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DETERMINANTS OF ARTERIAL HYPERTENSION CONTROL IN THE HYPERTENSIVE POPULATION RECEIVING MEDICAL THERAPY

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Highlights

• The leading factor of ineffective arterial hypertension (AH) control in the population taking medications was the number of metabolic risk factors (RF). In addition, in men, the odds of reaching the blood pressure targets were lower if there was a history of kidney disease and bronchitis, and higher, if statins and hypotensive drugs were taken together, respectively. In women, heart rate equal or higher than 75 beats/min and total carotid atherosclerotic plaque thickness were associated with lower and a visit to a physician in the past year – with higher odds of effective hypertension control, respectively.

Aim	Analysis of factors associated with reaching blood pressure targets in hypertensive population taking medications.
Methods	We examined men and women of 25–64 y.o., randomly drawn from general population, having hypertension and receiving medications. All participants underwent standardized cardiac screening, including a survey on a number of socio-demographic, psychosocial, behavioral variables, traditional and metabolic cardiovascular risk factors, life quality. We measured anthropometric and blood pressure variables, "intima-media" thickness, presence and total thickness of carotid atherosclerotic plaques. Analysis included data from 480 respondents. Parametric and nonparametric statistics were used. To analyze relationships, multivariable logistic regression was used. An error probability <5% was considered statistically significant.
Results	After adjustment for age, wealth level, cardio-vascular diseases and the number of antihypertensive drugs, the following factors increased the chances of effective treatment for hypertension in men – statins, positive answer to the question “Do you feel pain or discomfort?” on the EQ5D scale. Lower odds for detecting target blood pressure levels were associated to the count of metabolic syndrome components according to IDF criteria except arterial hypertension (0–4), kidney disease, previous bronchitis, age. A direct association with the effectiveness of treatment for hypertension in women was shown by a visit to the doctor during the past year, and the opposite – the number of metabolic syndrome components, heart rate ≥ 75 per minute and the total thickness of carotid atherosclerotic plaques, respectively.
Conclusion	Lack of hypertension control was associated to metabolic risk factors count, age, kidney disease, heart rate ≥ 75 per minute, previous bronchitis, lack of visit to a doctor over the past year, as well as total thickness of carotid atherosclerotic plaques. The situation can be improved by deliberately losing weight, taking statins by all people at very high and high risk, and seeing a doctor regularly. It is necessary to further study the factors that hinder achievement of blood pressure targets, as well as methods aimed at the prevention and effective correction of metabolic disorders.
Keywords	Arterial hypertension • Antihypertensive therapy • Achievement of treatment goals • Population

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Список сокращений

AH	– arterial hypertension	DBP	– diastolic blood pressure
AND	– antihypertensive drugs	HR	– heart rate
ASP	– atherosclerotic plaque	MS	– metabolic syndrome
BP	– blood pressure	OR	– odds ratio
CI	– confidence interval	RF	– risk factors
CKD	– chronic kidney disease	SBP	– systolic blood pressure
CVD	– cardiovascular diseases		

Introduction

Arterial hypertension (AH) is the most important modifiable risk factor of cardiovascular diseases (CVD) which is closely related to the problem of morbidity and premature mortality of the population [1]. According to some estimates 48% of ischemic strokes and 18% of all cardiac events are associated with hypertension [2]. The decrease in mortality from coronary heart disease observed in a number of countries is directly related to the positive dynamics of systolic blood pressure (SBP) indicators [3]. The control of hypertension which is understood as the achievement of relatively safe (target) values of blood pressure by medications and other means, serves as one of the key tasks aimed at reducing cardiovascular morbidity and mortality. Undoubtedly, insufficient intake of antihypertensive drugs (AND) remains the most important problem. The treatment significantly improves the prognosis especially among high-risk individuals. An important issue is the failure to achieve the target blood pressure levels during drug treatment. According to modern research only a part of Russian patients taking antihypertensive drugs treat hypertension effectively [3]. Although certain factors complicating the achievement of target BP values are known, the causes of this problem have not been fully studied.

The aim of the study is the epidemiological analysis of the factors associated with the probability of detecting target blood pressure levels in the conditions of cardiologic screening in the hypertensive population of the Siberian region receiving drug therapy.

Materials and Methods

The object of the study was a random sample of the male and female population of Tomsk aged 25–64 years (n = 1,600). The program and protocol of the study corresponded to the principles of the Helsinki Declaration, reviewed and approved by the local ethical committee of Cardiology Research Institute, Tomsk National Research Medical Centre (Tomsk, Russia). All the surveyed signed a voluntary informed consent to participate in the study. The design of the study, the methodology of sampling, measurement of blood pressure and other biometric indicators were described

in detail by us earlier [4, 5]. The analysis included 480 respondents with hypertension who were taking antihypertensive drugs. Hypertension was diagnosed at the level of systolic blood pressure (SBP) ≥ 140 and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or if the respondent received AND. The analysis included the data from 480 respondents selected in accordance with the criteria for the presence of hypertension and taking antihypertensive drugs. Hypertension was determined at the level of systolic blood pressure (SBP) ≥ 140 and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or if the respondent received antihypertensive drugs (AND). The target blood pressure indices were SBP < 140 and DBP < 90 mmHg. The control of hypertension meant the achievement of target blood pressure levels. The presence of antihypertensive therapy was defined as taking one or more AND for at least 2 weeks prior to screening.

The following associative factors were analyzed: age, family status, the level of education, level of income; eating habits, opinion about the impact of hypertension on health, the awareness of the personal blood pressure, level of physical activity, alcohol consumption; presence of hypertension, CVD, diabetes mellitus in close relatives; awareness of the presence of CVD, rheumatoid arthritis, asthma, bronchitis; thickness of the intima – media complex, the presence of carotid plaques, height, indicators of quality of life (EUROQOL-EQ-5D); smoking, taking beta-blockers, calcium channel antagonists, I-ACE, angiotensin receptor blockers, diuretics, statins, the number of antihypertensive drugs taken, number of visits to a doctor over the past year, body mass index, obesity, diabetes mellitus, metabolic syndrome (MS; IDF) and its components, the number of active metabolic risk factors besides hypertension.

The criteria for moderate and excessive alcohol consumption were considered to be < 168 and ≥ 168 g of ethanol per week for men and < 84 and ≥ 84 g for women. Low level of physical activity was defined as < 150 min per week of moderate or < 75 min per week of intensive aerobic exercise. People who smoked at least one cigarette a day or those who quit smoking less than a year ago were considered smokers.

The habit of adding extra salt to food was considered as excessive salt intake. The level of wealth was determined from 1 to 5, ranking the categories of answers from "not enough even for the most necessary" (1) to "the opportunity to buy a house, apartment, expensive car" (5).

Statistical analysis

Data analysis was carried out in the statistical software packages SPSS (v.13) and R (v.2.15). Gender frequency comparisons were carried out by the chi-square method and the Fisher exact test if the former was not applicable. The McNemar criterion was used for paired frequency comparison. Comparisons of continuous variables were carried out using the t-test and the Mann–Whitney test. The method of multivariate step-by-step logistic regression was used to analyze the relationships. Age, level of affluence, the presence of CVD, the number of antihypertensive drugs taken, were introduced into the model as co-variants. The odds ratio (OR) of detecting the target blood pressure level in the surveyed population was evaluated, adjusted for the influence of other factors. The probability of error <5% was considered statistically significant.

Results

The characteristics of the surveyed are presented in Table 1.

Among those who received drug therapy, there were almost twice as many women as men. In general women were significantly more likely to control hypertension than men and in particular according to the criteria of SBP and DBP. The percentage of men controlling SBP and DBP did not differ ($p = 0.30$) while women were significantly more likely to reach the target level of DBP than SBP ($p<0.001$). Men had higher indicators of the income level, the frequency of smoking, CVD, the total height of atherosclerotic plaque; women had higher cholesterol levels and the occurrence of the "visit to the doctor over the past year" factor. According to other indicators, the males and females did not differ significantly. Both men and women had two metabolic RF in addition to AH on average. The odds ratio of target blood pressure levels in women compared to men was 2.0 (95% confidence interval (CI) 1.3–3.0; $p = 0.001$).

At the next stage, multivariate regression models were constructed to achieve target blood pressure levels in men ($22 = 59.23$; $df = 10$; $p<0.001$) and women ($\chi^2 = 87.41$; $df = 8$; $p<0.001$) (Table 2).

According to multivariate analysis, smoking, taking statins, and a positive response to a question about pain or discomfort are associated with higher chances of detecting target blood pressure values in men. The inverse association was shown by age, kidney disease, the number of metabolic RF and bronchitis. In women

Table 1. Comparative characteristics of the sample surveyed

Indicator	Men	Women	p
Age, years, m (SE)	53,2 (0,66)	54,2 (0,46)	0,24
Sex, %	34,2	65,8	–
SBP <140, mm Hg, %	32,9	47,5	0,02
DBP <90, mm Hg, %	38,4	64,9	<0,001
AH control, %	28,2	44,9	0,001
Higher education, %	42,1	35,1	0,14
Average income, %	31,7	26,6	0,24
Income higher than average, %	31,7	15,2	<0,001
Visit to a doctor for the past year, %	70,1	80,7	0,009
Regular smoking, %	34,8	8,5	<0,001
Cardiovascular diseases, %	32,9	22,1	0,01
ACE inhibitors, %	18,9	15,5	0,34
Beta-blockers, %	28,1	33,2	0,25
Diuretics, %	31,1	34,5	0,45
Hypotensive medication count, m (SE)	1,57 (0,05)	1,66 (0,04)	0,20
Monotherapy, %	54,3	50,3	0,41
Statins, %	11,6	7,6	0,15
Total carotid plaque thickness, m (SE)	2,65 (0,26)	1,10 (0,11)	<0,001
Total cholesterol, mmol/L, m (SE)	5,8 (0,11)	6,1 (0,06)	0,02
Glucose, mmol/L, m (SE)	6,2 (0,17)	6,0 (0,09)	0,21
IDF metabolic risk factor count except AH, m (SE)	2,04 (0,08)	1,96 (0,07)	0,41
Kidney diseases, %	25,6	26,6	0,82

Note: ACE – angiotensin-converting-enzyme; AH – arterial hypertension; DBP – diastolic blood pressure; SBP – systolic blood pressure.

“a visit to the doctor over the past year” correlated with a higher probability of detecting target BP values but the number of metabolic RF, heart rate (HR) ≥ 75 beats/min and the total height of carotid ASP - with the lower one. The absence of correlations of the studied indicator with the presence of CVD is obvious; the number of antihypertensive drugs in sexes and the level of income in women; in men, such an association can be traced as the trend level. After correction for age, smoking, the level of wealth and education, the presence of CVD, bronchitis, kidney diseases in the anamnesis, the total height of ASP, heart rate, “a visit to the doctor over the past year”, the number of antihypertensive drugs and metabolic RF, statins, the detection of target blood pressure values in women compared to men was 3.0 (95% CI 1.7–5.2; $p < 0.001$).

Two-thirds of the variation in effective hypertension control was determined by four factors: kidney disease, age, smoking and the number of metabolic RF in men and heart rate, the total height of ASP, “a visit to the doctor over the past year” and the number of metabolic RF in women. The independent contribution of these factors in was approximately equal (15–17%), while in women the overwhelming role belonged to the number of metabolic RF (52%).

Discussion

Accelerated development of atherosclerosis due to faster penetration of atherogenic lipoproteins into intima in conditions of elevated blood pressure is

recognized as one of the main mechanisms of the influence of hypertension on the risk of CVD.[6]. According to the studies, hypertension is associated with an increased frequency of ASP detection, the number of affected carotid segments, the probability of detection and the severity of coronary atherosclerosis [7, 8]. To reduce cardiovascular morbidity, it is necessary to contain blood pressure at relatively safe (target) levels, since the indicators increase with age, exceeding the recommended norm in the vast majority of the population [4].

The effectiveness of hypertension treatment remains one of the most urgent public health problems. Not more than half of people with hypertension in the Russian population taking antihypertensive drugs reach the target blood pressure levels [3]. According to one-dimensional analysis, the value of this indicator in the surveyed sample of the population was 28.2% for men and 44.9% for women [4]. The epidemiological analysis of the situation demonstrates to what extent the achievement of target blood pressure levels is associated with the current socio-demographic and medical factors and thus helps to identify areas that require more attention from medical specialists.

According to the data obtained earlier, the factors associated with the detection of hypertension in the examined population were age, biometric indicators of body weight, the presence of hypertension in close relatives, heart rate, excessive salt intake, educational status, etc. [1]. Contributing to higher blood pressure

Table 2. Association of factors to reaching blood pressure targets in the multivariable logistic regression models			
Factor	χ^2	OR (95% CI)	p
Men			
Age	8,89	0,92 (0,87–0,97)	0,003
Cardiovascular diseases	0,04	0,89 (0,33–2,44)	0,825
Hypotensive medication count	1,07	0,69 (0,34–1,39)	0,300
Wealth level	3,38	1,53 (0,97–2,42)	0,067
IDF metabolic risk factor count except AH	7,76	0,52 (0,33–0,82)	0,005
Kidney diseases	8,70	0,15 (0,04–0,53)	0,003
Statins	5,64	5,54 (1,35–22,8)	0,018
Feeling of pain or discomfort	5,12	2,97 (1,16–7,61)	0,024
Bronchitis	4,19	0,27 (0,08–0,95)	0,041
Regular smoking of ≥ 20 cigarettes	12,7	8,07 (2,56–25,5)	<0,001
Women			
Age	3,87	0,96 (0,93–1,00)	0,049
Cardiovascular diseases	0,13	1,13 (0,59–2,17)	0,716
Hypotensive medication count	1,67	0,80 (0,56–1,13)	0,198
Wealth level	0,64	0,89 (0,67–1,18)	0,422
IDF metabolic risk factor count except AH	37,6	0,46 (0,35–0,59)	<0,001
Heart rate ≥ 75 bpm	8,21	0,45 (0,26–0,78)	0,004
Total carotid plaque thickness (effect of the indicator increase by 1 mm)	4,31	0,84 (0,71–0,99)	0,038
Visit to a doctor for the past year	4,14	2,01 (1,03–3,93)	0,042

Note: AH – arterial hypertension; CI – confidence interval; OR – odds ratio.

values, these, as well as some other factors may reduce the effectiveness of drug therapy. In a recent study [3], the authors analyze the influence of the main CVD RF on the effectiveness of hypertension treatment in the Russian population. The important role of age, increased heart rate, alcohol intake, individual metabolic CVD RF, educational status has been established. The aim of the presented work was to analyze the state of the issue with the inclusion of a number of additional social and clinical variables in the analysis.

Ageing influences the achievement of target blood pressure levels and it was detected less frequently in both sexes, but mainly in men, these numbers are consistent with the trends observed in the national sample as a whole [3]. A significant role of age is noted in the German population [9]. As it is known, age is the “accumulator” of the influence of most, if not all, known CVD RF, however, the data obtained do not allow us to assert that age is the leading factor complicating the effective treatment of hypertension.

The chances of detecting target blood pressure levels were significantly higher in women than in men, which also reflects the situation in the Russian sample as a whole [3]. In the German population, women treated hypertension as effectively as in the examined sample, but the difference between the sexes was minimal [9]. A possible explanation for such gender differences is a less attentive attitude to health in the male population, as has been reported in domestic studies re than once In particular, women are more committed to hypertension therapy than men, which triple the chances of achieving target blood pressure levels in 3–12 months after a visit to the doctor [10].

It is known that the progression of central obesity underlying MS contributes to the cascade manifestation of other components of MS – dyslipidemia, hyperglycemia, hypertension. The role of overweight in reducing the effectiveness of hypertension treatment is progressively increasing and this is a global problem [1, 3]. At the same time, it is not always clear which factor makes effective treatment the most difficult: overweight, general obesity, MS, its individual components or their number. The study shows that the variation of the studied indicator was most explained by the number of active components of MS except AH. The obtained fact is consistent with the results of studies [3, 9] and indirectly confirms the important role in the discussed problem of obesity and other manifestations of MS. The number of MS components reflects the severity of metabolic disorders, with an increase in which the intensity of compensatory mechanisms, including hypertension, aimed at maintaining adequate metabolism, probably increases. Correction of two or more metabolic RF by intentionally reducing excess weight can be a significant contribution to improving the effectiveness of drug treatment of hypertension in both male and female populations.

Kidney diseases and hypertension are largely united

by the problem of chronic kidney disease (CKD), characterized by a progressive decrease in renal function and the development of nephrosclerosis. The most common causes of this condition are diabetes mellitus, hypertension, glomerulonephritis, and polycystic disease. The complexity of the relationship between AH and CKD is that hypertension can be both a cause and a consequence of the latter. However, in any scenario, a decrease in renal function significantly complicates the effective control of hypertension. Most people with CKD fail to fully achieve the target BP values even with maximum support [11]. The association of the studied indicator with kidney diseases was revealed only in the male population, which may be explained by exposure to hypertension at an earlier age [1].

Chronic lung pathology refers to preventable, treatable diseases, in the structure of causes of death in which 25% is assigned to CVD. A large cross-sectional study showed an independent association of chronic obstructive pulmonary disease with the probability of detecting hypertension in men [12]. Long-term smoking and environmental factors make a significant contribution to the development of chronic lung diseases. This pathology is characterized by the development of periodic, and eventually persistent hypoxia, which causes hypertension due to increased heart rate and SBP [13]. This mechanism largely explains the data obtained on less effective drug treatment of hypertension in men who have had bronchitis.

Chronic hyperactivation of the sympathetic nervous system is the most important stimulator of heart rate and blood pressure, and probably contributes to the development of persistent hypertension. The association of these two factors is reported both in cross-sectional and prospective epidemiological studies [1, 14]. In particular, it is known about the correlation of heart rate with the risk of hypertension in the future [14]. A moderate contribution of this factor to the inefficiency of hypertension control in women was revealed. In men, other factors probably interfere with this association: smoking, bronchitis, the amount of metabolic RF.

The severity of carotid atherosclerosis (total height of ASP) showed an inverse relationship with the effectiveness of blood pressure control in the female population. The revealed association is known from many studies – previously we reported on the conjugacy of SBP and the number of affected segments in a subsample of individuals with carotid atherosclerosis [7]. The data obtained indicate the relevance of such an association in the hypertensive population receiving AND. This factor was not selected in the male model, which is largely due to age and does not indicate the absence of a male relationship as such [7].

According to the data obtained in men, taking statins can make a significant contribution to the effectiveness

of hypertension control. The conjugacy of these factors was previously reported as part of the problem of insufficient statin intake in the general population [15]. The nature of the observed association is not completely clear. The presence of hypertension implies the mandatory use of statins at very high risk and high (in many representatives) risk. Both hypotensive and hypolipidemic therapy are based on the concept of target levels. It can be assumed that people who additionally take statins better understand the purpose and criteria for the effectiveness of hypertension treatment, which allows them to be active, contributing to the control of the disease.

According to the analysis of the national sample, a decrease in the quality of life in the hypertensive population receiving AND is reported in comparison with the rest, regardless of the effectiveness of treatment [16]. The data obtained indicate that there is an inverse relationship between the quality of life in terms of "pain/discomfort" and the probability of achieving target blood pressure levels in men. Presumably, patients can treat hypertension more effectively if they associate discomfort/pain syndrome with hypertension. The nature of this association will probably be studied in more detail in the future.

The average level of education in the Russian population is associated with less effective treatment of hypertension compared to a more educated population group [3], which is not confirmed by the data we have obtained. As the social variables show, the level of wealth in men shows only a weak relationship with the studied indicator.

According to experts, regular visits to the doctor are mandatory for people taking AND [17]. "A visit to the doctor over the past year", according to our data, increased the chances of identifying target blood pressure levels in women. The population reserve regarding the improvement of this indicator was small, which is explained by the high percentage of women who visited the doctor over the past year.

Literature data on the nature of the relationship between regular smoking and blood pressure levels cannot be called unambiguous [18, 19]. [21]. Two possible reasons for the detection of lower blood pressure values in smokers are discussed: the vasodilating effect of cotinine – one of the main metabolites of nicotine [20], and quitting smoking on the day of cardiological screening, which is provided for by the protocols of most studies and leads to a temporary decrease in the activity of the sympatho-adrenal system, blood pressure and heart rate [21]. Undoubtedly, it is a mistake to interpret the paradoxical association of smoking and blood pressure as a beneficial effect, since prolonged smoking leads to irreversible structural and functional changes in blood vessels through other mechanisms.

In this work, the probability of achieving the target

blood pressure levels in the examined population practically did not depend on social factors, the attitude to hypertension as a RF, salt intake, knowledge of one's blood pressure level, low physical activity, the presence of CVD, specific classes and the number of antihypertensive drugs taken. The results obtained do not refute the significance of these variables for the control of hypertension, but rather indicate the absence of their independent contribution in the context of the revealed patterns.

Restrictions

The restrictions include the one-time design of the study, which does not allow considering many issues from a causal point of view. All the assumptions made in the article are probabilistic in nature. Classes were taken into account in this work, but other aspects of taking AGP, including adherence to treatment, which play an important role in the problem under consideration, were not affected.

Conclusion

This study analyzes the association of a wide range of social, clinical and instrumental factors with the effectiveness of drug control of hypertension in the hypertensive population of working age. According to multivariate analysis, statin intake, a decrease in the quality of life in the measurement of the "pain/discomfort" indicator, and to a lesser extent, the level of income are associated with higher chances of identifying target blood pressure values in men. The inverse association was shown by age, the number of metabolic RF, previous or existing kidney diseases and bronchitis. In women with a higher probability of detecting target BP values, "a visit to a doctor over the past year" correlated with a lower one – the number of metabolic RF, heart rate ≥ 75 beats/min and the total height of carotid ASP. The hypothesis about the significant role of social factors, the attitude to hypertension as a RF, salt consumption, alcohol consumption, knowledge of the level of one's blood pressure, low physical activity, the presence of CVD, taking specific classes and the number of antihypertensive drugs taken is not confirmed by the data obtained.

Achieving the target blood pressure levels is the most important task aimed at combating hypertension and its health consequences. The results of this work emphasize the ineffectiveness of hypertension control with the help of factors such as the number of metabolic RF, age, kidney disease, high heart rate, bronchitis, non-attendance of a doctor over the past year, as well as the severity of carotid atherosclerosis. The situation can positively be affected by intentional reduction of excess weight, taking statins by very high and high-risk individuals, as well as regular visits to the doctor. It is necessary to further study the factors that make it

difficult to achieve the target blood pressure levels, as well as methods aimed at the prevention and effective correction of metabolic disorders.

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Conflict of Interest

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Author Contribution Statement

KVS – contribution to the concept of the study, data collection and analysis, manuscript writing, approval of the final version, fully responsible for the content

SVN – contribution to the concept of the study, data collection and analysis, editing, approval of the final version, fully responsible for the content

TIA – contribution to the concept of the study, data collection and analysis, editing, approval of the final version, fully responsible for the content

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