

STATIN THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Our aim was to assess the outcome of using statins in patients with cardiovascular modifications associated with ankylosing spondylitis. We selected 14 patients with ankylosing spondylitis with at least a score of four on The Bath Ankylosing Spondylitis Disease Activity Index scale. From this group, eight patients presented with evident clinical cardiovascular modifications (group I: >10 years, n=8) and six patients had subclinical manifestations (group II: <10 years, n=6). Seven patients underwent statin therapy for eight weeks, followed by an observational phase of another eight weeks. We evaluated the effects of statins on reducing the inflammation and lipids, through the assessment of plasma concentrations of C reactive protein (CRP), erythrocyte sedimentation rate (ESR), total cholesterol, LDL – cholesterol, HDL-cholesterol, triglycerides. Patients who underwent treatment with statins had significant improvements of CRP after eight weeks. Total and LDL – cholesterol were also reduced. Statin therapy for patients with cardiovascular manifestations of ankylosing spondylitis is beneficial not only through the reduction of lipoprotein metabolism, but also through the suppression of inflammatory processes, thus, improving the life quality and life expectancy in patients with cardiovascular complications of ankylosing spondylitis.

Keywords: ankylosing spondylitis, statins, cardiovascular diseases, inflammation

INTRODUCTION

It has been shown that statins have anti-inflammatory properties and thus beneficial cardiovascular effects, inhibiting the formation of intracellular isoprenoids¹. For patients with ankylosing spondylitis, treatment consists mainly of non-steroidal anti-inflammatory drugs combined with physical therapy, the use of disease modifying antirheumatic drugs being less efficient than in other rheumatic diseases, even though tumour necrosis factor α -blocking agents have proven to be quite effective². Nonetheless, with all these classes of drugs there comes a notable array of possible adverse events. Recent evidence shows that patients with ankylosing spondylitis (AS) have a 43% higher risk for vascular mortality, a 60% higher risk for cerebrovascular mortality and a 35% higher risk for cardiovascular mortality than those without ankylosing spondylitis³. By lowering the lipids, statins can be used in the prevention of coronary heart disease and other cardiovascular complications in AS patients. The aim of this study was to determine the outcome of using statins in patients with both clinical and subclinical modifications of ankylosing spondylitis by assessing the levels of the lipids in the plasma of this group of patients.

MATERIAL AND METHODS

We enrolled 14 patients with ankylosing spondylitis who had been managed at our institutions between January-October 2015. All patients were men, aged between 25 and 45 years old, fulfilling the 1984 New York criteria (1/14 fulfilled the ASAS classification criteria for axial spondyloarthritis) and with a disease score with a minimum of 4/10 on the both BASDAI scale and VAS pain score. They all had plasma modifications of the total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, CRP and ESR. We divided our patients into two groups: group I - with AS lasting for more than 10 years (n=8), and group II - with AS lasting for less than 10 years (n=6). Seven patients underwent statin therapy with atorvastatin (20 mg/day) for eight weeks, followed by an observational phase of another eight weeks. The main exclusion criteria consisted of cardiovascular and cerebrovascular events within the last three months, current lipid lowering therapy, kidney pathology, liver pathology, hypothyroidism and alcohol addiction. All patients were under targeted treatment for axial spondyloarthropathy, consisting of: NSAIDs (10/14), infliximab (3/14), etanercept (1/14) and physical therapy (14/14). The patients signed the informed consent before inclusion and the study was approved by the Ethical Committee.

Rheumatological evaluation The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Metrology Index (BASMI), as well as the Bath Ankylosing Spondylitis Global score (BASG) were determined by the rheumatologist of our team. We assessed them at baseline and weeks 8 and 16. The clinical evaluation included an interview and routine blood tests, as well as the X-ray of the hips and spinal joints. All our patients were interviewed about their low back pain lasting for longer than 3 months, which improves with exercise, but is not relieved by rest and at an age of onset below 45 years old. We assessed the limitation of motion of the lumbar spine in the sagittal and frontal planes, as well as the limitation of chest expansion. We also looked for the SpA features, represented by: arthritis, enthesitis of the heel, uveitis, dactylitis, psoriasis, Crohn's colitis, good response to NSAIDs, family history of SpA, HLA-B27 and elevated CRP.

Cardiovascular evaluation All our 14 patients underwent echocardiography and ECG. The echocardiography machine used was an iE33 xMatrix

Ecocardiography System (Phillips). Our expert cardiologist also assessed the patients clinically and through the blood tests. The clinical cardiovascular manifestations revealed high blood pressure (<140/90 mmHg), cardiac failure NYHA II-III, as well as aortic insufficiency. On the other hand, the subclinical manifestations was represented by the dilatation of the aortic ring (2/14 patients) at echocardiography. We did not find any modifications on the ECGs. All our patients presented increased levels of the lipids in the plasma (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides).

Statistical analysis

In order to measure the levels of the lipids, CRP (C reactive protein), ESR (erythrocyte sedimentation rate), as well as of the functional parameters at various times (baseline, 8 weeks, 16 weeks) we used a longitudinal linear regression analysis. Our study determined the relationship between lipid levels and inflammation markers over time, as well as disease activity, corrected for age. The statistical analysis was performed with SPSS 14.0 for Windows command and values with a $p < 0.05$ were found to be significant.

RESULTS AND DISCUSSIONS

Our patients showed significant changes ($p < 0.05$) as compared to baseline at 8 weeks in the levels of total cholesterol, LDL-cholesterol and CRP. This indicates us the efficiency in reducing the inflammation, as well as the

lipids in the blood. Significant results ($p < 0.05$) were also found at 16 weeks, after stopping atorvastatin, as compared to 8 weeks, during the treatment, which might prove the longlasting effects of statins (Table1).

Variables	Baseline	At 8 weeks	At 16 weeks
		With atorvastatin	After stopping atorvastatin
Age (years)	35 ± 10		
BASDAI	6.3	5.8	5.4
BASMI	4.4	4.0	4.0
BASG	6.2	6.1	6.0
BASFI	4.7	5.2	5.0
Pain score	6.5	6.3	6.4
Total cholesterol (mmol/l)	5.0	4.2*	5.6**
LDL – cholesterol (mmol/l)	2.8	1.7*	3.2**
HDL – cholesterol (mmol/l)	1.3	1.3	1.3
Triglycerides (mmol/l)	1.4	1.3	1.6
CRP (log mg/l)	15.0	11.7*	13.8
ESR (mm/1 st h)	22.0	20.3	21.0

*significant changes compared to baseline ($p < 0.05$); **significant changes compared to 8 weeks ($p < 0.05$);

Table 1 Clinical and paraclinical parameters in AS patients under treatment with atorvastatin

The functional parameters slightly improved during and after the treatment, as well. However, our study is limited because it was done on a short period of time and with a small batch of patients being under different targeted treatments for ankylosing spondylitis. Nonetheless, it is a start into further discovering and investigating the anti-inflammatory effects of statins in patients with cardiovascular manifestations of ankylosing spondylitis.

Previous studies determined the cardiovascular risk in patients with ankylosing spondylitis, showing that this group of patients have an increased risk for vascular, cerebrovascular and cardiovascular complications than those without the disease^{3,4}. Other study shows that statins might be beneficial in patients with ankylosing spondylitis, both through the reduction of the inflammatory markers, as well as the lipids in the plasma². However, we found no studies to investigate the effects of statins on patients with ankylosing spondylitis who already have cardiovascular manifestations, clinical or subclinical.

In the case of patients with ankylosing spondylitis, literature demonstrates that through the reduction of the inflammation markers, the levels of lipids in the blood also decrease⁴. However, it is not investigated whether lowering of the levels of lipids might influence the inflammation markers, as well as the functional parameters in patients with ankylosing spondylitis.

In this group of patients, it has been proven that cardiovascular complications are more often seen, being mostly represented by aortic insufficiency and conduction disturbances⁵.

Other studies show that patients without clinically evident cardiovascular disease have a high prevalence of subclinical atherosclerosis, in the form of increased carotid IMT, as well as carotid plaques⁶, which are good predictors for inflammatory processes such as atherosclerotic disease⁷.

As inflammatory markers such as CRP or ESR are good predictors concerning the evolution of spondylarthropathies⁸, it is very important to reduce them early in the course of the disease. Statins, as anti-inflammatory agents, might be a good option in this case, being also beneficial in the reduction of cardiovascular events through the reduction of lipids⁹.

Ankylosing spondylitis is a chronic inflammatory autoimmune disease¹⁰, with a disease activity characterized by various functional parameters, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the Bath Ankylosing Spondylitis Metrology Index (BASMI), as well as the Bath Ankylosing Spondylitis Global score (BASG), all with great validity¹¹. As these scores reveal the active ankylosing spondylitis¹², the disease might be held under control through anti-inflammatory treatment, which was also observed during our study, even though we did not record any notable statistical result, due to the limitations of our study.

However, the total-cholesterol, LDL-cholesterol and CRP had significant statistical results, which encourage us into further investigating the effects of atorvastatin on the progression of ankylosing spondylitis in patients with clinical and subclinical cardiovascular modifications.

CONCLUSION

The main conclusion is that statin therapy in patients with clinical and subclinical cardiovascular manifestations of ankylosing spondylitis might be beneficial not only through the reduction of lipoprotein metabolism, but also through the suppression of inflammatory processes, and thus, improving the life quality and also the life expectancy in this group of patients.

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