Original Article

Comparative assessment of the clinical efficacy of various amlodipine isomers in 1st and 2nd degree arterial hypertension patients

Dmitriy Ermakov[1], Olga Pashanova[2]*

Abstract

Objective: The paper presents the results of clinical trials of medications based on S-amlodipine and S/R-amlodipine. ***Materials and methods:*** A total of 140 patients diagnosed with arterial hypertension of I and II degree were included into study, in particular, 70 patients with 1st degree and another 70 patients with 2nd degree hypertensive disease. A group consisted of 80 male (57%) and 60 female patients (43%) aged from 45 to 73 years. The average age of the examined patients was 62.1±5.8 years. Duration of the disease was established between 1 and 22 years (12.5±1.2 years on average). ***Results and discussion:*** The stereoselectivity mechanisms of the studied amlodipine enantiomers were found to initiate the activity of only one S-amlodipine isomer. Applying S-amlodipine in treatment was proved to improve significantly the clinical results, facilitate the course of hypertensive disease, and normalize the structure and functional heart condition. After 8 weeks of amlodipine-based treatment, the diastolic pressure in groups receiving S-amlodipine reduced by 20-25% and systolic pressure reduction was between 20% and 31%. Among patients taking the original amlodipine medication consisting of S and R enantiomers, the diastolic pressure decrease was between 19.4% and 24%, and the systolic pressure reduced from 16.7% to 27.37%. ***Conclusions:*** By using S-amlodipine, the prescribed medication dosage can be reduced by 50%, which allows diminishing the drug load on the body and lessen the side effects.

Keywords: arterial hypertension; R-amlodipine; S-amlodipine; stereoselectivity; the structure and functional heart condition.

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Introduction

Arterial hypertension (AH) is one of the most common diseases of the cardiovascular system[1,2]. According to the Russian Ministry of Health, a number of patients diagnosed with AH currently amounts to about 12 million. However, hypertensive diseases significantly influence the quality of life and plays a key role in development of pathological changes of the cardiovascular system, viscera, retina, as well as other tissues and organs. Due to its asymptomatic manifestation at an early stage, hypertension can cause numerous pathological conditions, complications of related diseases and increased mortality rate[3].

Effective approaches for hypertension treatment are being developed due to the increasing need for selective and safe medications[4]. According to the latest trends in medicine, it is recommended to use prolonged forms of antihypertensives. The controlled release of the target component allows correcting an adequate profile of arterial pressure (AP) values by a single drug receiving[5]. Calcium antagonists (CA)[6] are often used in arterial hypertension treatment tactics.

Calcium channel antagonists have a broad spectrum of activity, good drug tolerance, minimal contraindications, and can be used for simultaneous elimination of increased leg swelling. The known positive properties of amlodipine allow prescribing

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it as a drug of choice for a wide range of age categories. Amlodipine is especially indicated for elderly patients suffering from arterial hypertension, including severe stages of the disease[7]. Amlodipine is often prescribed at I and II stages of AH in the absence of contraindications and complications of the cardiovascular system[5]. However, many authors[8-10] point to the efficacy of amlodipine therapy also in patients with heart defects, ischemic heart disease (IHD) and ischemia cerebrale, heart failure, etc. Amlodipine preparations are recognized as effective in the treatment of patients with metabolic syndrome and diabetes mellitus type I and type II. Treatment with pure amlodipin or a combination of amlodipine with other drugs like perindopril, is often used in the therapeutic tactics of hypertension management in patients with kidney diseases and isolated systolic arterial hypertension[11]. Out of all modern calcium antagonists, the vasoselective amlodipine of the third generation consisting of S (-) and R (+) isomers mixture is most often used. The advantage of this medication lies in its prolonged effect. Due to the controlled release of the drug, its anti-hypertensive properties are preserved for a long time. The study[6] presents clinical results for the treatment effect of hypertension management of I and II types with amlodipine silicate medications. Investigations of the efficacy and safety profiles of low doses of L-amlodipine besylate are consistent with the results of amlodipine malate ($P<0.01$) pharmacokinetics. The bioavailability of amlodipine besylate was 83% on average. Amlodipine in the form of capsules and pills is also used to increase the bioavailability of drugs and reduce their photosensitivity and degradation[8]. However, it is important to examine different enantiomers of amlodipine as antihypertensive medication.

This work aimed to optimize the arterial hypertension management by including in complex therapy S-amlodipine (Azomex) and the original amlodipine medication, which is a racemic mixture of enantiomers, and to determine the efficacy and safety of both enantiomers.

The most important problem in cardiology is arterial hypertension (AH), which affects more than 1/3 of the adult population. Effective antihypertensive therapy reduces the risk of the stroke by 35–50%, myocardial infarction by 16–25%, and cardiac insufficiency by more than 50%. Among the antihypertensive drugs of the I series recommended by the European Society of Cardiologists, calcium antagonists (CA) play significant role due to their high clinical effectiveness and lack of individual side effects that could limit the use of other groups of medication[7]. Many studies indicate that CAs from the dihydropyridine derivatives are particularly effective in reducing the risk of stroke. Among the latter, amlodipine is most noteworthy[12].

Amlodipine free base is quite unstable[8]. To provide maximum bioavailability and safety, acidic-additive forms of amlodipine are applied. For therapeutic purposes, amlodipine is used in the form of salts like amlodipine gentisate, malate, besylate, etc.

In practice, the most common side effect of amlodipine-based treatment is peripheral edema, which is diagnosed in about 8% of patients according to literature. This problem is the main reason for the withdrawal of medication[9,10]. The solution to this problem was proposed to solve with employing levorotary isomer S-amlodipine. Like many organic compounds, amlodipine manifests optical activity due to the presence of a chiral carbon atom.

Enantiomers (mirror isomers) of amlodipine except for its spatial structure and optical properties differ in pharmacological properties[13-15]. The original amlodipine medicine is a racemic mixture (1:1), in which only (S)-(–)-amlodipine is a blocker of calcium channels and exhibits antihypertensive activity according to the literature[16,17]. The dextrogyrate isomer (R)-(+)-amlodipine is inactive in this respect. In fact, the reason for the inactivity of R(+)-enantiomer is the inability to stereoselective binding to specific blood plasma proteins[15,18-20]. Based on available literature resources, the antihypertensive activity of (S)-(–)-amlodipine is twice as high as that of racemic R/S-amlodipine[21-23].

Objective: To compare the antihepertensive activity of amlodipine enantiomers in the treatment of arterial hypertension of 1st and 2nd degrees.

Methods

Characteristics of the drug

In the trials were used S-amlodipine (Azomex 2.5 mg and 5 mg) and R/S-amlodipine (Amlodipine 5 mg and 10 mg).

A group of 140 patients with clinically verified

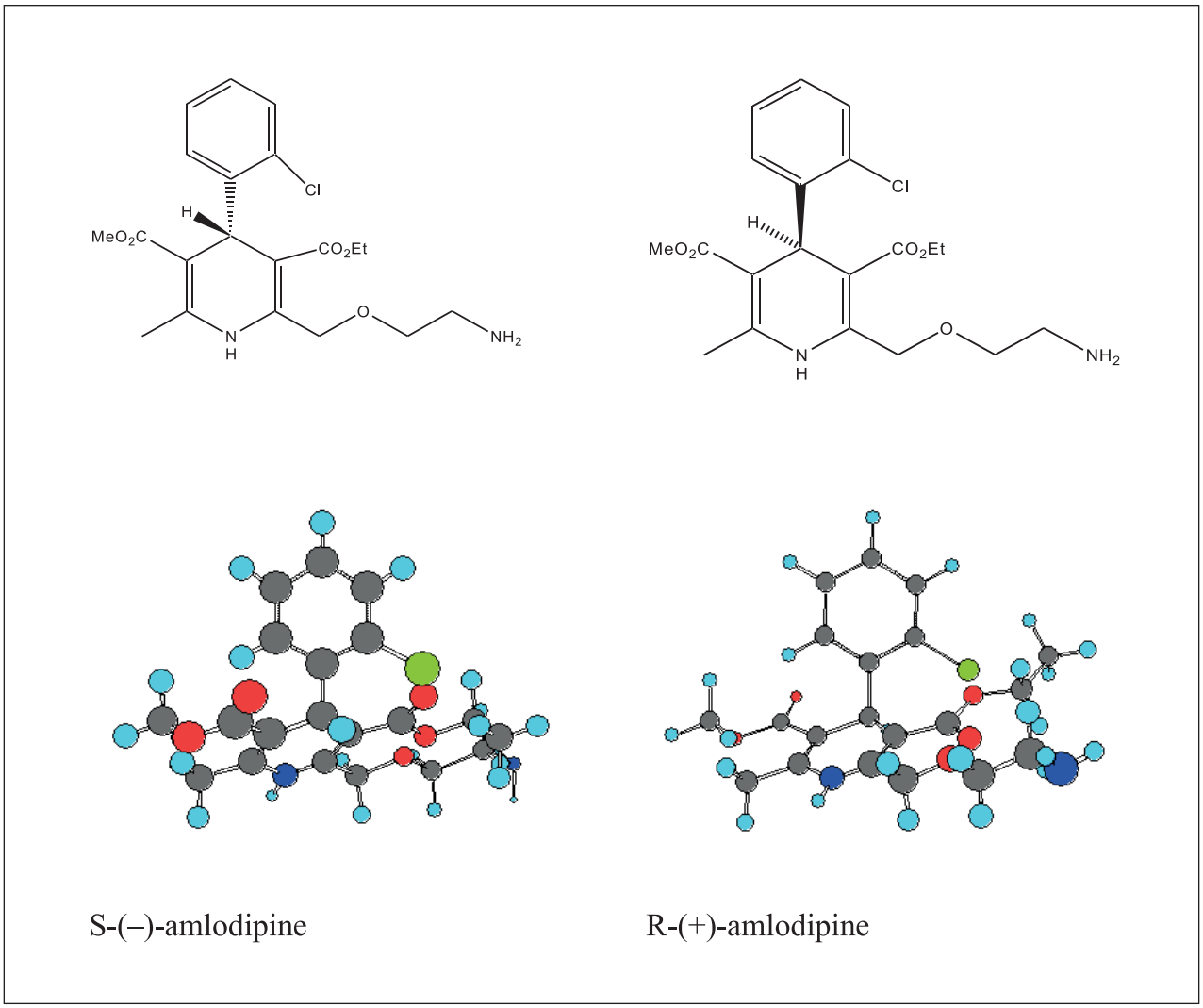

Figure 1 shows 2D and 3D images of amlodipine isomer molecules performed in Chemsoft Office 6.0 interface.

arterial hypertension of I and II degrees were under observation. Among them, 70 patients with AH of I degree and 70 patients with AH of degree II according to ACC/AHA Hypertension Guidelines (2017).

The experiment involved 60 women (43%) and 80 men (57%) aged from 45 to 73 years (average 62.1±5.8 years) suffering from 1-2 stage arterial hypertension from 1 to 22 years. Patients were divided into two groups by medication type. In turn, each group was divided into subgroups by disease stage.

Patients of Group I (70 people) were assigned with S-amlodipine (Azmex, Aktavis).

Group Ia with diagnosed arterial hypertension of the 1st degree received S-amlodipine in a dose of 2.5 mg, once per day.

Group Ib with diagnosed arterial hypertension of the 2nd degree received S-amlodipine in a dose of 5 mg, once per day.

Patients of group II (70 people) were prescribed with the original amlodipine, which is a racemic mixture of R- and S-amlodipine.

The group IIa with arterial hypertension of the 1st degree received the the R/S – amlodipine in a dose of 5 mg, once per day.

The group IIb with arterial hypertension of the 2nd degree received the the R/S – amlodipine in a dose of 10 mg, once per day.

All groups of patients were consistent in age and sex, as well as by the levels of systolic and diastolic blood pressure.

The study did not include patients with symptomatic arterial hypertension, myocardial infarction, diabetes mellitus, chronic obstructive pulmonary disease,

bronchial asthma, hepatitis, cirrhosis, and chronic renal disorder.

The efficacy of amlodipine was assessed by the clinical course of the disease, blood pressure dynamics, heart rate, and with the help of echocardiography. Drug safety was estimated by circumstantial evidence considering pharmacological recommendations of the drug clinical application.

The research was conducted before treatment with antihypertensives or against the background of antihypertensive medication withdrawal within 5-7 days. Treatment results were compared after 8 weeks.

Statistical analysis

To assess the results of the treatment with drugs based on various amlodipine isomers, the ANOVA – analysis with software Statistica and Microsoft Excell were applied. The statistical analysis was based on combining the results of ≥2 individual tests. Statistical heterogeneity of the results was determined after Pearson's criterion χ^2 (P=0.05).

Ethical clearence: The research was approved by ethical committee of I.M. Sechenov First Moscow State Medical University

Results

The dynamics of changes in systolic (SAP) and diastolic (DAP) arterial pressure during treatment are shown in Tables 1, 2, and Figures 2, 3.

Table 1. Impact of amlodipine enantiomers on blood pressure changes in patients with AH of the 1st degree

Stages of research	S-amlodipine 2,5 mg		S/R-amlodipine 5 mg	
	Δ SAP	Δ DAP	Δ SAP	Δ DAP
Difference in blood pressure values after 8 weeks of treatment, mmHg.	33	27	27	21

Table 2. Influence of amlodipine enantiomers on AP change in patients with AH 2nd degree

Stages of research	S-amlodipine, 5 mg		S/R-amlodipine, 10 mg	
	Δ SAP	Δ DAP	Δ SAP	Δ DAP
Difference in blood pressure values after 8 weeks of treatment, mmHg.	57	22	49	26.9

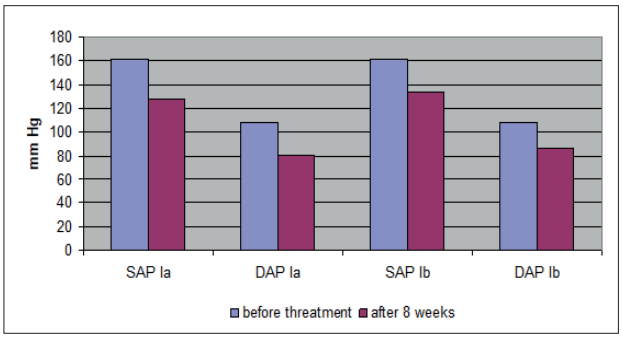

Fig. 2. Dynamics of AP change in patients with AH 1st degree against the background of amlodipine intake, mm Hg p≤0.0001.

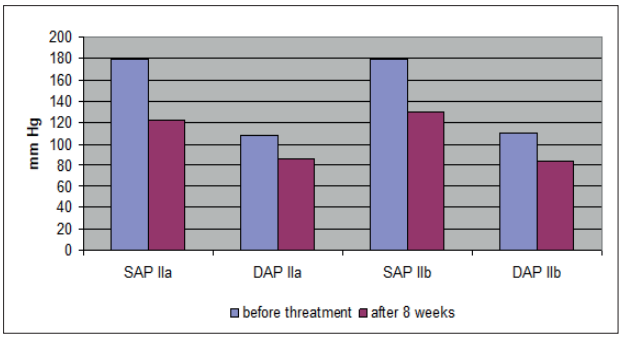

Fig. 3. Dynamics of AP change in patients with AH 2nd degree against the background of amlodipine intake, mm Hg p≤0.00001

Tables 3 and 4 present the results of Doppler echocardiography of structural and functional heart parameters in hypertensive patients before and after treatment with amlodipine isomers.

Table 3. Structural and functional condition of the heart in patients with arterial hypertension of 1st and 2nd degrees during S-amlodipine-based treatment

Stages of research	LVEF*, %	LA, mm	LAWL, mm	IVST, mm	HR, bpm
Before treatment	69.7 ±0.3	34.7±0.5	12.1±0.2	11.1±0.4	73.7±0.9
After 8 weeks	62.2±0.3	35.0±0.6	10.8±0.2	10.1±0.4	76.5 ±0.5

* LVEF – left ventricular ejection fraction; LA – left atrium; LAWL – left atrium wall thickness; IVST – intervascular septum thickness; HR – heart rate.

Table 4. Structural and functional condition of the heart in patients with arterial hypertension of 1st and 2nd degrees during S/R-amlodipine-based treatment

Stages of research	LVEF*, %	LA, mm	LAWL, mm	IVST, mm	HR, bpm
Before treatment	69.7 ±0.3	34.7±0.5	12.1±0.2	11.1±0.4	73.7±0.9
After 8 weeks	65.3 ±0.4	34.9±0.6	11.1±0.3	10.4±0.5	75.6 ± 0.5

* LVEF – left ventricular ejection fraction; LA – left atrium; LAWL – left atrium wall thickness; IVST – intervascular septum thickness; HR – heart rate.

The results of evaluating the amlodipine bioavailability in the daily dosage of 2.5 and 5 mg/day of S-amlodipine and 5 and 10 mg/day of S/R-amlodipine in terms of S-amlodipine are presented in Figure 4.

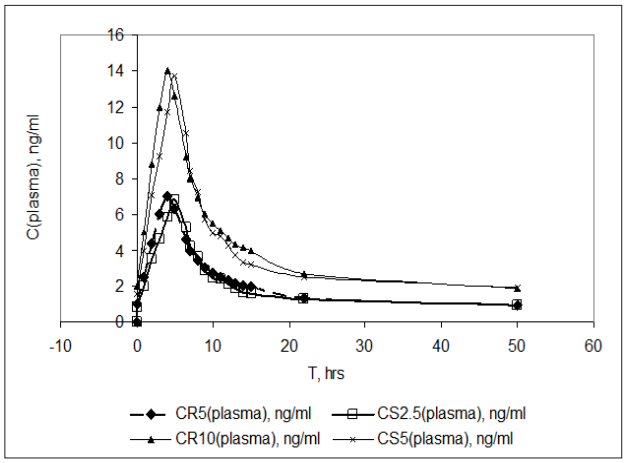

Fig. 4. Comparison of S-amlodipine and S/R-amlodipine bioavailability

The figure shows that S-amlodipine products manifested almost the same bioavailability as S/R-amlodipine. It should be noted that the maximum serum concentration was reached almost at the same intervals for all forms of amlodipine, although S-amlodipine showed a slightly more prolonged effect. The reason for this is the denser consistency of the pharmaceutical form of the factory-made S-amlodipine.

To calculate the half-life of amlodipine, the results of studies presented in Figure 4 will be provided in logarithmic form (Figure 5). Half-life period of amlodipine is .

where $t_{1/2}$ is the half-life period, equal to $tg\alpha$, and k_{el} is the constant of elimination rate[6,17].

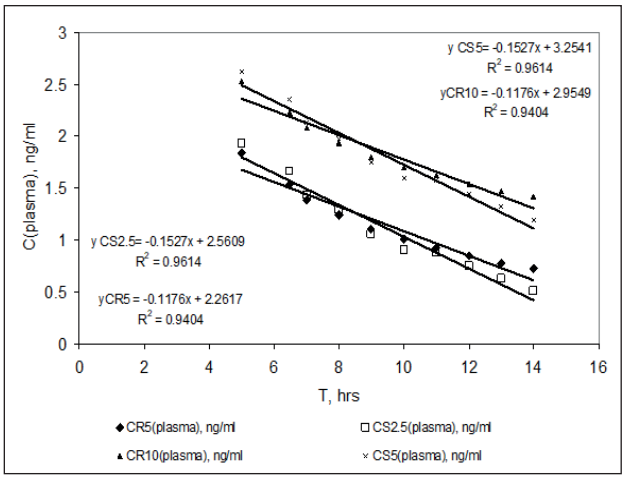

Fig. 5. Elimination kinetics of S-amlodipine and S/R-amlodipine in plasma

Tables 5–10 show the elimination coefficients of amlodipine enantiomers.

Table 5. Estimation of the half-life of amlodipine enantiomers in AH treatment

Title	Half-life period $t_{1/2}$, h	Elimination rate constant k_{el}
S-amlodipine 2.5 mg	4.5392743	0.1527
S-amlodipine 5 mg	5.8941087	0.1176
S/R-amlodipine 5 mg	4.5392743	0.1527
S/R-amlodipine 5 mg	5.8941087	0.1176

Table 6. Changes in clinical parameters during AH of 1st degree management with S - amlodipine in a dose of 2.5 mg/day.

Parameter	S-amlodipine 2.5 mg			
	Before treatment	After treatment	R1	p
SGOT*	15.44 ± 0.1	15.44 ± 0.1	0.01	0.9
SGPT	16.12 ± 0.3224	15.43 ± 0.3086	0.2	0.882353
LDL	133.1 ± 6.5219	126.34 ± 6.19066	0.49	0.85796
Total cholesterol	210.01 ± 4.2002	195.11 ± 3.9022	0.2	0.882353
Triglicerides	177.22 ± 14.1776	170.6 ± 13.648	0.8	0.833333
Serum Creatinine	0.81 ± 0.0324	0.81 ± 0.0324	0.4	0.865385

* SGOT – serum glutamic oxaloacetic transaminase; SGPT – serum glutamic pyruvic transaminase; LDL – low density lipoprotein

Table 7. Changes in clinical parameters during AH of 1st degree management with S/R- amlodipine in a dose of 5 mg/day.

Parameter	S/R-amlodipine 5 mg			
	Before treatment	After treatment	R1	p
SGOT*	15.46 ± 0.004637	15.50176 ± 0.004651	0.003	0.89973
SGPT	16.14 ± 0.806806	15.49172 ± 0.774586	0.5	0.857143
LDL	133.23 ± 5.729023	126.8454 ± 5.45435	0.43	0.862895
Total cholesterol	210.22 ± 1.828914	195.8904 ± 1.704247	0.087	0.892238
Triglicerides	177.40 ± 19.51369	171.2824 ± 18.84106	1.1	0.810811
Serum Creatinine	0.82 ± 0.00082	0.81324 ± 0.000813	0.01	0.899101

* SGOT – serum glutamic oxaloacetic transaminase; SGPT – serum glutamic pyruvic transaminase; LDL – low density lipoprotein

Table 8. Changes in clinical parameters during AH of 2nd degree management with S-amlodipine in a dose of 5 mg/day.

Parameter	S-amlodipine 5 mg			
	Before treatment	After treatment	R1	p
SGOT*	15.5944 ± 0	15.5944 ± 0	0	0.84
SGPT	16.2812 ± 0.113968	15.5843 ± 0.10909	0.07	0.834161
LDL	134.431 ± 3.898499	127.6034 ± 3.700499	0.29	0.816327
Total cholesterol	212.1101 ± 5.090642	197.0611 ± 4.729466	0.24	0.820313
Triglicerides	178.9922 ± 13.7824	172.306 ± 13.26756	0.77	0.779944
Serum Creatinine	0.8181 ± 0.03436	0.8181 ± 0.03436	0.42	0.806142

* SGOT – serum glutamic oxaloacetic transaminase; SGPT – serum glutamic pyruvic transaminase; LDL – low density lipoprotein

Table 9. Changes in clinical parameters during AH of 2nd degree management with S/R-amlodipine in a dose of 10 mg/day.

Parameter Before treatment	S/R-amlodipine 10 mg			
	After treatment	R1	p	
SGOT*	15.61 ± 0.3122	15.65678 ± 0.313136	0.2	0.872549
SGPT	16.30 ± 0.668197	15.64664 ± 0.641512	0.41	0.854947
LDL	134.57 ± 5.651748	128.1138 ± 5.38078	0.42	0.854127
Total cholesterol	212.32 ± 1.698578	197.8493 ± 1.582795	0.08	0.882937
Triglicerides	179.17 ± 16.12541	172.9952 ± 15.56957	0.9	0.816514
Serum Creatinine	0.82 ± 0.0082	0.821372 ± 0.008214	0.1	0.881188

* SGOT – serum glutamic oxaloacetic transaminase; SGPT – serum glutamic pyruvic transaminase; LDL – low density lipoprotein

Table 10. Frequency of side effects incidence in the treatment of 1st and 2nd degree arterial hypertension with amlodipine isomers

Side effect	Group I (70)		Group II (70)	
	Ia (35)	Ib (35)	IIa (35)	IIb(35)
Nausea	-	-	1	2
Fatigue	3	7	5	9
Vertigo	1	2	1	3
Headache	2	3	3	4
Epigastric pain	0	–	1	1
Total	6	13	11	19

Discussion

At the beginning of the study, the fluctuations of blood pressure values in patients of the main and control groups were not statistically significant and amounted to 171.2±9.7 mmHg in Group I and 173.4±9.2 mm Hg in Group II (P>0.05). Blood pressure frequency above 160 mmHg was registered in 78.8% and 79.2% cases, respectively (p>0.05). After 2 weeks, the blood pressure of all patients in both groups did not exceed 140 mmHg and was on average 129.2±4.8 in Group I and 134.5±4.3 in Group II (p>0.05).

At the moment of inclusion in the study, the heart rate was 70.0±5.1 beats per minute in Group I and 72.1±5.8 beats per minute in Group II. The asymptotic significance of the results throughout the whole period of observation in both groups was p<0.05. Positive changes in blood pressure were observed against the background of treatment with both amlodipine drugs. Average blood pressure decreased by 24.4% (p<0.05) in the treatment with S-amlodipine and by 22.01% (p<0.05) in the treatment with the original amlodipine medication.

Before S-amlodipine therapy the arterial hypertension patients experienced general weakness, fatigue, headache, tinnitus, increased heartbeat, fluctuating blood pressure, vertigo, sleep disturbances, etc. Thus, general weakness was observed in 140 patients (100%), increased fatigue, especially after psycho-emotional and physical activity, manifested

in 110 patients (78.57%), and 82 patients (58.57%) complained of sleep disturbance. After sleep, the patients felt tired and complained of increased fatigue, reduced productivity, and morning headache. All patients had a fast heartbeat. Headache expressed in 103 patients (73.57%) and was observed more often in patients with increased AP. Vertigo was noticed in 68 patients (48.57%), and cardialgia occurred in 112 patients (80%).

The application of S-amlodipine during 8 months resulted in the improvement of the clinical course of arterial hypertension. Thus, the general weakness was noted only in 42 patients, which was 30% against 100% before treatment. The patients complained much less of increased fatigue, which was noted only for 24 patients (14%). During the period of S-amlodipine therapy, most of the examined patients did not have significant complaints about vertigo, i.e., only 7 patients or 5% cases. These positive changes contributed also to better sleep. The number of patients with sleep disturbance decreased by 3 times and was only 28 (20%). Increased heart rate was noted by 4 patients (8.5%) against 27 (57.4%) before treatment. The number of patients who experienced cardialgia was also reduced by 4 times (21.3%). Only 7 patients (14.8%) mentioned dyspnea.

When analyzing obtained results of AP measurement, it was revealed that the AP indicators improved significantly in essential arterial hypertension (EAH) patients after 8 weeks of treatment with S-amlodipine. Thus, in the group with AH of the 1st degree receiving S-amlodipine, the level of AP decreased by 20.5%, and the DAP value – by 25% compared to the upward level. In the group with AH of the 1st degree receiving R/S-amlodipine, SAP decreased by 16.7% and DAP – by 19.44%. Patients with AH of the 2nd degree observed a stronger pressure decrease (up to 31.84%), apparently due to a higher dosage of the drug. Similarly, despite twice the higher dosage of the drug, R/S-amlodipine was noted to be less effective. On average, S-amlodipine was 9% more effective than a racemate. In general, the target AP level was achieved in 88.57% cases or in 124 patients. In the other 16 patients with AH, both SAP and DAP levels were close to the target. Side effects were observed in 49 patients (35%). The most frequent complaints were fatigue and general weakness. 13 patients (9.3%) suffered from a headache. The majority of patients noted a decrease in swelling of the lower legs, but 2% of patients who used S-amlodipine observed an increase in turgidity and swelling of the lower legs. Such a problem was sometimes reported by other researchers[24,25].

In terms of statistics, no significant differences in heart rate in EAH patients before and after S-amlodipine therapy were noticed. The HR rate before treatment was 73.7±0.9 beats per minute. After S-amlodipine treatment it changed to 76.1±0.4 beats per minute, and after R/S-amlodipine intake amounted to 75.6±0.5 beats per minute. Thus, as indicated in other sources, the use of S-amlodipine does not lead to a significant increase in HR in patients with AH[26,27].

The analysis of the obtained results showed that the state of left ventricular systolic function remained almost unchanged by the left ventricular ejection fraction indicator. Only the tendency to improvement of left ventricular systolic function was observed. For racemic amlodipine, the indices were close to those obtained for S-amlodipine (Tables 3 and 4), but it should be considered that the dose of racemic amlodipine was twice as high as of S-amlodipine. Thus, the R (+) isomer played the role of "ballast" in relation to the antihypertensive activity of the drug.

It has been established that the diameter of the left atrium decreased by 0.6% for S-isomer and 0.5% for R-isomer. The thickness of the interventricular septum decreased by 10% and 9%, respectively. The wall thickness of the left atrium decreased by 10.7% and 7.6%. Left ventricular ejection fraction decreased by 6.2.-10.7%. Thus, the obtained results can be regarded as a slow regression of left ventricular hypertrophy in patients with AH, which coincides with the results of other researchers[10,13,18].

The use of S-amlodipine during 8 weeks in EAH patients has shown its sufficient safety, as evidenced by the frequency incidence of side effects given in Table 5.

In particular, peripheral edema, tachycardia, and vertigo were noted in only one case, hyperemia and fatigue in 24 patients, and headache in 12 patients. However, these side effects passed quickly and did not become a significant reason for drug withdrawal. All patients continued to apply it by the specified date.

Proved efficacy of monotherapy with S-amlodipine in a dose of 2.5-5 mg in patients with AH coincides with the data of other researchers[22]. Obtained results confirm the possibility of effective S-amlodipine application in monotherapy to reduce blood pressure in different categories of patients with AH. The results presented in Tables 6–9 are consistent with

that of other authors[28], which confirms the effect of S-amlodipine in reducing the cardiovascular risk, the wide antihypertensive action of the drug, metabolic neutrality, and good therapy tolerance[17].

It should be noted that S-amlodipine almost did not cause an increase in heart rate and, accordingly, no complaints of pounding pain, afflux, and redness were reported. This advantage in comparison with short-acting calcium antagonists (nifedipine) is due to the relative neutrality of the medication for the functional state of the sympathoadrenal system[18].

The anti-hypertensive action of S-amlodipine is manifested through the mechanism of blocking the flow of calcium cations. At the same time, the bioavailability of S/R amlodipine comprised half of that for S-amlodipine, as follows from Figure 4. The release rate of S-amlodipine was reported to be slightly lower than that of S/R amlodipine. The concentration of amlodipine in cell membranes is $1 \cdot 10^5$ times higher than in intercellular space. At that, amlodipine interacts with calcium channels of various cells. Especially selective interaction is manifested with smooth muscle cells of vessels. A high concentration of amlodipine weakens the aggregation of low-density lipoproteins with cell membrane lipids, which negatively affects the condition of cell membranes. The effect of S-amlodipine reduces the peripheral resistance of blood vessels unless the cardiac alternation is affected. Application of S-amlodipine leads to the slow development of the hypotensive effect and decrease of blood pressure, which is not accompanied by reflex tachycardia. After intake, the maximum concentration of the drug in the patient's plasma was reached after 6–7 hours (Figure 4). The half-life of both amlodipine enantiomers was t1/2=4.5392743 in a 5 mg dosage and t1/2=5.8941087 for S/R-amlodipine in a dose of 10 mg. The elimination rate constant for S-amlodipine in a 2.5 mg dose was k_{el}=0.1527, in a 5 mg dose k_{el}=0.1176, and for the S/R-amlodipine in a 5 mg dose k_{el}=0.1527, in a 10 mg dose k_{el}=0.1176. (Figure 5). Constant drug concentration in blood is reached on the 7th-8th day of intake and provides a stable hemodynamic profile during treatment with S-amlodipine[5,18].

Conclusions

According to the AP indicators in patients with essential arterial hypertension of 1st and 2nd degrees, the antihypertensive efficacy of S-amlodipine in a daily dosage of 5 mg does not differ from that of the original amlodipine in a dosage of 10 mg. The maximum equilibrium concentration of S-amlodipine in a daily dosage of 2.5 mg is compared to that of 5 mg racemic amlodipine for the treatment of AH of the 1st degree, and 5 mg S-amlodipine is compared to the dose of 10 mg racemic amlodipine for the treatment of AH of the 1st degree. Against the background of S-amlodipin therapy, the incidence of peripheral edema is lower than by the application of racemic amlodipin in a dose of 10 mg.

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Authors's contribution:

Data gathering and idea owner of this study: Dmitriy Ermakov

Study design: Olga Pashanova

Data gathering: Olga Pashanova

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