

STUDY OF THE INFLUENCE OF DIFFERENT TYPES OF STATINS IN THE TREATMENT OF ATHEROGENESIS

Osser Gyongyi¹, Cecilia Avram⁴, Murg Sergiu², Pletea Movileanu Ioana Maria³,
Annamaria Pallag², Hulbar Aurelia¹, Maria Orodan⁴

¹"Vasile Goldiş" Western University, the Faculty of Pharmacy, Arad, L Rebreanu street

²The University of Oradea, the Faculty of Medicine, Pharmacy and Dental Medicine

³University of Medicine and Farmacy Carol Davila Bucharest

⁴"Vasile Goldiş" Western University, the Faculty of Medicine, Arad, L Rebreanu street

ABSTRACT. The discovery of statins has led to significant progress in both primary and secondary prevention of coronary heart disease. Although the angiographic changes following statin therapy were modest, the clinical benefits associated with therapy were significant. Numerous clinical trials have correlated the reduction in blood cholesterol induced by these compounds by reducing the number of major coronary events as well as reducing overall mortality in coronary patients

KEYWORDS: statins, UV spectrum, heart disease, cholesterol

INTRODUCTION

Statins are the most effective drugs in the treatment of atherogenesis, but they are only one of a number of other lipid-lowering medications that act by various mechanisms: fibrates, bile acid-binding resins and the latest acquisition, ezetimibe, an absorption inhibitor intestinal cholesterol. (1-6).

The first commercially available statin, lovastatin, was introduced by the Merck Pharmaceutical Industry. (9) It was subsequently confirmed that statins effectively reduce LDL cholesterol. Japanese biochemist Akira Endo was awarded 30 years later with the prestigious Lasker Award for discovering an agent that blocks cholesterol synthesis (12-22).

The pharmaceutical industry continuously modifies statin molecules. After lovastatin, fluvastatin, pravastatin and simvastatin, atorvastatin, cerivastatin, pitavastatin and recently most effective, rosuvastatin (7-11).

Intravascular ultrasound imaging studies performed in clinical trials with rosuvastatin and atorvastatin revealed regression of atheromatous plaques (5).

Currently, statins are part of the second category of drugs most commonly prescribed for anticancer drugs. In the 2003-2004 period statins were used by 24 million North Americans (22-28).

Some statins (like lovastatin - Mevacor, pravastatin - Lipostat, Pravachol and simvastatin-Zocor) are obtained by fungal fermentation, and others are obtained by synthesis: fluvastatin (Lescol), atorvastatin (Sortis, Lipitor) and cerivastatin (Baycol). It should be

noted that on August 8, 2001, Bayer AG banned cerivastatin on the pharmaceutical market worldwide, after 31 patients died with acute renal failure due to rhabdomyolysis, and the FDA (Food and Drug Administration) supported this decision. (15 to 19).

Only 6 statins are currently used: lovastatin, simvastatin, pravastatin, atorvastatin, fluvastatin and rosuvastatin (29-30).

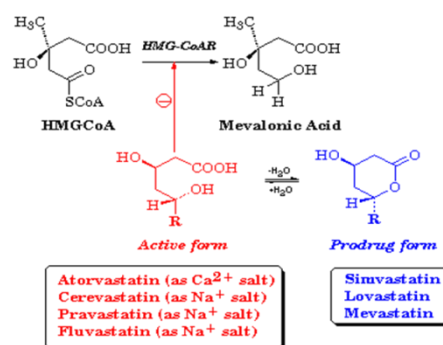


Fig no 1. Statin synthesis

(www.auburn.edu/~rileytn/py421graphics/statins.gif)

MATERIAL AND METHODS

The present study is a retrospective review of the clinical observation sheets of patients admitted to the Cardiology Clinical Section of the Arad County Emergency Clinical Hospital in October 2016. The patients were hospitalized with various pathologies and some of them required lipid-lowering treatment with statins (the one studied - Atorvastatin).

During October 2016, 151 patients were hospitalized in this section, of which 75 (49.67%) required statin-treated lipid-lowering treatment. Patients in the study group had a mean age \pm SD (standard deviation) of 60.09 ± 11.431 years (age range 32 years to 86 years).

Of the total of 75 patients who received statin-treated hypolipidemic therapy, 42 (56%) were female and 33 (44%) were male; with regard to the environment of these patients it was for 40 patients (53.33%) the urban environment and for the remaining 35 patients (46.66%), the rural environment.

RESULTS AND DISCUSSIONS

During the testing, 151 patients were hospitalized in this unit, of which 75 (49.67%) required statin-treated lipid-lowering treatment.

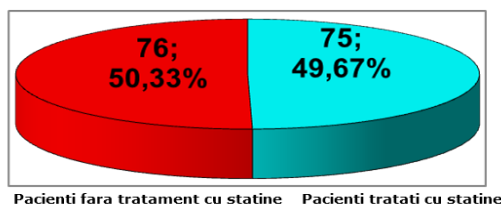


Fig.no.2 Representation of patients who had statin therapy

Patients in the study group had a mean age \pm SD (standard deviation) of 60.09 ± 11.431 years (age range 32 years to 86 years).

Of the total of 75 patients who received statin-treated hypolipidemic therapy, 42 (56%) were female and 33 (44%) were male; with regard to the environment of these patients it was for 40 patients (53.33%) the urban environment and for the remaining 35 patients (46.66%), the rural environment.

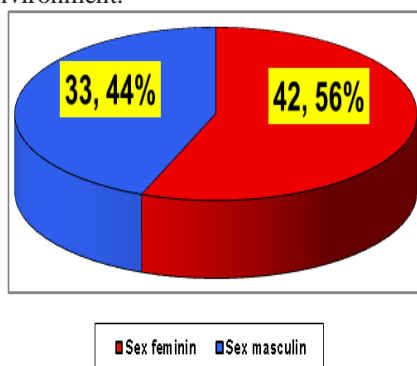


Fig.no.3 Distribution of patients in the study group after sex

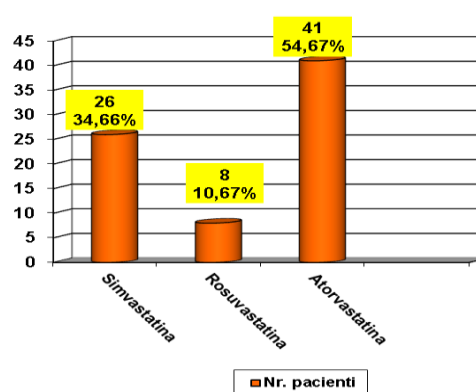


Fig.no.4 The distribution of patients according to the type of statin taken

Following the distribution of patients in the study group by the amount of rosuvastatin (crest) taken, it can be seen that all eight patients (100%) taking this statin used the 10 mg / day dose. In terms of gender distribution, 5 (62.5%) were male and 3 female (37.5%) were female.

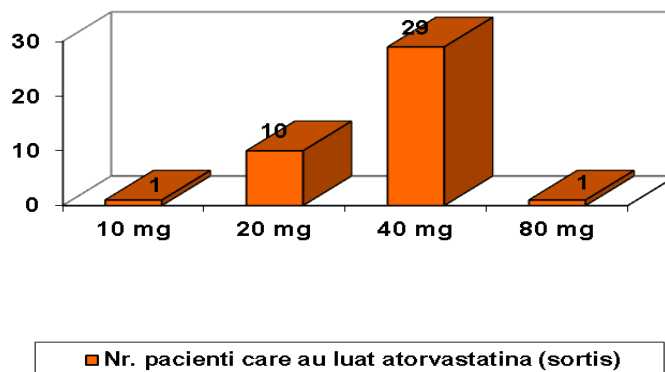


Fig.no 5 The distribution of patients taking atorvastatin (sortis) after the statin dose taken.

The distribution of patients in the study group by the amount of atorvastatin (sortis) taken, it can be seen that the vast majority (29 patients, 70.73%) took a daily dose of 40 mg of atorvastatin; At the same time, 10 patients (24.39%) took a daily dose of 20 mg, one patient (2.44%) took 10 mg daily and one patient (2.44%) took the daily maximum dose of 80 mg of atorvastatin. As regards the distribution of these patients by sex, it was found to be approximately equal, ie 23 patients (56.09%) were female and 18 patients (43.91%) were male

Statins or 3-HMG-CoA reductase inhibitors are the most effective drugs for reducing LDL-cholesterol and total plasma cholesterol, which significantly reduces cardiovascular morbidity and mortality and overall mortality

Statins are well tolerated and have well documented safety, rarely cause adverse effects, the most important being muscle (myositis, rhabdomyolysis) and hepatic (elevated liver transaminases).

Lipid-lowering treatment consisted of atorvastatin (54.67%), simvastatin (34.66%) and rosuvastatin (10.67%); Daily doses were varied atorvastatin (10, 20, 40 and 80 mg / day), simvastatin (20, 40 and 80 mg / day) and rosuvastatin 10 mg / day.

Evolution was favorable for all patients, and continued discontinuation of hypolipidemic therapy with statins, predominantly sortis (atorvastatin), treatment of associated diseases as well as hygienic-dietary regimen and periodic specialized controls

BIBLIOGRAPHY

1. Hunninghake D.B. - *HMG-CoA reductase inhibitors*, Curr. Opin. Lipidol., 1992, 3: 22-8
2. Ghinghină Carmen, Enache Roxana - *Dislipidemia și riscul cardiovascular: de la factorii clasici la noile fracțiuni lipidice*, Stetoscop, Mai 2006, Anul 5, Nr. 50, pag. 20-23
3. Pârvolescu V-N, și colab. - *Dislipidemiile și relația lor cu patologia generală*, Practica Medicală, 2007, Vol. 2, Nr. 4(8), pag. 254-260
4. Rusu Emilia, Cheța DM - *Trigliceridele și riscul cardiovascular*, Stetoscop, Anul 6, Nr. 61, Aprilie 2007, pag. 16-20
5. Efthimiades A. - *Rosuvastatin and cardiovascular disease: did the strongest statin hold the initial promises?*, Angiology, 2008, 59: 62S-64S
6. Vaughan C.J., Gotto A.M., Basson C.T. - *The evolving role of statins in the management of atherosclerosis*, J. Am. Coll. Cardiol., 2000, 35: 1-10
7. Bellosta S., Ferri N., Bernini F., Paoletti R., Corsini A. - *Non-lipid-related effects of statins*, Ann. Med., 2000, 32: 164-176
8. Lennernas H., Fager G. - *Pharmacodynamics and pharmacokinetics of the HMG-CoA reductase inhibitors: similarities and differences*, Clin. Pharmacokinet., 1997, 32: 403-425
9. Corsini A., Bellosta S., Baetta R., Fumagalli R., Bernini F. - *New insights into the pharmacodynamics and pharmacokinetic properties of statins*, Pharmacol. Ther., 1999, 84: 413-28
10. Sehayek E., Butbul E., Avner R. - *Enhanced cellular metabolism of very low density lipoprotein by simvastatin: a novel mechanism of action of HMG-CoA reductase inhibitors*, Eur. J. Clin. Invest., 1994, 24: 173-8
11. Blum C.B. - *Comparison of properties of four inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase*, Am. J. Cardiol., 1994, 73: 3D-11D
12. Rizzo M., Rini GB, Berneis R. - *Effects of statins, fibrates, rosuvastatin and ezetimibe beyond cholesterol: the modulation of LDL size and subclasses in high-risk patients*, Adv. Ther., 2007, 575-582
13. Thavandiranathan P., bagal A., Brookhart A., et al. - *Primary prevention of cardiovascular diseases with statin therapy. A meta-analysis of randomized controlled trials*, Arch. Intern. Med., 2006, 166: 2307-2313
14. Afilalo J., Majdan AA, Eisenberg MJ - *Intensive statin therapy in acute coronary syndromes and stable coronary heart disease: a comparative meta-analysis of randomised controlled trials*, Heart, 2007, 93: 914-921
15. Fauchier L., Pierre B., de Labriolle A., et al - *Antiarrhythmic effect of statin therapy and atrial fibrillation. A meta-analysis of randomized controlled trials*, J. Amer. Coll. Cardiol., 2008, 51: 828-835
16. Blumenthal RS. - *Statins: effective antiatherosclerotic therapy*, Am. Heart. J., 2000, 139: 577-83
17. Kostner G.M., Gavish D., Leopold B., Bolzano K., Weintraub M.S., Breslow J.L. - *HMG-CoA reductase inhibitors lower LDL cholesterol without reducing Lp(a) levels*, Circulation, 1989, 80: 1313-1319
18. Stein E.A., Lane M., Laskarzewski P. - *Comparison of statins in hypertriglyceridemia*, Am. J. Cardiol., 1998, 81: 66B-69B
19. Gaw A., Packard C.J., Murray E.F. - *Effects of simvastatin on apoB metabolism and LDL subfraction distribution*, Arterioscler. Thromb., 1993, 13: 170-89
20. Marais A.D., Naumova R.P., Firth J.C., Penny C., Neuwirth C.K., Thompson G.R. - *Decreased production of low density lipoprotein by atorvastatin after apheresis in homozygous familial hypercholesterolemia*, J. Lipid Res., 1997, 38: 2071-2078
21. Raal F.J., Pilcher G.J., Illingworth D.R., Pappu A.S., Stein E.A., et al. - *Expanded dose simvastatin is effective in homozygous familial hypercholesterolemia*, Atherosclerosis, 1997, 135: 249-256
22. Hoffman R., Brook G.J., Aviram M. - *Hypolipidemic drugs reduce lipoprotein susceptibility to undergo lipid peroxidation: in vitro and ex vivo studies*, Atherosclerosis, 1992, 93: 105-13
23. Chen L., Haught W.H., Yang B. - *Preservation of endogenous antioxidant activity and inhibition of lipid peroxidation as common mechanisms of antiatherosclerotic effects of vitamin E, lovastatin and amlodipine*, J. Am. Coll. Cardiol., 1997, 30: 569-75
24. Aviram M., Hussein O., Rosenblat M., Schleisinger S., Hayek T., Keidar S. - *Interactions of platelets, macrophages, and lipoproteins in hypercholesterolemia: antiatherogenic effects of HMG-CoA reductase inhibitor therapy*, J. Cardiovasc. Pharmacol., 1998, 31: 39-45,
25. Pietsch A., Erl W., Lorenz R.L. - *Lovastatin reduces the expression of the combined adhesion and scavenger receptor CD36 in human monocytic cells*, Biochem. Pharmacol., 52: 433, 1996
26. Bernini F., Didoni G., Bonfadini G., Bellosta S., Fumagalli R. - *Requirement for mevalonate in acetylated LDL induction of cholesterol*

esterification in macrophages, Atherosclerosis, 1993, 104: 19-26

27. Bellosta S., Via D., Canavesi M., Pfister P., Fumagalli R., Paoletti R. - *HMG-CoA reductase inhibitors reduce MMP-9 secretion by macrophages*, Arterioscler. Thromb. Vasc. Biol., 1998, 18: 1671-8

28. Ballantyne C.M., Herd J.A., Dunn J.K., Jones P.H., Farmer J.A., Gotto A.M.J. - *Effects of lipid lowering therapy on progression of coronary and*

carotid artery disease, Curr. Opin. Lipidol., 1997, 8: 354-361

29. Libby P. - *Atherosclerosis: the new view*, Sci. Amer., 2002, 286: 47-55

30. Libby P. - *The molecular mechanisms of the thrombotic complications of atherosclerosis*, J. Intern. Med., 2008, 263: 517-527

CORRESPONDENCE ADDRESS

annamariapallag@yahoo.com