

<https://doi.org/10.15407/dopovidi2020.11.092>

UDC 616.12-009.72-085.272.4 :612.112.94 :577.352.3:577.115.3

T.V. Bogdan

Bogomolets National Medical University, Kyiv

E-mail: taviza@mail.ua

Effect of atorvastatin and rosuvastatin on the fatty acid spectrum of lymphocyte membranes in patients with unstable angina

Presented by Corresponding Member of the NAS of Ukraine V.P. Shyrobokov

Numerous studies have demonstrated the superiority of rosuvastatin over other statins in the treatment of cardiovascular disease. It has been proven that rosuvastatin is more effectively lowers low-density lipoprotein cholesterol in patients with cardiovascular disease than other members of this drug group. Despite the known mechanisms of action of statins on blood lipids, their effective use in patients with cardiovascular disease, as well as side effects, the influence of these drugs on the fatty acid spectrum of lymphocyte (LC) membrane phospholipids in patients with ischemic heart disease remains unexplored. The results of the studies cited in the article indicate that, in patients with unstable angina who received the therapy that included rosuvastatin, unlike patients receiving the basic treatment with atorvastatin, the relative phosphate lipid contents of palmitic, stearic, and stearin arachidonic polyunsaturated fatty acids and the amount of unsaturated fatty acids are normalized, which testifies to the stabilization of membranes as dynamic structures.

Keywords: *unstable angina, atorvastatin, rosuvastatin, lymphocytes, fatty acids.*

Randomized clinical trials have demonstrated a high efficacy of statins in reducing the incidence of recurrent coronary heart disease (CHD): myocardial infarction, unstable angina, and sudden death by more than 25–40 %. The mechanism of action of all statins is due to the inhibition of the main enzyme involved in the synthesis of cholesterol (cholesterol) – HMG-CoA reductase of liver [1].

The use of statins is recommended for all patients with coronary heart disease, in the absence of reservations and provides for the level of low-density lipoprotein cholesterol (LDL) < 1.8 mmol/l, if this is not possible, it is recommended to reduce this figure by at least 50.0 % of the initial value [1]. Clinical studies have shown that the prophylactic effect of statins is to reduce the concentration of LDL cholesterol, highly sensitive C-reactive protein, and to increase the level of high-density lipoprotein cholesterol (HDL) [2]. Numerous studies have now shown

Цитування: Bogdan T.V. Effect of atorvastatin and rosuvastatin on the fatty acid spectrum of lymphocyte membranes in patients with unstable angina. *Допов. Нац. акад. наук Укр.* 2020. № 11. С. 92–95. <https://doi.org/10.15407/dopovidi2020.11.092>

the superiority of rosuvastatin over other statins in the treatment of cardiovascular disease (CVD). Rosuvastatin has been shown to reduce the LDL cholesterol levels more effectively in patients with CVD than other members of this group of drugs [3]. The role of rosuvastatin in the primary prevention of CVD was proven in the METEOR study, which evaluated the effect of taking rosuvastatin at a dose of 40 mg per day on the subclinical course of atherosclerosis in the carotid arteries [4].

According to a meta-analysis [5], 10 mg of rosuvastatin provide the same reduction in LDL cholesterol levels as 30 mg of atorvastatin. Thus, in a 6-week open-label randomized study, STELLAR studied the hypolipidemic efficacy of rosuvastatin at doses of 10, 20, 40, or 80 mg per day compared with atorvastatin 10, 20, 40, or 80 mg per day, simvastatin 10, 20, 40, or 80 mg per day, and pravastatin 10, 20 or 40 mg per day in patients with hypercholesterolemia [6].

Material and research methods. Seventy-five NS patients aged 59-67 years (mean age 66 years \pm 5.2 years) were examined and divided into two groups: Group I – 35 people received bisoprolol at doses of 5 mg, enalapril 10 mg, atorvastatin 20 mg, acetylsalicylic acid 75 mg during the day, fondaparinux sodium 2.5 mg subcutaneously, isosorbide dinitrate 20 mg; group II – 37 patients received bisoprolol at doses of 5 mg, enalapril 10 mg, rosuvastatin 10 mg, acetylsalicylic acid 75 mg, fondaparinux sodium 2.5 mg subcutaneously, isosorbide dinitrate 20 mg. Examination of patients was performed at the beginning of the treatment and after 20 days. The control group (CG) included 18 healthy individuals aged 49-58 years (mean age – 53.4 years \pm 4.7 years).

Gas-chromatographic analysis of the spectrum of fatty acids of PL in membranes of LCs was performed using a gas chromatograph “Color-500” with a flame ionizing detector in the isometric mode. In the LC membranes, the following LCDs were identified: C14:0 – myristic acid, C15:0 – pentadecanoic acid, C16:0 – palmitic acid, C17:0 – margaric acid, C18:0 – stearic acid, C18:1 – oleic acid, C18:2 – linoleic acid, C18:3 – linolenic acid, C20:4 – arachidonic acid. Of these – saturated LCD (NLC): myristic (C14:0), pentadecane (C15:0), margarine (C17:0),

Effect of atorvastatin and rosuvastatin on the fatty acid spectrum of lymphocyte membranes in patients with unstable angina, % ($M \pm m$)

Indicators	KG, n = 18 (1)	Before treatment	After treatment		PI-2	PI-3
			atorvastatin, n = 35 (2)	rosuvastatin, n = 37 (3)		
C14:0	13.9 \pm 0.5	9.7 \pm 0.05	10.2 \pm 0.07	10.5 \pm 0.07	< 0.05	< 0.05
C15:0	2.4 \pm 0.03	4.4 \pm 0.06	3.9 \pm 0.05	4.0 \pm 0.06	< 0.05	< 0.05
C16:0	12.3 \pm 0.4	9.6 \pm 0.3	8.7 \pm 0.5	11.5 \pm 0.4	< 0.05	> 0.05
C17:0	2.3 \pm 0.07	2.6 \pm 0.06	2.7 \pm 0.06	2.9 \pm 0.06	> 0.05	> 0.05
C18:0	3.2 \pm 0.06	4.8 \pm 0.05	4.7 \pm 0.06	3.4 \pm 0.05	< 0.05	> 0.05
C18:1	42.8 \pm 1.2	51.2 \pm 1.8	49.7 \pm 1.5	47.3 \pm 1.5	< 0.05	< 0.05
C18:2	11.7 \pm 0.4	12.5 \pm 0.4	12.7 \pm 1.5	11.4 \pm 1.6	> 0.05	> 0.05
C18:3	2.7 \pm 0.05	2.5 \pm 0.06	3.2 \pm 0.07	1.2 \pm 0.04	> 0.05	< 0.05
C20:4	8.7 \pm 0.05	2.7 \pm 0.05	4.2 \pm 0.05	7.8 \pm 0.05	< 0.05	> 0.05
Σ SFA	34.1 \pm 1.0	31.1 \pm 1.5	30.2 \pm 1.6	32.3 \pm 1.6	< 0.05	> 0.05
Σ NFA	65.9 \pm 1.2	68.9 \pm 1.7	69.8 \pm 1.9	67.7 \pm 1.8	< 0.05	> 0.05
Σ PFA	23.1 \pm 1.7	17.7 \pm 0.7	20.1 \pm 1.5	20.4 \pm 1.5	< 0.05	< 0.05

palmitic (C16:0), stearic (C18:0); unsaturated LC (NLC): oleic (C18:1); polyunsaturated LC (PUFA): linoleic (C18:2), linolenic (C18:3), arachidonic (C20:4).

Results and Discussion. The effects of atorvastatin and rosuvastatin on FSW membranes in patients with NA have been studied.

In patients with NS treated with rosuvastatin unlike patients whose basic therapy included atorvastatin, the relative contents of palmitic acid (C16:0) and stearic acid (Table) were normalized in comparison with KG in PL membranes.

It should be noted that, in patients of group II, unlike patients of group I, the relative content of linolenic acid (C18:3) in the PL membranes of LCs was significantly lower compared to KG by 55.6 % ($p < 0.05$).

Due to the decrease in the relative content of linolenic acid (C18:3), which is a substrate for the synthesis of arachidonic acid (C20:0), the relative content of arachidonic acid in PL LC membranes in patients receiving rosuvastatin significantly increased compared with the indicator before the treatment by 65.4 % ($p < 0.05$) and normalized compared with CG (8.7 ± 0.5 and 7.8 ± 0.5 , $p > 0.05$). Against the background of receiving rosuvastatin in patients with NA in PL LC membranes compared with KG, the relative content of NNZHK also normalized (65.9 ± 1.2 and 67.7 ± 1.8 , $p > 0.05$).

Therefore, against the background of taking rosuvastatin compared with atorvastatin in patients with NA in PL LC membranes, the dynamics of some higher LCD was revealed. Normalization of the relative content of saturated palmitic (C14:6) and stearic LCD in PL LC membranes in patients receiving rosuvastatin may indicate the stabilization and a decrease in the fluidity of LC membranes. The normalization of the arachidonic acid content (C20:4) in comparison with the indicator before the treatment also testifies to the improvement of the structure of LC membranes against the background of the rosuvastatin administration.

Conclusions.

1. In patients with emergencies, who received the therapy that included rosuvastatin, unlike patients receiving the low-dose atorvastatin treatment, the relative content of palmitic and stearic saturated LCDs was normalized in the PL membranes of lymphocytes.

2. In patients with NA, who received rosuvastatin, unlike patients whose antianginal therapy included atorvastatin, in the PL LC membranes, the relative content of arachidonic PAH of PA NNZHK was normalized, indicating the stabilization of LC membranes as dynamic structures.

REFERENCES

1. Fayura, O. P. (2014). European Society of Cardiology guidelines on the management of stable coronary artery disease (2013). *Lviv. Klinich. Visn.*, No. 1-2, pp. 58-69. <https://doi.org/10.25040/lkv2014.01.058> (in Ukrainian).
2. Crouse, J. R., Raichlen, J. S., Riley, W. A., Evans, G. W., Palmer, M. K., O'Leary, D. H., Grobbee, D. E., Bots, M. L. & METEOR Study Group (2007). Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR Trial. *JAMA*, 297, No. 12, pp. 1344-1353. <https://doi.org/10.1001/jama.297.12.1344>
3. Kjekshus, J., Apetrei, E., Barrios, V., Böhm, M., Cleland, J. G. F., Cornel, J. H., Dunselman, P., Fonseca, C., Goudev, A., Grande, P., Gullestad, L., Hjalmarsen, Å., Hradec, J., Jánosi, A., Kamenský, G., Komajda, M., Korewicki, J., Kuusi, T., Mach, F., Mareev, V., McMurray, J. J. V., Ranjith, N., Schaufelberger, M., Vanhaecke, J.,

- van Veldhuisen, D. J., Waagstein, F., Wedel, H. & Wikstrand, J. for the CORONA Group (2007). CORONA Group Rosuvastatin in older patients with systolic heart failure. *N. Engl. J. Med.*, 357, No. 22, pp. 2248-2261. <https://doi.org/10.1056/NEJMoa0706201>
4. Luvai, A., Mbagaya, W., Hall, A. S. & Barth, J. H. (2012). Rosuvastatin: a review of the pharmacology and clinical effectiveness in cardiovascular disease. *Clin. Med. Insights. Cardiol.*, 6, pp. 17-33. <https://doi.org/10.4137/CMC.S4324>
5. Nicholls, S. J., Brandrup-Wognsen, G., Palmer, M. & Barter, P. J. (2010). Meta-analysis of comparative efficacy of increasing dose of Atorvastatin versus Rosuvastatin versus Simvastatin on lowering levels of atherogenic lipids (from VOYAGER). *Am. J. Cardiol.*, 105, No. 1, pp. 69-76. <https://doi.org/10.1016/j.amjcard.2009.08.651>
6. Pharmaceutical Benefits Advisory Committee July 2006. (2006). Positive recommendations. Canberra: Australian Government Department of Health and Ageing. Retrieved from <http://www.ag.gov.au/cca>

Received 06.02.2020

Revised version: 23.10.2020

T.B. Богдан

Національний медичний університет ім. О.О. Богомольця, Київ

E-mail: taviza@mail.ua

ВПЛИВ АТОРВАСТАТИНУ ТА РОЗУВАСТАТИНУ НА ЖИРНОКИСЛОТНИЙ СПЕКТР МЕМБРАН ЛІМФОЦИТІВ У ХВОРИХ НА НЕСТАБІЛЬНУ СТЕНОКАРДІЮ

Численними дослідженнями показано перевагу розувастатину над іншими статинами в лікуванні серцево-судинних захворювань. Доведено, що розувастатин ефективніше знижує рівень холестерину ліпопротеїдів низької щільності у хворих із серцево-судинними захворюваннями, ніж інші представники цієї групи лікарських препаратів. Попри відомі механізми дії статинів на ліпіди крові, їх ефективне застосування у хворих із серцево-судинними захворюваннями, а також побічну дію, залишається не вивченим вплив цих препаратів на жирнокислотний спектр фосfolіпідів мембран лімфоцитів у хворих на ішемічну хворобу серця, зокрема стабільну стенокардію. Результати досліджень, наведені у повідомленні, вказують на те, що у хворих на нестабільну стенокардію, які отримували терапію, яка включала розувастатин, на відміну від хворих, що приймали базисне лікування з аторвастатином, у фосfolіпідах мембран нормалізувався відносний вміст пальмітинової та стеаринової насичених жирних кислот, відносний вміст арахідонової поліненасиченої жирної кислоти і суми ненасичених жирних кислот, що свідчить про стабілізацію мембран як динамічних структур.

Ключові слова: *нестабільна стенокардія, аторвастатин, розувастатин, лімфоцити, жирні кислоти.*