Research Article

Analysis of the Controlled Essential Hypertension's Pharmacotherapy in General Doctor in Russian Federation (Pharmacoepidemiological Analysis)

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Abstract

Aim of the Study: To analyze pharmacotherapy of essential hypertension in patients, who have achieved a controlled course of the disease.

Materials and Methods: In this study 274 patients with controlled course of stage 2 arterial hypertension and no comorbidities were recruited. Blood pressure indicators, the volume of drug therapy for hypertension were analyzed.

Results: The study included 543 drug prescriptions. In 97 (35.3%) patients only one drug was prescribed, in 112 (40.7%) - two drugs, in 46 (16.7%) - three drugs from various pharmacological groups, among which monodrugs were in the lead: angiotensin-converting-enzyme inhibitors (ACE-inhibitors) - 31.86%, cardioselective β-blockers - 23%, angiotensin 2 receptor blockers - 9.3%. Combined drugs were present in 18.4% of general doctors` prescriptions.

Conclusion: Pharmacotherapy in patients with stage 2 essential hypertension, belonging to the group of high risk of cardiovascular complications, does not fully comply with modern clinical recommendations in general medical practice.

Keywords: Essential Hypertension; Arterial Hypertension; Pharmacological Therapy

Introduction

Arterial hypertension (AH) is one of the most common cardiovascular diseases in adults and remains the main cause of disability and mortality in the population, including patients of working age.

Currently completed large multicenter studies have proven the positive effect of lowering blood pressure (BP) on the incidence of cardiovascular complications (CVC) [1,2].

The level of blood pressure is the leading factor that affects the magnitude of the individual risk of developing CVC, as determined by the SCORE scale.

Despite the availability of a wide range of drugs with proven clinical efficacy, achieving the target level of blood pressure is often a difficult task in clinical practice.

According to the Russian AH Registry, the achievement of target BP is observed only in 20% of patients [3,4].

Obviously, clinical (office) measurement of blood pressure and home monitoring of blood pressure is required to assess the level of blood pressure. To achieve an assessment of blood pressure in real medical practice, it is necessary to research the features of therapy, risk factors and lifestyle of patients on the background of antihypertensive therapy.

The purpose of this study is to identify the structure of antihypertensive therapy in patients with well controlled levels of arterial hypertension according to the attending physicians.

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Materials and Methods

Patients` characteristics

The study involved 274 patients on observation in 55 general practice doctors (family doctors) from various medical institutions in the city of Samara and Samara region. The study was conducted during 2019. In accordance with the design of the study, each doctor had to fill out a protocol for a patient with controlled stage 2 hypertension and without comorbidity (Table 1).

Indicators	Mean	Median	Std.Dev.
Average age	55,03	56	10,2
Male (n(%))	93 (33,8%)	-	-
Age of AH onset	44,1	45,5	10,99
Smoker index (pack/years) (n = 31 patient)	15,2	15	13,02
Body mass index (BMI) kg/m^2	30,11	29,05	4,89
Total cholesterol (mmol/l)	5,49	5,3	3,2
Low density lipoproteins (mmol/l)	3,07	3	1
Systolic BP (SBP) (at the doctor's office) mm Hg	136,02	133	12,97
Diastolic BP (DBP) (at the doctor's office) mm Hg	88,42	82,5	7,35
Systolic BP (home) mm Hg	122,32	122	8,78
Diastolic BP (home) mm Hg	75,19	75,9	6,28
Systolic BP (average) mm Hg	112,8	111,25	9,01
Diastolic BP (average) mm Hg	69,6	69,25	6,15

Table 1: Characteristics of the studied patients.

Excluding criteria were stage 1 and 3 AH, ischemic heart disease, chronic heart failure, oncological and psychiatric diseases.

Written voluntary consent were collected from all the patients, who participate in the study. The study was approved by the decision of the Biomedical Ethics Committee of the Samara State Medical University.

All patients underwent blood pressure monitoring for two weeks, some cardiovascular risk factors were recorded: smoking, body mass index, total cholesterol, high and low density lipoproteins.

Questionnaires of all 274 patients were analyzed and 543 appointments were selected (total sample). The structure of prescribed drugs is presented in table 2.

Statistical analysis

The collected data were processed using the statistical data analysis package Statistica 64 (StatSoft, inc., USA). The Shapiro-Wilk

No	Drug, group	Number of prescriptions - n(%)
1	Amlodipine	39 (7,18%)
2	Nifedipine	4 (0,73%)
3	Bisoprolol	99 (18,23%)
4	Metoprolol	14 (2,58%)
5	Other β-blockers	12(2,21%)
7	Captopril	36 (6,63%)
8	Enalapril	49 (9,02%)
9	Perindopril	45 (8,29%)
10	Other ACE-inhibitors	7 (1,29%)
11	Valsartan	7 (1,29%)
12	Losartan	31(5,71%)
13	Other angiotensin-2 receptor blockers	12 (2,21%)
14	Diuretics	48 (8,83%)
15	Combinations of ACE-inhibitor and Ca^{2+} antagonist	29 (5,34%)

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16	Combinations of an ACE-receptors blocker (ARB) and a Ca^{2+} antagonist	6 (11,04%)
17	ACE-inhibitor and diuretic combinations	42 (7,73%)
18	ARB and diuretic combinations	22 (4,05%)
19	Other combined drugs	4 (0,73%)
20	Drugs from other groups	3 (0,55%)
21	Total	543 (100%)

Table 2: Number of prescriptions for antihypertensive drugs in the study group.

criteria was used to test the hypothesis of normal distribution of data. Data analysis was caried out using the methods of parametric and nonparametric statistics.

Results

Current research includes only patients with well-controlled AH. The median age of a patient was 55.03 ± 10.21 years. Women accounted for 66.2% of patients. Many of them noted AH ten and more years ago, at the age of ± 44-45 years.

Most of the patients were overweight. The average BMI was 30.1 ± 4.89 kg/m^2. Only 24 (8.8%) patients had a normal BMI (less than 24.5 kg/m^2) (Figure 1).
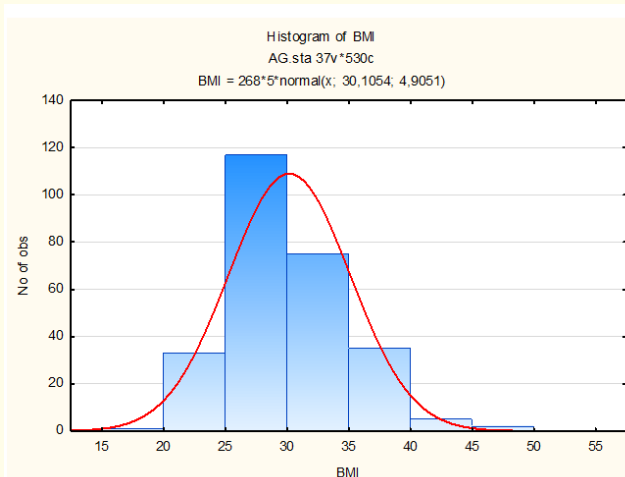

Figure 1: Histogram of distribution by body mass index in the studied patients.

Smoking as a cardiovascular risk factor was noted only in 31 patients with AH. The average smoking index was 15 pack/years.

The levels of total cholesterol and low density lipoproteins were increased in most cases and amounted to 5.49 ± 0.94 mmol/l and 3.06 ± 1 mmol/l respectively.

The medium daily arterial pressure (AP) was stable in every included patient and was slightly below the norm, amounting to SBP=112.8 ± 9.01 mm Hg and DBP = 69.6 ± 6.14 mm Hg; by contrast, at a doctor`s appointment, the BP value was higher: SBP = 136.02 ± 12.97 mm Hg and DBP = 88.42 ± 7.35 mm Hg.

Analysis of the pharmacotherapy of AH revealed, that physicians actively use various combinations of antihypertensive drugs from different groups. Only 97 (35.3%) patients had used a single drug, including short-acting medicines: captopril - 6.63%, nifedipine - 0.73%. The most part of the patients had controlled their AH with multi-drugs prescriptions: 112 (40.7%) patients were prescribed 2 drugs, 46 (16.7%) - 3 drugs from different pharmacological groups.

Combinations of ACE-inhibitors or ARBs-blockers with diuretics and calcium antagonists occurred in 35 (36%) of the group of 97 patients (100%) as monotherapy. Among patients with 4 and 5 prescribed antihypertensive drugs(n=20), combined drugs were observed only in 5 patients.

Analysis of the pharmacotherapy structure (Figure 2) showed that ACE-inhibitors are the leaders in the frequency of prescriptions - 173 (31.86%). In second place were β-blockers - 125 (23%). Combinations of ACE-inhibitors and angiotensin-II receptor blockers with diuretics or calcium antagonists (100 prescriptions (18.4%)) took the third position in terms of the frequency of prescriptions from a general practitioner. Next come angiotensin-II receptor blockers (50 prescriptions - 9.2%), diuretics (48 - 8.84%), calcium antagonists (43 - 7.9%).

According to the clinical recommendations, combination therapy is recommended for all patients with high-risk hypertension (stage 2 hypertension) as initial therapy. Preference is given to combinations that include: a blocker of the renin-angiotensin system - RAS (either an ACE inhibitor or an ARB) with a calcium channel blocker (CCB) or a diuretic. There is evidence that combination therapy at low doses is more effective than

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Figure 2: Structure of antihypertensive drugs prescriptions in patients with controlled hypertension.

monotherapy at the highest dose. Analysis of pharmacotherapy in our study showed that combined therapy was used in 18.4% of cases, while fixed combinations of drugs were practically not used.

Discussion

The feature of this study is determined by the group of patients themselves - patients with stage 2 arterial hypertension, without comorbid pathology, who had, according to the local doctor, well controlled blood pressure. This fact explains why among 274 patients, woman predominated, accounting for 66.2% of patients. Age about 50 years old, increased BMI in 91.2% of the patients and dyslipidemia are distinctive characteristics of the studied group of patients.

It is important to notice, that in a number of currently completed studies, the relationship between blood pressure and overweight has been established. As pointed out, a decrease in body weight to optimal values in patients with hypertension is accompanied by a decrease in blood pressure and improves the effectiveness of antihypertensive therapy [5-7]. Reduction of cardiovascular risk in all patients with AH could also be provided by decreasing of total cholesterol and low-density lipoproteins to the target levels - less than 4.5 mmol/l and less than 2.5 mmol/l respectively. Besides, patients with high-risk AH should be prescribed statins, which additionally reduce the risk of myocardial infarction by 1/3 and the risk of stroke by 1/4, even when the target BP level is reached. The above facts indicate that the studied patients with achieved target level of BP, have modifiable risk factors that must be corrected by the doctor in the process of preventive work and dispensary observation.

The average daily BP during the two-week home monitoring was stable in all the presented patients, and was slightly below normal,

while at the doctor's appointment, the BP levels were higher (Table 1). This may be due to the "white coat" effect. In accordance with clinical guidelines, SBP during treatment in all categories of patients should not be lower than 120 mm Hg, and DBP - 70 mm Hg. Currently available research results show that a decreased SBP less than 120 mm Hg., especially in patients at high risk, increases the likelihood of adverse events in the intensive therapy group.

Analysis of the pharmacotherapy prescribed by general practitioners for patients with stage 2 AH from high-risk group revealed, that drugs are frequently still used as a monotherapy, while some patients are prescribed short-acting medications (captopril, nifedipine).

ACE-inhibitors are effective antihypertensive drugs with large evidence base. Medications from this class in addition to the antihypertensive action, have cardio-, nephro- and cerebroprotective effect, reduce the risk of cardiovascular complications development. Yet it is recommended to use only long-acting drugs. It is important to notice that ACE-inhibitors affect the metabolism of bradykinin, which can provoke the development of dry cough and angioedema. There were no data on low tolerability of this class of drugs in our study.

The antihypertensive effect of angiotensin-II receptor blockers is comparable to that of ACE inhibitors. This class of drugs is characterized by higher patient adherence to treatment, due to fewer side effects compared to ACE inhibitors.

In our study, the frequent prescription of β-blockers turned out to be unexpected. On the one hand, high frequent of β-blockers prescriptions raises many questions due to the low antihypertensive efficacy. On the other hand, the absence of coronary artery disease and chronic heart failure in patients makes the use of these drugs unreasonable in the light of the latest clinical recommendations [8,9]. According to the recommendations, β-blockers is recommended to prescribe in combination with any of the other main classes of antihypertensive drugs in certain clinical situations, such as angina pectoris, postinfarction cardiosclerosis, chronical heart failure, etc. When prescribing β-blockers, it is necessary to take into consideration the possibility of adverse metabolic effects developing: a violation of carbohydrate and lipid metabolism, an increase in body weight. It is not recommended to prescribe drugs of this class to people with metabolic syndrome

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and a high risk of developing diabetes mellitus. A number of studies have shown that β-blockers are less effective in preventing stroke than other antihypertensive drugs [10]. According to the results of our study, the widespread use of β-blockers as monotherapy (23%) is often unfounded.

In a small number of cases, drug therapy included several (from 3 to 5) drug prescriptions, which reduces patients' compliance. It is important to notice, that clinical recommendations pay great attention to patients` adherence to treatment. It has been established, that reducing the number of drugs increases compliance. In contrast, their increase reduces the patient's compliance, especially when it comes to 4 or 5 types of antihypertensive drugs.

In a recent cohort study of 33,728 patients, poor adherence to hypertension treatment was shown to increase the risk of myocardial infarction by 32%, the risk of all-cause death by 75%, and the risk of stroke by 92% [10]. Therefore, in order to improve patients' compliance to the treatment of hypertension, it is necessary to use a combination therapy consisting of 2 or 3 antihypertensive drugs in a fixed form, i.e. in one tablet. Modern combined fixed drugs include antihypertensive drugs with various dosages of each component, which makes it possible to individually select antihypertensive therapy and increase adherence to treatment.

Conclusion

The quality of therapeutic and preventive measures carried out in patients with stage 2 AH, high risk of developing cardiovascular complications and, according to doctors, well controlled arterial hypertension does not fully comply with clinical recommendations. Although doctors achieve the desired drug control of blood pressure levels, they do not use enough methods to correct other risk factors for cardiovascular complications.

Conflict of Interest

The authors state that no conflict of interest occurs with the present manuscript.

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