
Annualised relapse rate		0.18±0.57	
EDSS, *median (min-max)*	3.0 (2.0-5.0)	3.0 (2.0-5.5)	
Systolic blood pressure, *mmHg*	115.7±11.0	115.9±13.2	0.715
BMI, *kg/m²*	24.9±3.9	24.3±4.0	0.841
Uric acid, *mg/dL*	4.1±1.1	4.4±1.3	0.038*
Total Cholesterol, *mg/dL*	189.3±40.5	181.0±39.6	0.013*
LDL Cholesterol, *mg/dL*	111.1±38.3	106.4±36.6	0.053
HDL Cholesterol, *mg/dL*	58.4±16.4	53.2±14.0	0.017*
Triglycerides, *mg/dL*	108.3±100.6	97.3±66.9	0.094

EDSS: expanded disability status scale; BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein.

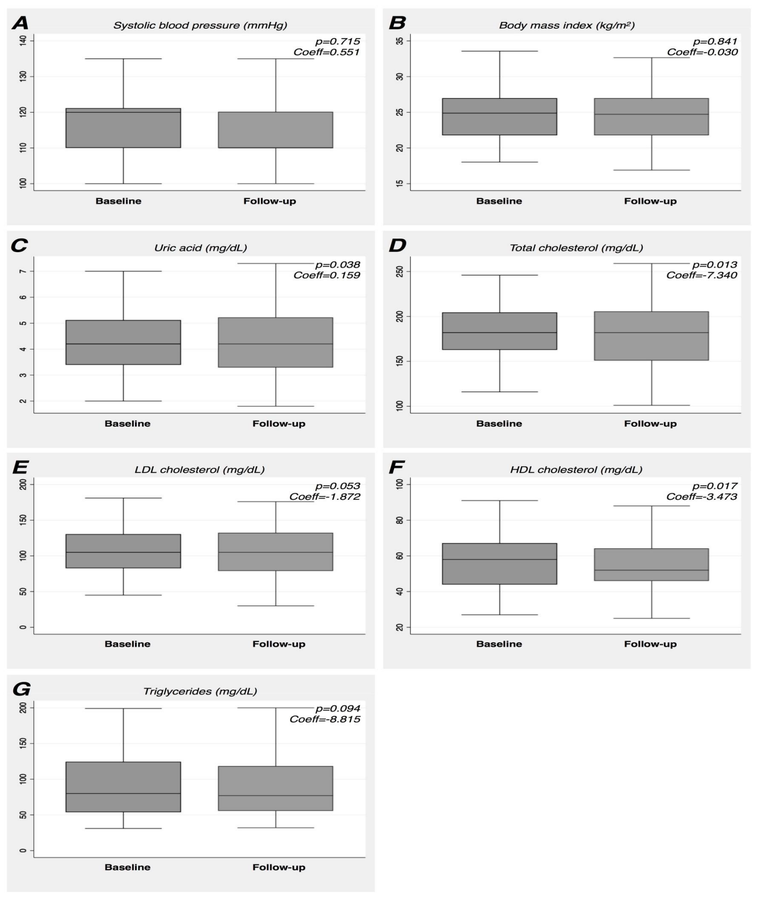

Figure 1. Cardiovascular risk factors at baseline and follow-up. Box-and-whisker plots show values of systolic blood pressure (A), body mass index (B), uric acid (C), total cholesterol (D), LDL cholesterol (E), HDL cholesterol (F), and triglycerides (G) at baseline and after 12.9±6.2 months. P-values and coefficients are shown from adjusted multilevel mixed-effects linear regression models.

References

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