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PHARMACOECONOMIC ANALYSIS OF MEDICINAL DRUG FOSINOPRIL IN PATIENTS WITH ARTERIAL HYPERTENSION

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Abstract:

Blockade of renin-angiotensin system (RAS) remains one of the most main strategies in treatment of arterial hypertension (AH), and drugs blocking this system, mainly angiotensin-converting-enzyme inhibitor (ACEI) and blockers of receptors to angiotensin II, are the main classes of antihypertensive drugs. The presence of different clinical effectiveness of drugs in these groups, as well as different frequencies of occurrence of undesirable cardiovascular events, side effects and formed the basis of pharmacoeconomic (PE) studies.

According to the conducted cost-effectiveness analysis, the treatment regimen using Monopril is characterized by lowest cost and the lowest coefficient of cost-effectiveness ratio in the treatment of patients with AH. The results of the budget impact analysis suggest that therapy with Monopril leads to budget savings. The results of the sensitivity analysis demonstrated the adequacy of the performed pharmacoeconomic analysis and the stability of the obtained data – during the change of the cost factors in the range of $\pm 97\%$ the therapy with the drug Monopril maintained its advantage expressed by the results of the cost-effectiveness analysis. Cost-effectiveness analysis and budget impact analysis were used in this study. The indirect comparison of two antihypertensive drugs was performed: ACEI (fosinopril, ramipril, lisinopril, perindopril) and ARB II (valsartan, losartan, telmisartan, candesartan). Both groups of drugs are not only one of the main classes of antihypertensive drugs, which can be prescribed to all patients with AH, but also have priority indications, such as diabetes mellitus, metabolic syndrome etc. Results of costs analysis show that fosinopril treatment scheme is characterized with total costs - 22 751 rub., with the lowest cost-effectiveness ratio – 285, during the treatment of AH and budget economy from 5 048 rub. to 46 805 rub. per 1 person per year compared with-ramipril, lisinopril, perindopril, valsartan, losartan, telmisartan, candesartan.

Key words: ACEIs, ARB, RAAS, fosinopril, ramipril, lisinopril, perindopril, valsartan, losartan, telmisartan, candesartan, arterial hypertension, infarction, stroke, cardiovascular diseases, , budget impact analysis, cost-minimization analysis, cost analysis, pharmacoeconomics.

Введение

Cardiovascular diseases are the leading cause of death in Europe and account for over 4.3 million deaths each year. Arterial hypertension (AH) is the leading risk factor for cardiovascular (myocardial infarction, stroke, coronary heart disease, chronic heart failure), cerebrovascular (ischemic or hemorrhagic stroke, transient ischemic attack) and kidney diseases (chronic kidney disease). Cardiovascular and cerebrovascular diseases, represented in official statistics, as of cardiovascular system diseases (CVD) are the leading causes of population mortality in the Russian Federation, their share in the number of deaths from all causes accounts for more than 55% of deaths [31-34]. In modern society there is a significant prevalence of AH, accounting for 30-45% of the adult population according to foreign studies and about 40% according to Russian studies. In Russian population the prevalence of AH among men is slightly higher in some regions it reaches 47%, whereas among women the prevalence of AH is about 40%. [43]

Renin-angiotensin-aldosterone system (RAAS) is considered as the main factor regulating blood pressure and homeostasis, it plays a central role in the occurrence of AH and its consequences, serves as an indispensable participant in the cardiovascular continuum starting with risk factors, the potentiation of atherosclerosis, endothelial dysfunction, ischemic heart disease (IHD), left ventricular hypertrophy, myocardial remodeling and final heart failure and chronic kidney disease (CKD) [35-39].

Currently, the treatment of hypertension in Russia is conducted on the basis of the clinical recommendations of the Russian Ministry of health for the diagnosis and treatment of hypertension from 2013, which recommended the 5

main classes of antihypertensive drugs: angiotensin-converting-enzyme inhibitors (ACEIs), Angiotensin II Receptor Blocker II (ARB), calcium channel blocking agents (CCBA), beta-blocking agent (BBA), diuretics [34]. The change in RAAS activity is possible on the background of antihypertensive therapy. One way of reducing the activity of RAAS is the suppression of synthesis of angiotensin II [41,42].

The purpose of this study is to determine, from the perspective of a pharmacoeconomic analysis of preemptive medications used for the treatment of hypertension based on the comparison between cost and efficiency, safety and quality of life in the treatment of drugs of two classes of antihypertensive drugs ACEIs: Fosinopril, Ramipril, Lisinopril, Perindopril and ARB: Losartan, Valsartan, Candesartan, Telmisartan.

Objectives:

1. To explore an informational material (scientific publications, guidelines for physicians, tutorials) about modern methods of treatment of patients with arterial hypertension.
2. To determine indicators of clinical efficacy of drug therapy of hypertension and types of cost, their use in comparative pharmacoeconomic study is most appropriate.
3. To calculate the costs for pharmacotherapy of ACEIs – Fosinopril, Ramipril, Lisinopril, Perindopril, ARB – Losartan, Valsartan, Candesartan, Telmisartan)
4. To conduct a pharmacoeconomic cost-effectiveness analysis and the budget impact analysis of the use of ACEIs drugs – Fosinopril, Ramipril, Lisinopril, Perindopril, ARB – Losartan, Valsartan, Candesartan, Telmisartan in the treatment of hypertension and to determine the optimal position of pharmacoeconomics of medical technology in the treatment of hypertension

Peculiarities of the study

In the first phase, to identify differences between the drugs ACEI and ARBS II, an analysis was conducted of various information sources: pharmacoeconomic and clinical research in foreign databases (DB) – in Pubmed, Medlink, etc. keyword: “angiotensin converting enzyme inhibitors, blockers of receptors of angiotensin-II, renin-angiotensin-aldosterone system, fosinopril, ramipril”, “lisinopril”, “perindopril”, “valsartan”, “losartan”, “telmisartan”, “candesartan”, “cardiovascular diseases”, “pharmacoeconomics”, “cost analysis”, “cost-effectiveness “analysis”, “budget impact”, “stroke”, “myocardial infarction”, “arterial hypertension”. Also, the information search was conducted in the Russian-language databases, Russian medicine, Central scientific medical library of the First MGSU named after I. M. Sechenov, scientific electronic library elibrary.ru, CyberLink and free search engine such as Yandex, Google etc. Information search in Russian database included the following keywords: ACEIs, ARB, RAAS, fosinopril, ramipril, lisinopril, perindopril, valsartan, losartan, telmisartan, candesartan, hypertension, myocardial infarction, stroke, cardiovascular diseases , analysis of the “impact on budget”, the cost-minimization analysis, cost analysis, pharmacoeconomics. In the search process, corresponding to the inquiry, it was found 113 publications. Next, duplicate publications and studies not related to the problem of treatment of hypertension with use of antihypertensive drugs were excluded; and was not included in further analysis of randomized clinical trials (RCTS) to compare drugs were evaluated in combination with other antihypertensive agents. The level of evidence was determined according to the scales assessing the levels of evidence results RCTS of drugs and the assessment of levels of credibility of evidence RCT LS. In the first place was out of the study with level of evidence A or b: the evidence summarized in the systematic review, meta-analysis, and evidence obtained in prospective RCTS, respectively. In the absence of such research was considered with a lower level of evidence. The results are summarized in a special table for analysis and subjected to peer review. Thus, after screening for detailed analysis included 22 publications (tab. 1).



Table 1. Results of information retrieval

Fosinopril							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
Treatment of Senile Hypertension Treatment of Senile Hypertension The Fosinopril in Old Patients Study (FOPS)	Vetter W	1997	Switzerland	fosinopril	Open-label study	757	12 weeks
Study of the efficacy and safety of fosinopril in general practice in 19,435 hypertensive patients (FLIGHT Study)	Berdah J1, Guest M, Salvador M.	1998	France	fosinopril	randomized, blind, multicenter	19 432	12 weeks
Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM	Tatti P1, Pahor M, Byington RP, Di Mauro et al.	1998	Italy	1)fosinopril 2)amlodipin	randomized	380	3,5 years
Long-term effects of fosinopril and pravastatin on cardiovascular events in subjects with microalbuminuria: Ten years of follow-up of Prevention of Renal and Vascular End-stage Disease Intervention Trial (PREVEND IT)	Brouwers FP1, Asselbergs FW, Hillege HL, de Boer RA et al.	2011	The Netherlands	1)fosinopril 2) pravastatin	randomized, double-blind,	864	4 years
Ramipril							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
The CARE Study: a postmarketing evaluation of ramipril in 11,100 patients. The Clinical Altace Real-World Efficacy (CARE) Investigators	Kaplan NM	1996	USA	ramipril	Open-label, multicenter	8261	2 months
Long-term effects of ramipril on cardiovascular events and on diabetes: results of the HOPE study extension	Bosch J1, Lonn E, Pogue J, Arnold JM, Dagenais GR, Yusuf S	2005	Canada	ramipril	randomized, double-blind, multicenter	4528	4,5 years
Lisinopril							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
Comparison of valsartan 160 mg with lisinopril 20 mg, given as monotherapy or in combination with a diuretic, for the treatment of hypertension: the Blood Pressure Reduction and Tolerability of Valsartan in Comparison with Lisinopril (PREVAIL) study	Malacco E1, Santonastaso M, Vari NA et al.	2004	Italy	1)valsartan 2)lisinopril	randomized, double-blind	1213	16 weeks
The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) Heart Failure Validation Study: diagnosis and prognosis	Einhorn PT1, Davis BR, Massie BM et al.	2007	USA	1) chlortalidon, 2)amlidipin, 3)lisinopril 4) doxazosin	randomized, double-blind, multicenter	42,418	5 years
Nocturnal reduction of blood pressure and the antihypertensive response to a diuretic or angiotensin converting enzyme inhibitor in obese hypertensive patients. TROPHY Study Group.	Weir MR1, Reisin E, Falkner B et al.	1998	USA	1)lisinopril 2)hydrochlorthiazide	randomized, multicenter	124	12 weeks
Perindopril							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study)	Fox KM	2003	England	1)perindopril 2)placebo	randomized, double-blind, multicenter	12218	4,2 years
Comparison of trough effect of telmisartan vs perindopril using self blood pressure measurement: EVERESTE study	Ragot S1, Ezzaher A, Meunier A et al.	2002	France	1)telmisartan 2)perindopril	randomized, double-blind	441	12 weeks

Losartan							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy	Brenner BM1, Cooper ME, de Zeeuw D et al.	2000	USA	1)losartan 2)placebo	randomized, double-blind,	1513	3,5 years
Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan	Dickstein K1, Kjekshus J	2002	Norway	1)losartan 2)captopril	randomized, blind, multicenter	5477	2,7 years
Сравнительная эффективность оригинального и генерического losartana у больных артериальной гипертензией	С.В. Недоуеys, Т.А. Чаляби и др.	2007	Russia	losartan	randomized, blind, multicenter	40	3 months
Valsartan							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
The Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trial: outcomes in patients receiving monotherapy	Julius S1, Weber MA, Kjeldsen SE et al.	2006	USA	1)valsartan 2)amlodipin	randomized, double-blind, multicenter	15245	3,2 years
Comparison of valsartan 160 mg with lisinopril 20 mg, given as monotherapy or in combination with a diuretic, for the treatment of hypertension: the Blood Pressure Reduction and Tolerability of Valsartan in Comparison with Lisinopril (PREVAIL) study	Malacco E1, Santonastaso M, Vari NA, Gargiulo A, Spagnuolo V et al.	2004	Italy	1)valsartan 2)lisinopril	randomized, double-blind	1213	16 weeks
Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both	Pfeffer MA, McMurray JJ, Velazquez EJ et al.	2003	USA	1)valsartan 2)captopril	randomized, double-blind, multicenter	14703	2,7 years
Telmisartan							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
Comparison of trough effect of telmisartan vs perindopril using self blood pressure measurement: EVERESTE study	Ragot S1, Ezzaher A et al.	2002	France	1)telmisartan 2)perindopril	randomized, open-label	441	12 weeks
Telmisartan to prevent recurrent stroke and cardiovascular events.	Yusuf S, Diener HC, Sacco RL et al.	2008	Canada	telmisartan	randomized, double-blind, multicenter	20 332	2,5 years
Telmisartan, ramipril, or both in patients at high risk for vascular events	Yusuf S, Teo KK, Pogue J, Dyal L et al.	2008	Canada	1)telmisartan 2)ramipril	randomized, double-blind, multicenter	25620	4,6 years
Candesartan							
Name of the study	Authors	Year	Country	Objects of study (medicines)	Design of study	Number of patients	Time horizon
The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial	Lithell H1, Hansson L, Skoog I et al.	2003	Sweden	1)candesartan 2)placebo	randomized, double-blind, multicenter	4964	3,7 years
Comparative effects of candesartan cilexetil and losartan in patients with systemic hypertension. Candesartan Versus Losartan Efficacy Comparison (CANDLE) Study Group	Gradman AH1, Lewin A, Bowling BT, Tonkon M et al.	1999	USA	1)candesartan 2)losartan	randomized, double-blind, multicenter	332	8 weeks
Effects of candesartan compared with amlodipine in hypertensive patients with high cardiovascular risks:candesartan antihypertensive survival evaluation in Japan trial	Ogihara T1, Nakao K, Fukui T et al.	2008	Japan	1)candesartan 2)amlodipin	randomized, open-label, multicenter	4728	3,2 years
Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial	Granger CB1, McMurray JJ, Yusuf S et al.	2003	USA	1)candesartan 2)placebo	randomized, multicenter	2028	2,8 years



Effectiveness analysis

For analysis of efficiency and analysis of “cost-effectiveness” on the basis of information found during the search of RCTS for each drug of the two groups of antihypertensive drugs - ACE-I (fosinopril, lisinopril, ramipril and perindopril) and ARBS II (losartan, valsartan, candesartan and telmisartan), we determined the criterion of effectiveness is the achievement of target blood pressure. In addition to the criterion of efficiency for analysis “cost-effectiveness” and cost analysis, we have identified unwanted cardiovascular events which included: THEY (fatal and nonfatal), stroke (fatal and nonfatal) and SN, as well as side effects of drug therapy such as hypotension, cough and angioedema. Data analysis of effectiveness are presented in table 2.

Table 3. Cost of drugs

Dosage form/ number	Price, rub.	Price of 1 mg, rub.	Mean price of 1 mg, rub.
Perindopril (Prestarium A)			
tabl. 5 mg № 30	456,21	3,04	2,66
tabl. 5 mg № 90	1 358,67	3,02	
tabl. 10 mg № 30	684,38	2,28	
tabl. 10 mg № 90	2 076,53	2,31	
Ramipril (Tritace)			
tabl. 2.5mg №28	809,60	11,57	7,22
tabl. 5mg №28	900,86	6,43	
tabl.10mg №28	1 022,50	3,65	
Lisinopril (Diroton)			
tabl. 2,5mg №14	60,00	1,71	1,15
tabl. 2,5mg №28	107,50	1,54	
tabl. 5mg №14	133,00	1,90	
tabl. 5mg №28	196,50	1,40	
tabl. 5mg №56	327,00	1,17	
tabl. 10mg №14	133,00	0,95	
tabl. 10mg №28	274,00	0,98	
tabl. 10mg №56	501,00	0,89	
tabl. 20mg №14	196,00	0,70	
tabl. 20mg №28	446,00	0,80	
tabl. 20mg №56	699,00	0,62	

The performance indicator for each of the studied drugs of antihypertensive drugs groups ACEI (fosinopril, lisinopril, ramipril and perindopril) and ARBS II (losartan, valsartan, candesartan and telmisartan) was taken from pre-registration studies phase III. Data on the incidence of adverse cardiovascular events and side effects mainly from post-marketing studies phase IV [1-24, 38].

Cost analysis

In the present study were evaluated only direct medical costs of using medicines: perindopril, ramipril, lisinopril, losartan, valsartan, candesartan and telmisartan in comparison with the medicine fosinopril. Prices on medicines were taken from the Internet resources www.medlux.ru and www.pharmindex.ru with further calculation of the average cost of 1 mg of active substance (tab. 3).

Dosage form/ number	Price, rub.	Price of 1 mg, rub.	Mean price of 1 mg, rub.
Fosinopril (Monopril)			
tabl. 20mg №28	410,00	0,73	0,73
Candesartan (Atacand)			
tabl. 8mg №28	1 598,47	7,14	4,75
tabl.16mg №28	1 935,81	4,32	
tabl.32mg №28	2 503,67	2,79	
Valsartan (Diovan)			
tabl. Coated 80mg №28	1 686,64	0,75	0,61
tabl. Coated 160mg №28	2 071,56	0,46	
Telmisartan (Micardis)			
tabl. 40mg №14	604,48	1,08	0,78
tabl. 80mg №28	1 086,64	0,49	
Losartan (Cozaar)			
tabl. coated 50mg №14	334,74	0,48	0,38
tabl. coated 100mg №28	772,62	0,28	

According to the data presented in table 3 – least cost of 1 mg for studied drugs: losartan – 0,38 rub., valsartan – 0,61 RUB.. and fosinopril – 0,73 RUB. The greatest value of 1 mg was observed in LP: ramipril – 7,22 RUB., candesartan – 4,75 RUB. and perindopril – 2,66 RUB.

Table 2 . Results of effectiveness analysis

INN	Achievement of target AH %	Fatal /non-fatal infarction %	Heart failure %	Stroke (fatal and non-fatal) %	Hypotension %	Cough %	Angioedema, %
Losartan	67,1 ^[14]	6,66 ^[12]	11,85 ^[12]	6,39 ^[12]	1,7 ^[13]	1 ^[13]	0,4 ^[13]
Valsartan	82,7 ^[7]	4,82 ^[15]	4,63 ^[15]	4,21 ^[15]	15,1 ^[16]	1,7 ^[16]	0,2 ^[16]
Candesartan	64 ^[18]	2,83 ^[19]	0,8 ^[20]	3,59 ^[19]	3,7 ^[21]	0,2 ^[21]	0,1 ^[21]
Telmisartan	58 ^[2]	1,66 ^[22]	1,19 ^[22]	8,67 ^[22]	3,9 ^[22]	1,1 ^[23]	0,2 ^[22]
Perinopril	46 ^[2]	4,83 ^[1]	0,7 ^[1]	1,6 ^[1]	1 ^[1]	2,65 ^[1]	N/A
Ramipril	85 ^[4]	9,88 ^[3]	9 ^[3]	3,36 ^[3]	1,89 ^[3]	7,32 ^[3]	N/A
Lisinopril	60 ^[6]	2,2 ^[5]	1,1 ^[5]	1,6 ^[5]	0,5 ^[7]	7,2 ^[7]	N/A
Fosinopril	79,8 ^[9]	1,8 ^[10]	0,2 ^[11]	0,7 ^[10]	0,6 ^[11]	5 ^[10]	N/A

The table below shows that the highest percentage of achievement of BP has been demonstrated in drugs: ramipril – 85%, valsartan – 82,7% and fosinopril – 79.8 per cent. The lowest incidence of mi was drugs: telmisartan and 1.66%, fosinopril – 1.8% and lisinopril was 2.2%. The lowest incidence of CH was drugs: fosinopril – 0.2 %, perindopril – 0.7% and candesartan and 0.8%. The lowest frequency of stroke was drugs: fosinopril – 0.6%, lisinopril – 1.3% of perindopril and by 1.6%. The lowest frequency of hypotension was for drugs: lisinopril – 0.5%, fosinopril – 0.6% and perindopril – 1%. The lowest incidence of cough was drug: candesartan and 0.2%, losartan – 1% and telmisartan – 1,1%. The incidence of angioneurotic edema was evaluated only for drugs of group II ARBS (losartan, valsartan, candesartan and telmisartan), drug from the group of ACE inhibitors (perindopril, ramipril, lisinopril, and fosinopril) of such data in RCTS has been presented.

Taking into account the results of information retrieval and recommendation of application guidelines, budget and planning of the health system in the treatment of hypertension, for further calculations we took the time interval in the amount of one years.

All calculations of the value of pharmacotherapy in the treatment of various conditions was based on the standards from table 4.

Table 4. The standards used in the calculation of direct costs

Nosology	Name of standard
Arterial hypertension (AH)	The standard of emergency medical care in diseases characterised by high blood pressure (Ministry of health Order No. 1513n of December 24, 2012)
	The standard of primary health care in primary arterial hypertension (Hypertensive disease) (Ministry of health Order No. 708n from November 9, 2012)
Myocardial infarction (MI)	The standard ambulance in acute coronary syndrome with ST segment elevation (Ministry of health Order No. 1383n of December 24, 2012)
	About approval of the standard of specialized medical care in acute myocardial infarction with ST-segment elevation of the electrocardiogram (Order of MH of the Russian Federation No. 839 of 24 May 2011)
Stroke	The standard of emergency medical care in stroke (Ministry of health Order No. 1282n of 20 December 2012)
	The standard of specialized medical care in myocardial injury (Ministry of health Order No. 1740n of December 29, 2012)
Cardiac insufficiency (CI)	The standard of emergency medical care in heart failure (Ministry of health Order No. 1283n of 20 December 2012)
	The standard of specialized medical care in heart failure (Ministry of health Order No. 1554n of 24 December 2012)
Angioneurotic edema	The standard ambulance in angioneurotic edema, hives (Ministry of health Order No. 1430n of 24 December 2012)

Feature of the present cost analysis was that in addition to the basic calculation of the cost of pharmacotherapy, we also calculated the compensation cost for the treatment of cardiovascular events and adverse effects from each specific PL.

Thus, the cost of providing out-patient or emergency medical care for hypertension at each stage was 9 501 rub. and **5 228** rub. respectively; during myocardial infarction at each stage - 375 255 rub. и 17 421 rub. respectively; during cardiac insufficiency - **67 757** rub. and 9 526 rub. respectively; during stroke - 289 715 rub. and 20 072 rub. respectively; during angioneurotic edema - 27 010 rub. The results of the cost analysis are presented in table 5.

Table 5. Structure of direct costs

INN	Costs:				Compensation of side effects, rub.	Total costs, rub.
	AH, rub.	CI, rub.	Stroke, rub.	CI, rub.		
Perindopril	13 328	538	4 949	18 960	19	37 795
Ramipril	13 374	6 916	10 409	38 794	50	69 543
Lisinopril	13 306	844	4 957	8 635	44	27 786
Fosinopril	13 329	154	2 169	7 068	32	22 751
Losartan	13 349	9 084	19 753	26 150	121	68 458
Valsartan	13 423	3 558	13 013	18 922	125	49 042
Candesartan	13 397	613	11 099	11 112	43	36 264
Telmisartan	13 380	915	26 859	6 518	76	47 747

INN- international nonproprietary name, AH-arterial hypertension, CI –cardiac insufficiency, IM - myocardial infarction, SE - side effects

From the above table it is seem that the lowest total costs have the following drugs: fosinopril – 22 751 rub., lisinopril – 27 786 rub. and candesartan – 36 264 rub.

Cost-effectiveness analysis

The calculations of cost-effectiveness analysis were performed separately for each drug. The result of the analysis is represented as a cost per unit of effectiveness with the subsequent comparison of the obtained results. Calculation in accordance with the methodology, was carried out according to the formula:

$$CER = (DC + IC) / Ef, \text{ where}$$

CER — cost-effectiveness ratio (defines costs, which are necessary for a unit of effectiveness, for example per 1 treated patient);

- DC — direct costs, including direct medical and direct non-medical costs;;
- IC — indirect costs;
- Ef — effectiveness (relative amount of treated patients).

After evaluating the cost and effectiveness of pharmacotherapy for AH with antihypertensive drugs values of the cost-effectiveness ratios (CER) as the ratio of total cost to percentage of patients achieved target arterial pressure level were calculated. (табл. 6).

Table 6. Cost-effectiveness ratio based on destination of target arterial pressure level

INN	Destination of target level of AP, %	Total costs, rub.	Cost-effectiveness ratio, rub.
Perindopril	46	37 808	822
Ramipril	85	69 591	819
Lisinopril	60	27 800	463
Fosinopril	79,8	22 719	285
Losartan	67,1	68 576	1 022
Valsartan	82,7	49 075	593
Candesartan	64	36 278	567
Telmisartan	58	47 762	823

During cost-effectiveness analysis is defined that Fosinopril has the lowest CER. From table 6 it is seen that the smallest lowest CER.have the following LP: fosinopril – 285, lisinopril – 463 and candesartan – 567.

Budget impact analysis

The next step was the implementation of budget impact analysis based on the data about the duration of treatment of patients suffering from AH, to assess the economic impact on the health care budget when choosing therapy. As part of this analysis by time horizon compared to the use of alternatives 365 days in accordance with the recommended instructions for use was analyzed.



The calculation of costs was conducted using formula:

$$BIA = Cost_1 - Cost_2,$$

где $Cost_1$ – total costs of the first type of treatment (rubles);
 $Cost_2$ – total costs of the second type of treatment (rubles);
 BIA (Budget Impact Analysis) – budget impact analysis (rubles).

Figure 1 shows the total cost of treatment of 1 patient with hypertension with different antihypertensive drugs.

in the treatment of hypertension.

Conclusions:

During direct costs analysis for AH therapy on the basis of current standards of rendering medical care for AH patients the total costs for two types of antihypertensive drugs were performed: fosinopril – 22 751 rub. compared with other drugs: perindopril – 37 795rub., ramipril - 69 543rub., lisinopril – 27 786rub., losartan - 68 458rub., valsartan – 49 042rub., candesartan – 36 264 rub., telmisartan– 47 747rub.

Basing on the cost-effectiveness analysis it is showed that Fosinopril

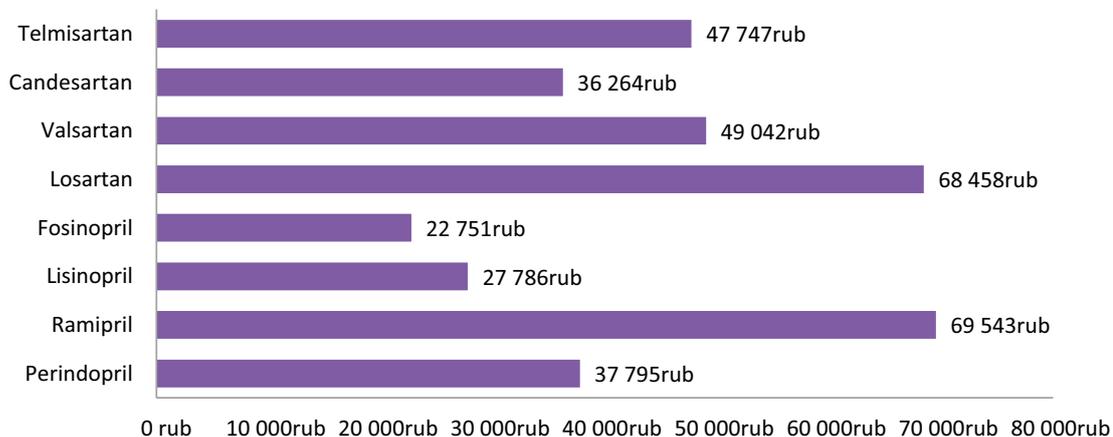


Figure 1. Total costs for each medicine

Figure 1 shows that drug fosinopril has the least total costs, therefore, the drug fosinopril comparison with the other drugs for the demonstration of economy of budgetary funds.

Next, we calculated of the transitions from different drugs to fosinopril as the drug with the lowest total cost

has pharmacoeconomic advantage 285 rub. in therapy of AH, as this type of treatment requires the least costs for 1 case of determination of target level of arterial pressure compared with drugs: Perindopril - 822 rub., Ramipril - 819 rub., Lisinopril - 463 rub., Losartan - 1 021 rub., Valsartan - 593 rub., Candesartan - 567 rub., Telmisartan - 823 rub.

Budget impact analysis showed that usage of Fosinopril in AH treatment

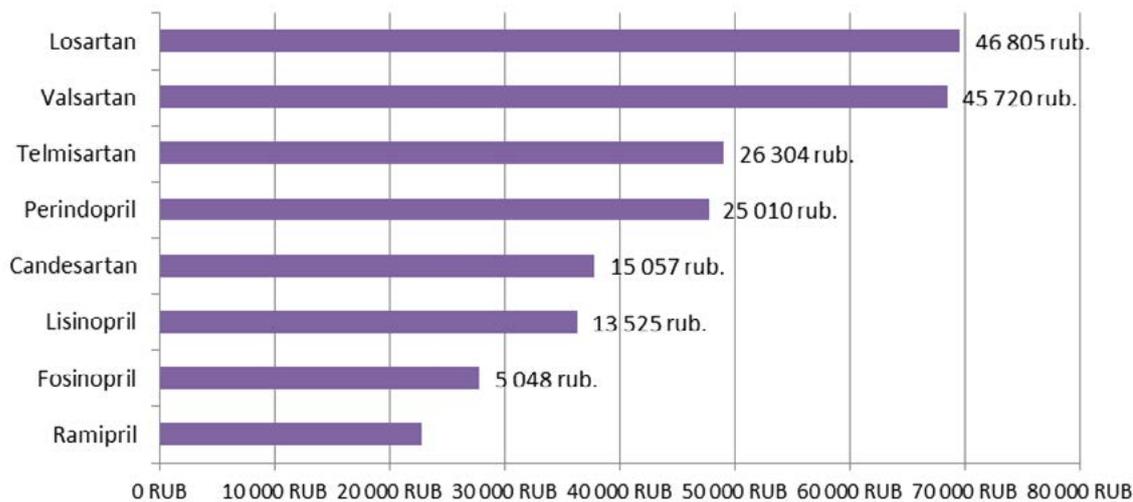


Figure 2. Monetary economy during transfer to fosinopril

The results obtained demonstrate fiscal savings when transferring all patients to other LP on treatment with fosinopril. With this transfer, the cost savings will be from 5 048 rub. to 46 805 rub. a year, depending on the drug. (fig.2).

Sensitivity analysis

For identification of the fact will be the usage of fosinopril still cost-effective under another profile of costs, the one-factor sensitivity analysis is conducted. As variables values of the main drugs of pharmacotherapy were considered. Sensitivity analysis defines, how the change in the value of two classes of antihypertensive drugs ACEIs and ARB will affect the cost – effectiveness ratios

compared with drugs: Perindopril, Ramipril, Lisinopril, Losartan, Valsartan, Candesartan and Telmisartan allows to save from 5 048 rubles to 46 805 rubles per 1 patient per year.

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