

Optimized management of hypertensive patients with anxiety: focus on non-pharmacological approaches

Viktorova IA, Lisnyak MV*, Trukhan DI

Omsk State Medical University of the Ministry of healthcare of the Russian Federation, Omsk, Russia

Authors

Inna A. Viktorova, M.D., PhD, professor, doctor of sciences, head of the Department of Internal Medicine and Outpatient therapy, Omsk State Medical University of the Ministry of healthcare of the Russian Federation, Omsk, Russia

Marina V. Lisnyak, M.D, PhD, assistant professor of the Department of Internal Medicine and Outpatient therapy, Omsk State Medical University of the Ministry of healthcare of the Russian Federation, Omsk, Russia

Dmitry I. Trukhan, M.D., Ph.D., doctor of sciences, professor of the Department of Internal Medicine and Outpatient therapy, Omsk State Medical University of the Ministry of healthcare of the Russian Federation, Omsk, Russia

Resume

Objective

To optimize the management of patients with hypertension and anxiety in order to increase the adherence to treatment by non-pharmacological approaches in addition to basis therapy.

Materials and methods

The study involved 209 patients with arterial hypertension and anxiety. Adherence to drug therapy was estimated by Moriski Green's questionnaire. Anxiety was diagnosed by the Hospital scale of anxiety and depression. The subjectively perceived stress was estimated by a visual analogue scale of stress at work and at home.

Results

We investigated 149 factors and determined factors influencing the adherence to treatment in this cohort of patients. Based on selected factors, the procedure of prediction of non-adherent behavior in patients with AH and anxiety using the results of binary logistical regression has been created. The authors have developed "Non-pharmacological approach" (Patent №2525736) based on works investigating progressive muscle relaxation and controlled mental visualization. The research for assessment of adherence to treatment dynamics after the cycle

* Corresponding author. Tel. +7 (3812)-74-44-27. E-mail: lisnyak80@mail.ru

of lessons in the "School of Health" with the standard program and using the "non-drug method of influence" (Patent №2525736) has been performed in 104 and 105 patients with AH of I and II groups respectively. It has been demonstrated, that progressive muscle relaxation exercises and controlled mental visualization (patent № 2525736) normalize blood pressure levels and increase patients' adherence to treatment, maintaining achieved results during 24 month observation.

Key words

Arterial hypertension, anxiety, non-pharmacological approach.

Anxiety is a personal feature, characteristic of temperament, caused by weakness of nervous processes and characterized by predisposition to frequent and intense experiencing of uneasiness [1]. According with numerous Russian and international studies, anxiety worsens the course of many somatic diseases and creates conditions for polytherapy [2]. Anxiety is diagnosed in 12-46% of arterial hypertension (AH) cases [2-5]. The presence of anxiety leads AH patients to violation of therapeutic regimen or even makes them refuse take drugs [6]. Studies of compliance to therapy in this category of patients are quite general [7, 8]. There are no data about the degree of distinct factors' impact on compliance, and up to date no techniques of non-compliant behavior prognosis have been developed in this cohort of patients.

Additional of non-pharmacological anxiety correction and formation of self-regulation skills to somatic disease treatment is one of variants to optimize the management of patients with AH allowing augmentation of therapy efficacy without increasing the number of prescribed drugs [2-9]. Relaxation techniques are more efficient, they reduce anxiety manifestations being used as a part of a complex approach for treatment of several diseases [10].

Behavioral methods reducing anxiety include progressive muscle relaxation developed by Jacobson E. and directive mental imagery devised by Simonthon C., Simonthon S. and Rossman M [9].

Methods directed on creation of positive mental images have been described just in elderly AH patients not receiving antihypertensive drugs exclusively with mental images of "heaviness" and "warmth" during autogenic training [10].

We developed "Non-pharmacological approach using progressive muscle relaxation, controlled mental visualization for treatment of patients with arterial hypertension" (Patent № 2525736, hereinafter "Non-pharmacological approach") based on Jacobson's method of progressive muscle relaxation and directive mental imagery worked out by Simonthon and colleagues [9]. "Non-pharmacological approach" provides blood pressure (BP) normalization, anxiety

levels reduction by means of consequent, specially selected exercises for contraction and relaxation of particular muscle groups, creation of mental images in mind in addition to basis antihypertensive therapy. This "non-pharmacological approach" is quite topical in terms of the World Health Organization (WHO) guidelines on reduction of cardiovascular disease (CVD) development and progression risk factors influence.

The aim of this study was to optimize the management of patients with AH and anxiety to increase their compliance to treatment using non-pharmacological approach in addition to pharmacological therapy.

This study has been performed in two phases. The first stage was designed as a "case-control" study involving 209 patients into the group, the second stage was characterized as a prospective crossover observation of previously formed cohort of patients.

Materials and methods

209 patients with AH and anxiety that have been separated into two groups (n=104 and n=105) using envelope method participated in this study. Number of males in the first group was 48.1% (n=50) and in the second one – 44.8% (n=47). Number of females in the first group was 51.9% (n=54) and in the second one – 55.2% (n=58). Median of age in the first group was 45(41; 50) years and 47 (43; 51) in the second group. Necessary number of observations was quantified using Lopez Gemenes formula and Boyarskiy tables [11]. The protocol of this study has been approved by local ethic committee of Omsk State Medical University. Every patient received detailed information about ongoing study and signed informed consent form.

Inclusion criteria for this study: 1) males and females aged 40-55 years; 2) verified AH of I, II, III stage diagnosis; 3) presence of anxiety according with the HADS questionnaire; 4) patient's consent to participation in the study.

Exclusion criteria for this study: 1) symptomatic AH in endocrine system diseases, kidney diseases, disorders of renal vessels and central nervous system,

other symptomatic hypertension; 2) excessive alcohol consumption; 3) patients with acute diseases and exacerbation of chronic diseases; 4) patient's refusal from participation in the study;

Patients' adherence to pharmacological treatment in this cohort of patients was estimated using Morisky-Green questionnaire. Anxious disorders were diagnosed using Hospital Anxiety and Depression Scale. Intensity of subjectively perceived stress as estimated using visual analogue scale of stress at home and at work, life quality was assessed using SF-36 questionnaire. 24-hours ambulatory BP monitoring (ABPM) was performed using "Valenta" gadget (limited liability company "Neo", Saint Petersburg, Russia).

Statistical estimation of results was performed with descriptive statistics and graphic analysis methods using standard . Microsoft Excel 2003 and Statistica 8.0 software. Results didn't have normal distribution, thus their quantitative estimation was performed using non-parametric methods and obtained results are presented as median, upper and lower quartile – Me, (P25, P75), absolute values (n) and percentage \pm error of the proportion ($\% \pm m$). Mann-Whitney test (Z) was used for comparison of two independent groups, Wilcoxon (z) test was performed for comparison of two linked groups. The χ^2 test was used for comparison of categorical data. Correlation between variables was evaluated with Spearman's rank correlation coefficient. Analysis of correlation between several variables was assessed using univariate and binary logistic regression analysis. The technique of non-compliant behavior of patients with AH and anxiety prediction has been created using regression equation. Results were considered significant if p-value was <0.05 [11].

In the beginning of the study only one fifth part of patients of both groups were adherent to pharmacological therapy of AH. These numbers are less by 9-17% comparing with the patients without comorbid anxiety [12].

Results

We investigated 149 factors and determined factors influencing compliance in this cohort of patients. These factors have been subdivided into three groups: socio-demographic and psychological, features of patients' behavior, patients' condition and prescribed therapy.

The first group of factors included: marital status, level of anxiety/depression, subjective attitude to stress, role functioning, caused by emotional condition, psychical health [3; 13].

The second group of factors included features of patients' behavior in terms of modifiable risk factors: addition of salt to food, smoking status, physical activity [14].

The third group consisted of: AH manifestations intensity, presence of concomitant pathology, BP values measured during ABPM, examples of treatment refusal in the past [15-18].

Spearman's rank correlation analysis revealed statistically significant negative correlations between characteristics of compliance to pharmacological treatment and several factors in patients with AH and anxiety. The majority of studied factors are linked directly, it restricts their use for further analysis in order to create the technique of non-compliant behavior prediction.

We selected four factors, correlation between which was not statistically significant. Then regression coefficients have been quantified (degree of each factor's impact on the model).

Parameters of binary logistic regression and their estimation are present in Table 1.

The factor of treatment refusal in the past was the most important one between factors participating in non-compliant behavior formation. The risk of non-compliant behavior in this case was 2.34 times higher than in case of this factor's absence. The probability of non-compliant behavior in anxious patients with AH in case of absent complaints during treatment is

Table 1. Contingency criteria value and relative risk of non-compliant behavior according with the results of univariate logistic regression

Factor	Regression coefficient, β	Wald's test	Level of significance
Constant, β_0	1,79		
Lack of a partner	2,06	12,56	0,043
Addition of salt to food	0,91	1,38	0,924
Low physical activity	0,76	2,65	0,563
Smoking	1,92	10,04	0,042
Persistent complaints during AH therapy	2,29	15,27	0,023
Examples of treatment refusal in the past	2,34	17,39	0,000

2.29 times lower than the same value in patients with preserved complaints during pharmacological AH treatment. Smoking and lack of a partner increased the risk of non-compliant behavior twice.

We created a technique of non-compliant behavior of patients with AH and anxiety based on selected factors and results of binary logistic regression [6]. Logistic regression equation (1):

$$Y = \frac{\exp[-1,79 + 2,34 \times X_1 + 2,29 \times X_2 + 2,06 \times X_3 + 1,92 \times X_4]}{1 + \exp[-1,79 + 2,34 \times X_1 + 2,29 \times X_2 + 2,06 \times X_3 + 1,92 \times X_4]}$$

where

Y – probability of non-compliant behavior expressed as decimal fraction;

X₁, X₂, X₃, X₄ – (predictors) factors influencing non-compliant behavior;

B₀ – absolute term (regression coefficient). Constant.

β₁, β₂, β₃, β₄ – regression coefficients for X₁, X₂, X₃, X₄ predictors;

exp – a power function, e – natural logarithmic base, approximately equal to 2.72.

Comorbid somatic pathology was present in 36.4±3.3% (n=76) of patients involved in this study. The majority of patients with comorbid somatic pathology had diabetes mellitus (DM) 2 type(68.4±5.3%). Patients with DM 2 type had more evident deviations of 24 hours BP profile during ABPM in comparison to patients without DM 2 type (Figure 1). Differences between these groups are statistically significant (χ²=2.093, p=0.043).

After selection of patients and their division into groups we performed a randomized prospective cohort crossover study with control examinations after 2, 12, 14 and 24 months after the beginning of the

study to estimate the changes of compliance of patients with AH and anxiety in the first group (n=104) and the second group (n=105) after a cycle of lessons at the School of Health using standard program [19] and “Non-pharmacological approach”.

According with the study design, patients of the second group attended standard lessons at the School of Health during first months, and patients of the first group attended the same lessons during 13 and 14 month after the beginning of observation. Education was performed according with the study guide for doctors “School of health for patients with arterial hypertension” [19]. Patients of the first group attended the School of Health lessons where “Non-pharmacological approach” was introduced during first months, and patients of the second group attended the same lessons during 13 and 14 month after the beginning of observation.

After two months of weekly education to perform exercises of “Non-pharmacological approach” patients received recommendations how to make the same exercises at home every week during 6-10 months. Exercise regimen was regulated taking into account how much busy were patients. Once in every two months patients of the first group (3-12 months of study) and patients of the second group (15-24 months of study) had to call the researcher and report their general state and BP dynamics. In parallel patients of the first group (3-12 months) and patients of the second group (15-24 months) were supervised once in 3 months by physicians and general practitioners in outpatient setting (according with the law of USSR Healthcare ministry from 30.05.1986 №770 “About the order of mass healthcare examination”. Information about the treatment was obtained dur-

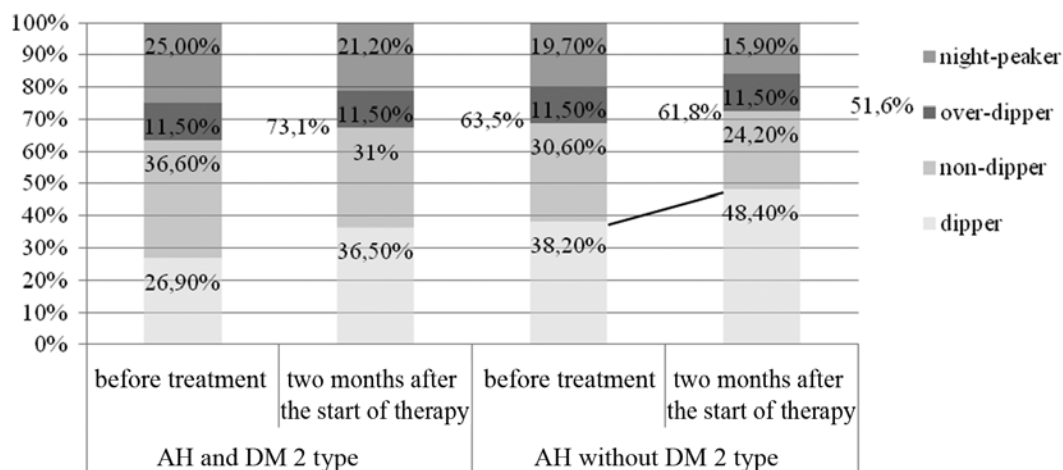


Figure 1. 24-hours BP profiles in patients with concomitant DM 2 type and without DM 2 type in the beginning of the study and 2 months after the start of “Non-pharmacological approach” use.

Table 2. Dynamics of subjective attitude to stress at work and presence of evident anxiety in patients with AH and anxiety during 24-years observation

Factors	Subjective attitude to stress at work			Anxiety with evident symptoms		
	Group I	Group II	Mann-Whitney test	Group I	Group II	Mann-Whitney test
	Abs	Abs.	Z; p	Abs	Abs	Z; p
0 months (start of the study)	76	77	0,219; 0,746	76	76	0,286; 0,732
2 months	29	59	8,913; 0,000	0	38	9,531; 0,002
12 months	21	62	8,734; 0,000	0	42	7,392; 0,003
14 months	17	15	0,903; 0,089	0	0	
24 months	15	14	0,841; 0,108	0	0	

ing personal talk 12 months after the beginning of the study because the majority of patients refuse to follow the treatment at this time [7].

Control examinations were performed 2, 12, 14 and 24 months after the beginning of the study.

Patients demonstrated the levels of compliance to antihypertensive therapy increased by $35.4 \pm 3.3\%$ after the end of education in the "School of health" using "Non-pharmacological approach". In comparison patients who attended standard lessons at the Health School increased compliance by $13.4 \pm 2.4\%$. 12 months after the beginning of observation $64.6 \pm 3.3\%$ of patients who followed the lessons of the School of health with the addition of "Non-pharmacological approach" remained compliant to pharmacological treatment of AH, whereas only $46.9 \pm 3.5\%$ of patients who followed standard lessons remained compliant.

After the cycle of lessons in the School of health with addition of "Non-pharmacological approach" the levels of subjectively perceived stress at work reduced by 45% and clinically evident anxiety was smoothed over (Table 2). Achieved results had been maintained until the end of the study in the first group and in the second one until 12 months of observation.

After obtaining statistically significant positive dynamics of compliance, reduction of subjectively perceived stress and anxiety levels we estimated BP changes during ABPM in this cohort of patients.

By the end of the cycle of lessons in the School of Health with addition of "Non-pharmacological approach" patients demonstrated reduction of average daily BP levels.

Optimization of management of patients with arterial hypertension and anxiety disorders after the education in the School of health with addition of "Non-pharmacological approach" in compliant patients of the first group was characterized with significant positive dynamics of average daily systolic BP (SBP), by its reduction. Achieved results had been maintained until the end of the study. Compliant pa-

tients of both groups after the education in the School of health with addition of "Non-pharmacological approach" demonstrated reduction of average daily BP: in the first group by 7 mm Hg ($Z=8.2369$; $p \leq 0.01$) and in the second group by 6 mm Hg ($Z=8.4976$; $p \leq 0.01$).

Average daily diastolic BP (DBP) values reduced in compliant patients of both groups after the education in the School of health with addition of "Non-pharmacological approach", DBP decreased by 5 mm Hg in the first group ($Z=8.5072$, $p < 0.01$) and by 4 mm Hg. in the second group ($Z=7.9364$; $p \leq 0.01$).

Patients with DM 2 type, selected during the first stage of the study from the patients with comorbid somatic pathology were characterized with more evident deviations of 24-hours BP profiles. As patients without DM 2 type, patients with comorbid DM 2 type demonstrated decrease of number of 24-hour BP profile deviations (figure 1) after the education in the School of health with addition of "Non-pharmacological approach", differences between groups are statistically significant ($\chi^2=2.164$, $p=0.047$).

Discussion

This study allowed to select factors that influence the most the compliance of patients with AH and anxiety independently on the presence of comorbid somatic pathology: socio-demographic factors: lack of a partner ($R=-0.493$, $p < 0.05$; $R=-0.506$, $p < 0.05$); factors reflecting patients' behavior: smoking ($R=-0.478$, $p < 0.05$; $R=-0.473$, $p < 0.05$); factors reflecting the course of disease - examples of AH treatment refusal in the past ($R=-0.519$, $p < 0.05$; $R=-0.523$, $p < 0.05$) and persistent complaints during antihypertensive treatment ($R=-0.431$, $p < 0.05$; $R=-0.363$, $p < 0.05$). We created the method of non-compliant behavior prediction in patients with AH and anxiety.

These results demonstrate that education of patients with AH and anxiety in the School of health with addition of "Non-pharmacological approach"

increases the levels of compliance to pharmacological treatment of AH by $35.4 \pm 3.3\%$ comparing with the standard education program ($\chi^2=8.96$; $p=0.049$).

Use of "Non-pharmacological approach" smoothed over clinically evident anxiety ($\chi^2=8.93$; $p=0.008$) and reduced subjective perception of stress at work $45.0 \pm 3.4\%$ ($\chi^2=6.74$; $p=0.047$), obtained results had been maintained during 24 months of observation.

It is necessary to notice that optimization of management of patients with AH and anxiety after education at the School of Health using the "Non-pharmacological approach" was accompanied with the reduction of average daily SBP by 7 mm Hg. in compliant patients of the first group ($Z=8.2369$; $p \leq 0.01$) and by 6 mm Hg. in the second one ($Z=8.4976$; $p \leq 0.01$); daily average DBP reduced by 5 mm Hg in compliant patients of the first group ($Z=8.5072$, $p < 0.01$) and by 4 mm Hg – in the patients of the second group ($Z=7.9364$; $p \leq 0.01$); it was also characterized by the reduction of deviations in 24-hours BP profile according with the ABPM results independently on the presence of comorbid somatic pathology from $61.8 \pm 3.9\%$ to $51.6 \pm 4.0\%$ in patients without DM 2 type and from $73.1 \pm 6.2\%$ to $63.5 \pm 6.7\%$ in patients with DM 2 type.

Thus, progressive muscle relaxation and controlled mental visualization "Non-pharmacological approach" exercises normalize BP values, increase the degree of patients' compliance to antihypertensive treatment, maintaining achieved results for 24 months of observation.

Conflict of interest: None declared

References

1. Large psychological dictionary. M.: Prime EVROZNAK. Ed. BG, Meshcheryakov, VP Zinchenko, 2002. 633s. Russian
2. Garganeeva NP, Belokrylova MF The main symptom and conditions of formation of neurotic and affective disorders in patients with cardiovascular disease. Siberian Medical Journal. 2009; 4: 11-7. Russian
3. Boitchev SA The structure of the factors of cardiovascular risk, and the quality of their prevention efforts in the primary care setting and Russia in European countries (according to the results of research EURIKA). Cardiovascular therapy and prevention. 2012; 11 (1): 11-6. Russian
4. Smulevich AB, Sirkin AL. Mental disorders in general medical practice. Psihokardiologiya. 2007; 4: 4-9. Russian
5. Bogner HR, de Vries HF. Integration of Depression and Hypertension Treatment: A Pilot, Randomized Controlled Trial. Ann Fam Med. 2008;6:295-301.
6. Garner JB. Problems of nonadherence in cardiology and proposals to improve outcomes. Am J Cardiol. 2010;105(10):1495-501.
7. Mazzaglia G, Ambrosioni E, Alacqua M, et al. Adherence to antihypertensive medications and cardiovascular morbidity among newly diagnosed hypertensive patients. Circulation. 2009; 120(16):1598-605.
8. Trukhan DI, Pozdnyakov YM Actual aspects of rational pharmacotherapy in cardiology. Pros and cons of fixed and arbitrary combinations of antihypertensive drugs. Consilium Medicum. 2016; 1: 25-31. Russian
9. Linden W, Moseley JV. The efficacy of behavioral treatments for hypertension. Appl Psychophysiol Biofeedback. 2006;31:51-63.
10. Ostir GV, Berges IM, Markides KS, et al. Hypertension in Older Adults and the Role of Positive Emotions. Psychosom Med. 2006;68:727-33.
11. Khalafyan AA. STATISTICA 6. Statistical analysis of the data. 2nd ed. M.: OOO "Bean-Press", 2010. 528 p. Russian
12. Garner JB. Problems of nonadherence in cardiology and proposals to improve outcomes. Am J Cardiol. 2010;105(10):1495-501.
13. Vorobyov OV. Stress and adjustment disorders. Russian Medical J. 2009; 11: 789-93. Russian
14. Jones DE, Carson KA, Bleich SN, et al. Patient trust in physicians and adoption of lifestyle behaviors to control high blood pressure. Patient Educ Couns. 2012;89(1):57-62.
15. Black HR. Controlling Hypertension: From Mechanisms to Management CME/CE. CME/CE Released: 06/15/2010. Available from: <http://www.medscape.org/viewarticle/723061>.
16. Ingersoll KS, Cohen J. The impact of medication regimen factors on adherence to chronic treatment: a review of literature. J Behav Med. 2008 Jun; 31(3):213-24.
17. Kettani FZ, Dragomir A, Cote R, et al. Impact of a better adherence to antihypertensive agents on cerebrovascular disease for primary prevention. Stroke. 2009; 40(1):213-20.
18. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005 (353): 487-97.
19. Chukaeva II, Orlova NV, OA Kislyak, et al. Health Schools for patients with cardiovascular diseases. Tutorial. M.: Russian State Medical University, 2011. 149 p. Russian