AB0601

RAPID AND SUSTAINED EFFICACY OF AN INDUCTION TREATMENT WITH A TRIPLE THERAPY INCLUDING HIGH-DOSE INTRAVENOUS IMMUNOGLOBULINS, METHOTREXATE AND GLUCOCORTICOIDS IN ANTI-3-HYDROXY-3-METHYLGLUTARYL-COENZYME A REDUCTASE MYOPATHY

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Background: Anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) myopathy is a new entity, which has been clearly associated to statin use, even if it can be diagnosed in patients without a history of exposure to statin or even in the childhood (1).

Objectives: The aim of the study is to describe the efficacy of a triple therapy regimen consisting in high-doses of intravenous immunoglobulins (IVIG), methotrexate (MTX), and glucocorticoids (GC) in 16 patients with Anti-HMGCR myopathy enrolled in 6 specialized centres.

Methods: A total of 16 patients with anti-HMGCR myopathy (7 females; 9 males) were collected. Mean ($\pm$ standard deviation) age at the onset of disease was 72.4 $\pm$ 10.3 years old. All patients were diagnosed having anti-HMGCR myopathy [anti-HMGCR antibodies were measured by chemiluminescence assay (Bio-Flash, Inova, CA)] (2). Median follow-up was 29.5 months (interquartile range: 15.75-60 months). Anti-HMGCR antibodies were available in the follow-up in 8/16 patients.

Results: Thirteen out of 16 patients (81.3%) had been exposed to statin (1/13 to red rice), 3/16 (18.7%) were not exposed. As induction therapy, 11/16 patients have been treated with triple therapy (high-dose IVIG, MTX and GC), 2/16 with double therapy (high-dose IVIG and GC), 2/16 have been treated with GC alone, the patient exposed to red rice resolved only with red rice suspension. Clinical remission and normalization of CPK values within month +24 were obtained in all the patients. All the patients were in remission at the last follow-up. Gradual improvement started soon from the first month, and among the 13 patients treated with an aggressive immunosuppressive therapy including IVIG (13/13), GC (13/13) and methotrexate (11/13), 9/13 normalized the CPK value within 6 months. Clinical and laboratory response was accompanied by significant decrease or normalization of the anti-HMGCR antibody titer. All the patients were either not taking GC (56.3%), or were taking low doses of GC (43.7%) at the last follow-up. Four patients had stopped GC within 6 months. No serious side effects were recorded. After persistent remission, a maintenance immunosuppressive therapy was then administered. Only 3 relapses in 3 different cases were recorded, all of them during drug-free remission in long-term follow-up. Reinduction was again effective in all.

Conclusion: Anti-HMGCR myopathy is a rare and serious myopathy which usually affects older people during statin treatment. After statin suspension, a rapid and sustained remission can be achieved by induction with a triple aggressive therapy consisting in medium-to high doses of GC, high-dose IVIG, and MTX (3). GC should be tapered as soon as possible. Relapse appears infrequent during maintenance treatment. Monitoring anti-HMGCR antibody titer may be clinically relevant.

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AB0602

SYSTEMIC SCLEROSIS: SUBCLINICAL ATHEROSCLEROSIS AND MORBIMORTALITY.

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Background: Rheumatic diseases are associated with accelerated atherosclerosis, and an increase in cardiovascular morbidity and mortality. This process is mediated by classic cardiovascular risk factors (CVRF), chronic inflammation and atherogenic treatments such as corticosteroids. In Systemic Sclerosis (SSc) cardiovascular complications have increased in recent decades, although the studies on subclinical atherosclerosis (sATS) in SSc show discordant results.

Objectives: To evaluate prospectively the relationship between subclinical atherosclerosis, cardiovascular morbidity and mortality in patients with SSc.

Methods: 120 consecutive patients with SSc who attended their medical regular review during November and December 2011 were included. We evaluated the presence of plaques and measured the right CCA IMT by B doppler US for the detection of sATS (IMT > 0.9mm and/or presence of plaque), review of classic CVRF and estimation of Medsger severity and EUSTAR activity index. Patients have been followed for 8 years, with at least annual consultation. In retrospect, the SCTC damage index, published in 2019, was obtained at the time of inclusion in the study. The clinical characteristics of the patients are collected since 1990 in a Prospective Longitudinal Observational Study (PLOS). Descriptive analysis was performed, using contingency tables for qualitative variables, and comparison of means for quantitative variables. The relationship between clinical characteristics, mortality, cardiovascular events (CVE), activity, severity and damage index, and sATS, was analyzed using binary logistic regression, adjusting for age and sex.

Results: 120 patients with SSc were included (93% female, age 60 $\pm$ 12 years). 42 of these patients (35%) had subclinical atherosclerosis. Age was statistically significant higher in patients with sATS compared to those without it (67.9 $\pm$ 11.5 vs. 56.1 $\pm$ 10.4 years, $p < 0.001$). We found no differences between groups in activity, damage and severity index (Table 1). Patients with sATS had higher levels of ESR and CRP, but the difference was not confirmed after adjusting for age (*). During the 8 years of follow-up, 9 CVE in 7 patients (5.8%): three myocardial infarction, one transient ischemic accident, one angor, one intermittent claudication and three refractory heart failure. The incidence of severe CVE was more than double in patients with sATS (10.25% vs. 3.7%), but the difference was not significant. We found no relationship between the mortality of any cause, or the secondary to CVE, with sATS, in the 32 patients who died during the follow-up, 3 due to CVE (9.4%). The results are similar when we analyze only the presence of plaques.

Table 1. Relationship between clinical characteristics and activity, severity and damage index with the presence of accelerated atheromatosis.

	Absent n=78	Present n=42	
Diffuse cutaneous SSc	37.18%	26.12%	NS
mRSS	7.71 $\pm$ 6.32	6.38 $\pm$ 4.92	NS
High mRSS	9.69 $\pm$ 8.33	7.57 $\pm$ 4.74	NS
Arthritis	32.05%	28.57%	NS
Lung involvement	33.33%	30.95%	NS
PAH	10.26%	7.14%	NS
Cardiac involvement	15.38%	9.52%	NS
Digital ulcers	35.90%	35.83%	NS
AntiScl70	25.64%	21.43%	NS
ESR	20.12 $\pm$ 13.77	26.88 $\pm$ 17.25	$p = 0.037^*$
CRP	0.65 $\pm$ 0.61	0.89 $\pm$ 0.7	$p = 0.041^*$
High activity index	11.54%	19.05%	NS
Damage index	6.67 $\pm$ 5.56	5.62 $\pm$ 4.9	NS
Σ Medsger index	5.37 $\pm$ 3.5	5.05 $\pm$ 3.45	NS

Conclusion: In our study subclinical atherosclerosis is not related to higher mortality in patients with SSc, but it does seem to influence the occurrence of cardiovascular events. In addition, our results suggest that SSc does not influence the onset of accelerated atheromatosis.

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