УДК 616-053.8: 616-08-059

COGNITION-MEDIATED PLEIOTROPIC EFFECTS OF AGE ORIENTED STATIN THERAPY IN THE ELDERLY

Fesenko E.V., [1] Zhiljakova E.T [1]

[1]Belgorod State National Research University, 85 ul. Pobedy, Belgorod 308015; e-mail: FesenkoE@bsu.edu.ru

Summary. The article presents the results of a study of medico-social significance of the conduct statinotherapy in elderly and senile age in conjunction with the pleiotropic effects of statins. The use of modern statins in addition to providing basic lipidnormalized effect able to increase the level of psychological well-being and the quality of life of the people as the middle, and older. In addition, in people of older age groups , age characteristic of the positive impact of statinotherapy on the General background of psychological prosperity is the effect on cognitive-mediated settings, such as depression and self-control. Thus, this article shows, what is the clinical significance and social feasibility of statinotherapy in high age groups of patients consist in their pleiotropic effects, such as reducing the level of depression, improved cognitive abilities, increasing the level of psychological well-being and quality of life.

Keywords. quality of life, pleiotropic effects, statins, depression, *cognitive function*, age oriented, elderly.

КОГНИТИВНО-ОПОСРЕДОВАННЫЕ ПЛЕЙОТРОПНЫЕ ЭФФЕКТЫ ВОЗРАСТ-ОРИЕНТИРОВАННОЙ СТАТИНОТЕРАПИИ У ПАЦИЕНТОВ СТАРШИХ ВОЗРАСТНЫХ ГРУПП.

Фесенко Э.В., [1] Жилякова Е.Т [1]

[1]Белгородский государственный национальный исследовательский университет, Белгород, Россия, 308015, ул. Победы 85,e-mail: Fesenko_E@bsu.edu.ru.

Резюме. В статье приведены результаты исследования медико-социальной значимости проведения статинотерапии у людей пожилого и старческого возраста в связи с плейотропными эффектами статинов. Применение современных статинов помимо обеспечения основного липиднормализующего эффекта способно повышать уровень психологического благополучия и качества жизни у людей как среднего, так и пожилого возраста. Кроме того, у людей старших возрастных групп возраста возрастной особенностью положительного влияния статинотерапии на общий фон психологического благополучия является воздействие на когнитивно-опосредованные параметры, такие как депрессия и самоконтроль. Таким образом, в данной статье показано, что клиническая значимость и социальная целесообразность применения статинотерапии в старших возрастных группах пациентов заключалась в их плейотропных эффектах, таких как снижение уровня депрессии, улучшение когнитивных способностей, повышение уровня психологического благополучия и качества жизни.

Ключевые слова: качество жизни, плейотропные эффекты, статины, депрессия, когнитивная функция, возрасториентированный, пожилой возраст.

The urgency of the problem. Currently, there is the problem of adequate medical management of patients in older age groups of the cardiological profile. This is due to the

existing objective laws of the pharmacodynamics and pharmacokinetics of drugs in elderly and senile age, the use of special forms of production of medicines, facilitating access to them, an elderly patient having, as a rule, the pathology of the organ of vision, the defeat of small joints of the hand with a reduction in its functions, cognitive disorders [Proshhaev K.I., Il'nickij A.N., 2012; Vahnina N.V., 2013].

According to the literature, many professionals ignore the use of statins in geriatric practice, age of patients, not feeling quick effect and fear of complications, have a low level of adherence to statins. This leads to a reduction in the quality of supervision of large groups of patients of elderly and senile age with lipid disorders [Smith, S. C. Jr., 2006]. At the same time, there is abundant evidence that statins have not only a corrective effect against atherogenic disorders, but have multiple pleiotropic effects, which can be very useful in the treatment of elderly patients with poly morbid background of pathological processes [Aronov D.M., 2004; Chokshi NP, 2012; Fitchett DH, 2014].

Purpose of the study. To substantiate the medical and social significance of statin therapy in elderly people due to the pleiotropic effects of statins.

Material and methods. To conduct age analysis of pleiotropic effects of statin therapy we have carried out a randomised prospective study in which two groups of patients of control and basic. The control group consisted of 32 patients of middle age (the average age was 54 years) and 31 patients of advanced age (average age was 71 years); the main group included 31 patients of middle age (the average age was 54 years) and 32 patients of advanced age (average age was 71 years). In the main group, 1 patient middle-aged (man) were excluded from the study due to the fact that it was canceled statins after 3 weeks of the start of administration in connection with a two-fold excess of the level of transaminases in blood serum.

In relation to elderly patients this section of the research has not been conducted because currently there is no generally accepted approach to the question whether the patients of senile age to start statin therapy , if before that age they are as received.

The inclusion criteria in the study were the following: presence of hypertension with normal blood pressure on the background of continuous use of antihypertensive therapy; Hyperlipidemia type IIb, the presence of abdominal obesity stage I, which together imply a moderate risk of cardiovascular complications, identified in the SCORE scale. The choice of these criteria for inclusion in the study due to the fact that a moderate risk of cardiovascular complications of the atherosclerotic process is the most common in the population that implies a high degree of social relevance of research in this area.

Exclusion criteria were the presence of diabetes type II, positive family history in terms of early development of cardiovascular events, Smoking, chronic immune-inflammatory diseases in the anamnesis, chronic renal pathology.

In the course of the study, the duration of which was three months, patients of the main group on the background they received antihypertensive therapy was appointed domestic drug "pravastatin" in a dose of 10 mg/day; the control group patients were recommended non-pharmacological measures-correction of lipid metabolism disorders, in particular, aerobic exercise, dietary recommendations.

The results and discussion.

At the end of the three month observation period in patients of control and basic groups was assessed the level of depression scale Montgomery-Asberg to Assess Depression (Montgomery-Asberg Depression Scale), anxiety level on a Scale of Covey (Covi Anxiety Scale) and as an Index of General Psychological well-being (Psychological General Well Being Index), level of cognitive ability on Questionnaire "Memory in Daily Life" (Everyday Memory Questionnaire).

Age and antilipidemic effects of statin therapy.

In the control group of patients, both middle and elderly age, who did not receive statin therapy , and received only non-pharmacological measures for the normalisation of lipid metabolism after 3 months failed to achieve positive changes in lipid status or in patients of middle or advanced age. In particular, patients of middle age lipid profile had the following dynamics during three-month observation: Ochs, respectively 5,7+0,2 mmol/l and 5.6+0.1 mmol/l, LDL cholesterol – 3,7+0,1 mmol/l and 3.5+0.3 mmol/l, HDL cholesterol of 1.2+0.1 mmol/l and 1.1+0.2 mmol/l, TG – 1,9+0,1 mmol/l and 1.7+0.2 mmol/l, for all lipid $p>0.05$. In the elderly with use-drug treatment also had a similar situation.

At the same time, application of the "Pravastatin", we obtained distinct antihyperlipidemic effects confirmed a statistically significant dynamics improve lipid metabolism (table 1). In particular, patients of middle age has been significantly ($p<0.05$) decrease in the cholesterol level by 12.5%, LDL cholesterol – by 12.6%, the level of TG – 16.7%, and the level of HDL cholesterol in these patients significantly ($p<0.05$) increased by 14.3%. That is especially important, similar positive shifts were noted in the elderly patients was significantly ($p<0.05$) decrease in the level of total cholesterol by 14.0%, LDL cholesterol – by 19.4%, the level of TG – 21.1%, and the level of HDL cholesterol in these patients significantly ($p<0.05$) increased by 14.3%.

Table *1*

Dynamics of lipid metabolism by statins influence

Indicators	Patients			
	Middle age (n=30)		Elderly patients (n=32)	
	Before studies	After three months	Before studies	After three months
Cholesterol (mmol/L)	5,6±0,10	4,9±0,20*	5,7±0,19	4,9±0,10*
LDL (mmol/L)	3,7±0,10	2,9±0,05*	3,6±0,06	2,9±0,04*
HDL (mmol/L)	1,2±0,11	1,4±0,08*	1,2±0,06	1,4±0,04*
TG (mmol/L)	1,8±0,09	1,5±0,03*	1,9±0,02	1,5±0,05*

*p<0,05 in comparison with the index before studies in the relevant age group

Age and the effect of statin therapy on the level of anxiety.

In our study in relation to "Pravastatin" was not evidence of its protective effect neither on average, and in old age. The average age of patients in the control group prior to surveillance total score characterising the level of anxiety was of 3.4+0.1 points, after three months and 3.4+0.2 points; the patients of the study group the total score of anxiety level was equal to 3.5+0,2 points, after a three-month follow-up period of 3.5+0.3 points, p>0.05. In old age also had a statistically significant dynamics of anxiety level in control and treatment groups. In the control group the total score before the observation was consistent with 3,4+0,2 points, after three months, and 3.4+0.1 points; in the main group it was equal 3,5+0,2 points to the start of the study and was not significantly changed after three months of therapy "Pravastatin" were consistent with a 3.5+0.3 points, p>0.05**.**

The influence of statin therapy on cognitive function in the elderly.

Initially, the cognitive deficit in the elderly patients, according to the Questionnaire "Memory in Daily Life" (Everyday Memory Questionnaire) was significantly (p<0.05) naturally more pronounced in elderly patients than in patients of middle age. The result of applying "Pravastatin" was a statistically significant improvement of cognitive abilities in patients of advanced age who took statins prior to the initial observation of 48.2+2.2 points, within three months, and 64.6+4.0 points, p<0.05. Despite the fact that older patients failed to achieve the level

of cognitive abilities similar to middle aged patients, it is important authentic the dynamics of this indicator. Interesting fact is that patients of middle age who took statins were not registered reliably the dynamics of cognitive status, there was a positive trend. This could be due to the initially better cognitive status of patients of middle age.

Age and antidepressant effects of station therapy.

If you use "Scale Montgomery-Asberg to assess depression revealed" that there has been a decrease in subjective feelings of depression under the influence of the applied "Pravastatin" in the group of elderly patients (table 2). If, prior to the start of treatment, this figure amounted to 1.6+0.2 points, after three months of 1.0+0.1 points, i.e. a reduction by 37.5%, $p<0.05$. In addition, there was lower reflecting the poor concentration of 33.3% – before treatment, this figure was 2.1+0.2 points, after three months and 1.4+0.2 points, $p<0.05$. The indicator of the intentions in the activities prior to the observation was 1.6+0.3 points, after three months – 0,9+0,1 score, i.e., decreased by 43.8%, $p<0.05$.

Table 2

Scale Montgomery-Asberg to assess depression revealed (in points)

Scale position	Patients							
	Control group				Main group			
	Middle age		Elderly patients		Middle age		Elderly patients	
	Before studies	After three months	Before studies	After three months	Before studies	After three months	Before studies	After three months
Subjective feelings of depression	1,7±0,1	1,8±0,3	1,7±0,2	1,6±0,3	1,6±0,2	1,5±0,3	1,6±0,2	1,0±0,1 *,**
Reduced sleep	1,9±0,2	1,8±0,3	1,8±0,3	1,7±0,3	1,8±0,2	1,7±0,3	1,7±0,2	1,1±0,1 *,**
Poor concentration	2,2±0,2	2,2±0,1	2,3±0,3	2,2±0,2	2,2±0,2	2,3±0,3	2,1±0,2	1,4±0,2 *,**

Intentions in the activities	1,8±0,2	1,7±0,3	1,6±0,3	1,7±0,2	1,6±0,2	1,8±0,4	1,6±0,3	0,9±0,1 *,**

* p<0,05 compared with the patients of middle age

** p<0,05 compared with the value of the index before studies

Thus, the application of statin therapy in the elderly was significantly decreased and levels of depression due to the cognitive component, in particular, contributing to reduced subjective symptoms of the depressive syndrome, increasing the concentration of attention and intention in activities. These data were corresponded with the obtained results of the study to study the effects of statins on cognitive abilities of older people. In patients of middle age, taking statins, this positive dynamics was not detected. This is because depression in patients included in the study, were linked by common pathogenesis of cognitive disorders, and middle-aged people initially, cognitive impairment was less pronounced dynamics of cognitive status in the process of therapy was not significant.

Age and the effect of station therapy on the level of General psychological well-being. In the analysis of issues of scale reflecting psychological well-being, a number of positions received significant positive changes in the application of statin therapy the elderly (table 3).

Table 3

Dynamics of self-control by the influence of statin therapy

Scale position	Group			
	Middle age		Elderly patients	
	Before studies	After three months	Before studies	After three months
Behavior monitoring	4,4±0,23	4,5±0,12	4,2±0,03	4,8±0,03*
Afraid losing control	4,6±0,02	4,6±0,08	4,0±0,01	4,6±0,22*
Self-doubt	4,8±0,14	4,8±0,06	4,2±0,03	4,9±0,12*

*p<0,05 in comparison with the index before the start of the observation

For example, scoring the question "if You controlled your behaviour, thoughts, emotions, feelings?" during the follow-up was 4.2+0.03 points and 4.8+0.03 points, respectively, $p<0.05$. Key evaluation question "did You have reason to believe that You lost control of your mind, memory, feelings, words?" were respectively 4,0+0,01 points and 4.6+0.22 points, $p<0.05$. Key evaluation question "did You have a sense of confidence, stability?" were respectively 4,2+0,3 points and 4.9+0.2 points for the elderly - $p<0.05$. It showed an improvement of psychological status of elderly patients treated with statin therapy. Note that in the group of patients who did not receive statin therapy, a positive trend for these items have not been received. In addition, patients in middle age, taking statins, this positive dynamics also was found. This situation is similar to the above situation, with the dynamics of depression and is explained in a similar way: psychological well-being is largely determined by the level of cognitive ability and the middle-aged people initially, cognitive impairment was less pronounced dynamics of cognitive status in the process of therapy was not significant.

Age and the effect of statin therapy on quality of life.

When using the SF-36 questionnaire in the control groups of patients of both middle and old age, have not been undergo statin therapy, we have shown the lack of statistically natural dynamics of the indicators of quality of life (table 4).

Table 4

The quality of life in control group patients who did not receive statins, in the dynamics of observation

Indicators	group			
	Middle age		Elderly patients	
	Before studies	After three months	Before studies	After three months
General health	25,2±2,2	25,4±2,4	25,5±2,2	25,1±2,5
Role-Physical Function	25,1±2,3	25,3±2,2	25,0±2,1	24,9±2,3
Bodily pain	14,4±1,9	14,6±1,8	14,5±1,8	14,6±1,9
Physical Functioning	24,9±2,3	25,0±2,4	24,8±2,3	24,9±2,4
Viability	25,1±2,2	25,2±2,3	25,0±2,3	25,2±2,2

Psychological health	21,9±1,7	22,1±1,8	22,2±1,8	21,8±1,9
Role emotional functioning	30,1±2,1	30,2±2,2	31,1±2,1	31,0±2,2
Social functioning	30,8±2,3	30,7±2,4	30,5±2,2	30,6±2,1

On the background of the use of statin therapy, the attitude of the core group, the quality of life in patients of middle age and older, significantly ($p<0.05$) improved by such indicators as General health (9.0 and 9.0 points, respectively), viability (6.5 and 6.9 points, respectively), role emotional functioning (5.6 and 5.8 points respectively), except in patients in middle age has been improving in terms of social functioning (4.6 points), and the elderly – in terms of psychological health (6.2 points) (table 5).

Table 5

The quality of life in patients, the background of the use of statin therapy

Indicators	group			
	middle age (n=31)		older (n=32)	
	Observational Before studies	After 3 month	Observational Before studies	After 3 month
General health	25,1±2,1	34,1±2,3*	25,2±2,2	34,2±2,4*
Role-Physical Function	25,2±2,4	25,3±2,2	25,4±2,3	25,1±2,1
Bodily pain	14,5±1,8	14,4±1,7	14,5±1,7	14,6±1,8
Physical Functioning	24,7±2,2	24,8±2,3	24,6±2,4	24,7±2,3
Viability	25,2±2,3	31,7±2,1*	25,1±2,2	32,0±2,2*
Psychological health	21,8±1,8	21,9±1,7	21,9±1,9	28,1±1,8*, #

Role emotional functioning	30,2±2,2	35,8±2,0*	30,3±2,1	36,1±2,1*
Social functioning	30,9±2,4	35,5±2,3*	30,7±2,2	30,6±2,3#

*p<0,05 in dynamics within the same age group

#p<0,05 between elderly patients and middle age

At the same time, the use of modern statins in addition to providing basic lipid normalised effect able to increase the level of psychological well-being and quality of life of the people of both middle and old age. In addition, people in older age groups age age characteristic of the positive impact of statin therapy on the General background of psychological well-being is the impact on cognitive-mediated settings, such as depression and self-control. In the end such a successful application of statins on the one hand, increases the interest of doctors in their appointment and promotion, on the other hand, patients of older age groups increases the motivation to further prolongation of statin therapy.

Conclusion.

The use of modern statins in addition to providing basic lipid normalised effect able to increase the level of psychological well-being and quality of life of the people of both middle and old age. In addition, people in older age groups age age characteristic of the positive impact of statin therapy on the General background of psychological well-being is the impact on cognitive-mediated settings, such as depression and self-control.

The clinical significance and social usefulness of statin therapy in the older age groups of patients is their pleiotropic effects, such as reducing the level of depression, improved cognitive abilities, increased levels of psychological well-being and quality of life.

List of references

1. Aronov D.M. Plejotropnye jeffekty statinov //Kardiologija. – 2004. – V. 10. – p. 85–94.
2. Aronov D.M., Bubnova M.G. Plejotropnye jeffekty statinov na sovremennom jetape ih izuchenija (fokus na atorvastatin). Chast' I // CardioSomatika.- 2012 – V. 3- p. 70–81.
3. Proshhaev K.I., Il'nickij A.N., Zezjulin P.N., Filippov S.V. Nejroimmunojendokrinnye aspekty hronicheskogo vospalenija v geneze serdechno-sosudistoj patologii u ljudej pozhilogo vozrasta // Gerontologija. – 2015. – V. 1.
4. K.I. Proshhaev, A.N. Il'nickij, V.V. Kriveckij [i dr.] Osobennosti klinicheskogo osmotra pacienta pozhilogo i starcheskogo vozrasta // Uspehi gerontologii. – 2013. – V. 26(3). – p. 472-475.
5. A.N. Il'nickij, K.I. Proshhaev, S.V. Trofimova [i dr.] Preventivnaja geriatrija, ili antivozrastnaja medicina // Uspehi gerontologii. – 2015. – V. 28 (3). – p. 589-593.
6. Proshhaev, K.I. Kachestvo zhizni pacientov starcheskogo vozrasta [Jelektronnyj resurs] / K.I. Proshhaev, S.G. Gorelik, A.I. Pritchina // Vestnik novyh medicinskih tehnologij. – 2013. – № 1.
7. Proshhaev, K.I. Molekuljarnye osnovy razvitija i progressirovanija hronicheskoj serdechnoj nedostatochnosti v pozhilom i starcheskom vozraste [Tekst] /K.I. Proshhaev, A.N. Il'nickij, V.I. Bessarabov, T.V. Pavlova, T.V. Kvetnaja, O.A. Bolhovitina, N.M. Pozdnjakova // Molekuljarnaja medicina. – 2012. – V. 6. – p. 60-63.
8. Vahnina N.V. Vedenie pacientov s kognitivnymi narushenijami // Spravochnik poliklinicheskogo vracha. – 2013 – V. 3 - p. 40—45.
9. Chokshi NP, Messerli FH, Sutin D et al. Appropriateness of statins in patients aged ≥80 years and comparison to other age groups // Am J Cardiol 2012 – V. 110 – p. 1477-1481
10. Fitchett DH, Mancini GB, Gregoire J, Anderson T, McPherson R. Risk stratification and selection for statin therapy: going beyond Framingham // Can J Cardiol. - 2014 Jun. –V. 30(6) – p.667-70.
11. Smith, S.C.Jr. AHA/ACC Guidelines for Secondary Prevention for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2006 Update / S.C.Jr Smith (and oth.) // Circulation. – 2006. – №113. – p.2363–72.