### **CLINICAL INVESTIGATIONS**

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# Evaluation of arterial hypertension control and treatment in daily practice of family physicians

Žaneta Petrulionienė<sup>1, 2</sup>, Daiva Asta Apanavičienė<sup>3</sup>

<sup>1</sup>Center of Cardiology and Angiology, Vilnius University Hospital Santariškių klinikos, <sup>2</sup>Department of Cardiovascular Medicine, Faculty of Medicine, Vilnius University, <sup>3</sup>"Sanofi-Aventis Lietuva," Lithuania

*Key words*: arterial hypertension; blood pressure control; antihypertensive drugs.

**Summary.** The objective of this study was to evaluate the percentage of patients with primary arterial hypertension treated with antihypertensive drug(s), who achieved target arterial blood pressure (ABP), and to compare the characteristics of patients with controlled and uncontrolled ABP, their current treatment, and treatment modifications.

Material and methods. A total of 429 18–80-year-old patients with primary arterial hypertension treated for  $\geqslant 1$  year participated in this study. General practitioners collected data on patients' demographic and clinical characteristics, current treatment for primary arterial hypertension, and treatment modifications.

Results. According to physicians, 45.4% of patients achieved target ABP levels. Adequately controlled ABP was documented more often in the group of low and moderate cardiovascular risk than in high- and very high-risk group (n=141, 62.9% versus n=54, 26.3%; P<0.0001). Based on ABP measurements, 160 (37.3%) patients had ABP of <140/90 mm Hg. The majority of patients were treated with a combination of two (n=153, 35.7%) to three (n=144, 33.6%) antihypertensive drugs. Patients with uncontrolled ABP more frequently than patients with controlled ABP were given combination therapy. Treatment was not modified in 37.8% (n=162) of patients, more commonly in those with controlled ABP.

Conclusions. The level of hypertension control in study population was far from optimal, especially in the group of patients at high- and very high-risk where target ABP was lower. Almost 12% of patients with uncontrolled ABP were still undergoing monotherapy, whereas 16% of patients were not recommended any modifications of antihypertensive treatment despite their ABP was not controlled.

#### Introduction

Arterial hypertension is one of the main risk factors of atherosclerosis. High blood pressure increases the risk of coronary heart disease, stroke, peripheral artery disease, and heart failure (1). Arterial hypertension is diagnosed for almost every second Lithuanian adult: in 1999, arterial hypertension was diagnosed for 59.3% of men aged 25–64 years and 42.1% of women of the same age (2).

Despite a number of medicines, efficacy of which was proved in clinical trials, comprehensive treatment recommendations, and the increasing amount of knowledge related to the pathophysiology of hypertension, the arterial blood pressure (ABP) control is still not adequate over the world. The results of epidemiological studies indicate that less than half of patients suffering from increased blood pressure are treated systemically in advanced industrial countries; in addition, the percentage of patients constantly receiving an effective treatment is only

15–20% (3). The main reasons of such inadequate results are related to patients (noncompliance with the treatment regime, poor toleration of drugs) and physicians (noncompliance with the accepted treatment recommendations, absence of complex and nonpharmaceutical treatment) (4–7). The effective antihypertensive treatment reduces the risk of stroke, coronary heart disease, and cardiovascular death by 38%, 16%, and 21%, respectively (3). Additionally, effective treatment improves quality of life in patients who received it (8).

Lately, there are limited data published in Lithuania regarding blood pressure control of the patients who underwent treatment. The objective of this study was to evaluate the percentage of patients with primary arterial hypertension and treated with antihypertensive drugs, who achieved target blood pressure defined in the Lithuanian guidelines on diagnostics and outpatient treatment of arterial hypertension (9) and to compare the characteristics of

Correspondence to D. Apanavičienė, "Sanofi-Aventis Lietuva," A. Juozapavičiaus 6/2, 09310 Vilnius, Lithuania E-mail: daiva.apanaviciene@sanofi-aventis.com Adresas susirašinėti: D. Apanavičienė, "Sanofi-Aventis Lietuva", A. Juozapavičiaus 6/2, 09310 Vilnius El. paštas: daiva.apanaviciene@sanofi-aventis.com

patients who achieved and did not achieve the target blood pressure, their current treatment, and recommended treatment modifications.

#### Material and methods

The permission to carry out this study was obtained from the Lithuanian Bioethics Committee. This epidemiologic trial was conducted in accordance with the ethical principles outlined in the Helsinki declaration accepted by the 18th General Assembly of the World Medical Association (Helsinki, 1964) and in the subsequent amendments of the declaration (1975, 1983).

The study was carried out during the period of November 2006 to January 2007. In order to see the real reflection of blood pressure control among hypertensive patients from various regions of Lithuania (both urban and rural population), randomly chosen physicians were asked to participate in the study. A total of 24 general practitioners from the cities of Klaipėda, Šilutė, Plungė, Telšiai, Skuodas, Šiauliai, Akmenė, Panevėžys, Kaunas, Šakiai, Kaišiadorys, Širvintos, and Vilnius and regions participated in this study. Each physician was allowed to include up to 15 patients. Every third patient who came for a regular visit was asked to participate in this trial. If the patient did not meet the inclusion criteria, the next one was asked to participate in this study. A total of 429 patients meeting inclusion criteria (18-80-year-old men and women, suffering from essential arterial hypertension and treated at least 1 year) participated in the study. In a single visit, physicians collected information about age, sex, duration of arterial hypertension, concomitant diseases, and risk factors, antihypertensive agents used, measured ABP and heart rate. Demographic and clinical data were recorded in accordance with patients' medical records. There were no specific laboratory tests carried out. Only ABP and heart rate were measured on the visit day. ABP was measured using a calibrated mechanic aneroid sphygmomanometer (manufacturer Rudolf Riester GmbH, Big Ben® model) after 5-minute rest; the test was performed in a sitting position. ABP was measured twice for each patient. In case of the difference in SBP and/or DBP by 10 mm Hg or more during the first two measurements, the physician was required to perform the third ABP measuring. The average value calculated from these measurements was entered into the data collection forms. Heart rate (beats in 1 minute) was also recorded after rest in a sitting position.

Risk factors of the patients were evaluated based on the following diagnostic criteria according to the European Society of Hypertension–European Society of Cardiology guidelines for the management of arterial hypertension (10):

- − Microalbuminuria: albumin concentration of >30 mg/24 h (corresponds to >20 μg/min in the morning urine sample or albumin-creatinine ratio of >22 mg/g for men and >31 mg/g for women in the random urine sample, or >20 mg/L determined using a reagent strip).
- Dyslipidemia: total cholesterol concentration of >6.5 mmol/L (250 mg/dL) or low-density lipoprotein cholesterol concentration of >4.0 mmol/L (155 mg/dL) or high-density lipoprotein cholesterol concentration of <1.0 mmol/L (40 mg/dL) for men and <1.2 mmol/L (48 mg/dL) for women.</li>
- Obesity: body mass index (BMI) of  $\geqslant 30 \text{ kg/m}^2$ .
- Smoking.

Patients were assigned by physicians to the groups of low or moderate risk for cardiovascular diseases or to high or very high risk for cardiovascular diseases. Evaluation of patients' risk was based on the Lithuanian guidelines on diagnostics and outpatient treatment of arterial hypertension (9) and data in the medical records regarding the risk factors, damages of target-organs, and diagnosis of concomitant diseases. Based on the criteria outlined in these guidelines, patients classified in the low or moderate cardiovascular risk groups had a high normal ABP or grade 1 hypertension plus 1-3 risk factors (except resistance to insulin and/ or diabetes). Patients at high or very high cardiovascular risk had only grade 2 hypertension or grade 1 or 2 hypertension and ≥3 risk factors (resistance to insulin, intolerance of glucose or diabetes was sufficient) and/or damages of target-organs caused by arterial hypertension and/or concomitant clinical disorders aggravating the course of hypertension or complicating its treatment. Following the evaluation of the patients' cardiovascular risk, physicians were required to assign them to one of the target ABP groups (<140/90 mm Hg in case of low and moderate risk, and <135/85-125/75 mm Hg in case of high and very high risk), to assess whether the target ABP was achieved or not, and to prescribe recommendations for a further treatment. ABP control was considered sufficient for the patients who achieved (based on physician's records) the target ABP. ABP control was considered insufficient for the patients who did not achieve (based on physician's records) the target ABP.

All information was registered anonymously into the standard data collection forms.

The descriptive statistical analysis was carried out. The frequency tables were prepared for the categorical variables. Descriptive statistical parameters (average, median, minimal value, maximal value, standard deviation, 5% ant 95% percentiles) were calculated for the continuous variables. Statistical differences were evaluated using the chi-square or Fisher's exact test for categorical variables and Stu-

dent's *t* test for continuous variables. Statistical differences were interpreted using a 5% significance level (two-sided). Statistical analysis was performed using the software SAS 9.1.2.

#### Results

A total of 429 patients suffering from essential arterial hypertension were enrolled into the study. There were 125 (29.3%) men and 301 (70.7%) women (gender of 3 patients was not indicated). The mean age of the patients was 61.7 years (SD, 10.7 years). Comparing men and women, there was no difference in the mean age (60.2 [SD, 11.6] and 62.3 [SD, 10.2] years, respectively) and mean ABP (143.3 [18.1]/87.3 [12.0] mm Hg and 144.2 [18.4]/85.2 [10.2] mm Hg, respectively). The mean duration of arterial hypertension of the patients was 12.7 years (SD, 9.1).

In accordance with the Lithuanian guidelines on diagnostics and outpatient treatment of arterial hypertension (8), 224 (52.2%) patients were assigned to the low or moderate cardiovascular risk group, and 205 (47.8%) patients to the high- and very high-risk group. There were more men than women in the high- and very high-risk group (53.6% and 45.5%, respectively), but the difference was not significant (P>0.05).

Based on physicians' evaluation, almost half of the patients (45.4%) achieved the proposed target ABP. In the low- and moderate-risk group, the target ABP (<140/90 mm Hg) was achieved in 141 (62.9%) patients, whereas in the high- and very high-risk group, the target ABP (<135/85-125/75 mm Hg) was achieved only in 54 (26.3%) patients (P<0.0001). The mean blood pressure of the patients was lower in the low- and moderate-risk group than those in the high- and very high-risk group (140.1 [16.4]/83.8 [9.3] mm Hg and 148.1 [19.2]/87.9 [11.9] mm Hg, respectively; P < 0.0001). The proportion of men and women who achieved the target ABP was similar in different cardiovascular risk groups: the target ABP was achieved by 36 (62.1%) men and 103 (62.8%) women from the low- and moderate-risk group and by 19 (28.4%) men and 35 (25.6%) women from high- and very high-risk group.

Based on measurements of blood pressure, ABP was appropriately controlled (<140/90 mm Hg) in 160 (37.3%) patients. The distribution of patients by different arterial blood pressure measured during the visit is presented in Fig.

All the patients who participated in this study were given antihypertensive agents at least for 1 year. Angiotensin-converting enzyme (ACE) inhibitors were most frequently prescribed drugs; 323 (75.3%) patients were given ACE inhibitors. Many patients used  $\beta$ -blockers (n=262, 61.1%), diuretics (n=204, 47.6%), and calcium channel block-

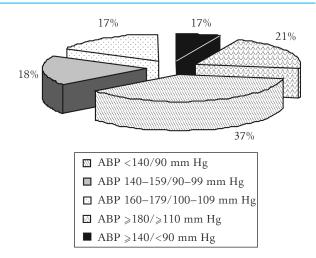


Fig. Distribution of patients by arterial blood pressure (ABP) achieved during the visit

ers (n=155, 36.1%). Angiotensin receptor blockers (n=51, 11.9%),  $\alpha$ -blockers (n=36, 8.4%), and other antihypertensive agents (n=39, 9.1%) were used less frequently. Only a small part of patients (n=68, 15.8%) used agents from one pharmacotherapeutic group. A combination of two and three antihypertensive agents was prescribed for 153 (35.7%) and 144 (33.6%) patients, respectively. Fifty-six (13.0%) patients used combination of the four groups and 8 (1.9%) of five. The most frequent combination of the two drugs was ACE inhibitors and  $\beta$ -blockers: this combination was used by 39.3% patients treated with two drugs. Patients treated with three drugs were given a combination of ACE inhibitors,  $\beta$ -blockers, and diuretics most frequently (27.4%).

Concomitant diseases, mostly coronary heart disease and heart failure, were present in 283 (65.9%) patients. Three hundred fifty-six (82.9%) patients had at least one risk factor, mostly obesity or dyslipidemia. There were more patients with several concomitant diseases or several risk factors in the group of patients who did not achieve target ABP (Table 1). In this group, more patients had diabetes mellitus, coronary heart disease or heart failure, metabolic syndrome or obesity.

Diuretics and calcium channel blockers were administered more frequently for the patients who did not achieve target ABP comparing with those who achieved target ABP; in addition, they were more frequently treated with combination of the two or more drugs. Distribution of patients by other antihypertensive drugs prescribed was similar (Table 2). Antihypertensive therapy was modified for 267 (62.2%) patients. Physicians recommended nonpharmacologic measures most frequently (diet, improved physical activity, changes in life style). Such recommendations were applied for almost half (48.0%) of the patients. Mostly, for the patients who achieved

Table 1. Clinical characteristics of patients who achieved and did not achieve target blood pressure

Characteristic	Patients who achieved target blood pressure (n=195)	Patients who did not achieve target blood pressure (n=234)
Age, mean (SD), years	61.0 (10.8)	62.2 (10.6)
Age ≽65 years	84 (43.1)	102 (43.6)
Systolic blood pressure, mean (SD), mm Hg	129.5 (7.5)	155.9 (15.7)*
Diastolic blood pressure, mean (SD), mm Hg	78.8 (6.8)	91.6 (10.1)*
Low and moderate risk	141 (72.3)	83 (35.5)*
High and very high risk	54 (27.7)	151 (64.5)*
No concomitant diseases	89 (45.6)	57 (24.4)*
More than one concomitant disease	65 (33.3)	113 (48.3)*
Concomitant diseases		
Diabetes mellitus	15 (7.7)	35 (14.9)*
Diabetic nephropathy	3 (1.5)	11 (4.7)
Coronary heart disease	74 (37.9)	127 (54.3)*
Peripheral artery disease	23 (11.8)	30 (12.8)
Heart failure	54 (27.7)	114 (48.7)*
History of atrial fibrillation	20 (10.3)	27 (11.5)
History of ischemic stroke	10 (5.1)	15 (6.4)
History of myocardial infarction	11 (5.6)	16 (6.8)
No risk factors	40 (20.5)	33 (14.1)
One risk factor	81 (41.5)	79 (33.8)
More than one risk factor	74 (37.9)	122 (52.1)*
Risk factors		,
Microalbuminuria	1 (0.5)	6 (2.6)
Metabolic syndrome	26 (13.3)	52 (22.2)*
Dyslipidemia	102 (52.3)	131 (55.9)
Obesity	90 (46.1)	150 (64.1)*
Smoking	20 (10.3)	27 (11.5)
Other	5 (2.6)	1 (0.4)

Values are number (percentage) unless otherwise indicated. \*P<0.05.

*Table 2.* Antihypertensive drugs used by patients who achieved and did not achieve the target blood pressure, and recommendations for treatment modifications

Antihypertensive drugs and recommendations for treatment modifications	Patients who achieved target blood pressure (n=195)	Patients who did not achieve target blood pressure (n=234)
Antihypert	ensive therapy	
1 antihypertensive drug	40 (20.5)	28 (11.9)*
≥2 antihypertensive drugs	155 (79.5)	206 (88.0)*
Antihypertensive drugs		
Diuretics	73 (37.4)	131 (55.9)*
Calcium channel blockers	59 (30.3)	96 (41.0)*
lpha-Blockers	15 (7.7)	21 (8.9)
eta-Blockers	118 (60.5)	144 (61.5)
ACE inhibitors	144 (73.8)	179 (76.5)
Angiotensin receptor blockers	21 (10.8)	30 (12.8)
Other antihypertensive drugs	16 (8.2)	23 (9.8)
Recommendations fo	r treatment modification	
Nonpharmacologic measures	66 (33.8)	140 (59.8)*
Only pharmacologic measures	58 (29.7)	48 (20.5)*
Increase of the dose of the used drug	4 (2.0)	70 (29.9)*
Administration of an additional drug	5 (2.6)	72 (30.1)*
Change of the used drug	0 (0.0)	20 (8.6)
Treatment was not changed	125 (64.1)	37 (15.8)*

ACE, angiotensin-converting enzyme. Values are number (percentage). \*P<0.05.

target ABP, only nonpharmacologic measures were recommended, whereas for the patients who did not achieve target ABP, usually nonpharmacologic recommendations were combined with an increased dose of the used drug or with administration of an additional drug (Table 2). Physicians did not change the treatment for almost 16% of the patients who did not achieve target ABP.

#### Discussion

The aim of this study was to evaluate the level of blood pressure control in patients treated with antihypertensive drugs. Based on evaluation of general practitioners, almost half (45.4%) of 429 patients suffering and treated for hypertension achieved target ABP (<140/90 mm Hg in patients at low and moderate cardiovascular risk and <135/85–125/75 mm Hg in patients at high and very high cardiovascular risk). A higher proportion of patients (62.9%) achieved target ABP in the low- and moderate-risk group than those in the high- and very high-risk group (26.3%). Based on the values of blood pressure measured during the study, 37.3% of patients had ABP of <140/90 mm Hg.

Epidemiological studies performed in America (United States, Canada) and Europe indicate that control of hypertension is insufficient despite pharmacotherapy: hypertension control (ABP <140/90 mm Hg) varies from 8.3% to 42% in different countries (11–21). The data from other published trials indicate that the level of ABP control in treated patients is lower than in the mentioned trial. According to the data obtained from the WHO-MONICA study carried out in the city of Kaunas from 2001 to 2002, the proportion of 35-64-old men and women effectively treated with antihypertensive agents was 15.8% and 19.9%, respectively (22). The study conducted in 5 primary health care institutions of Vilnius city in the year 2005 showed that target ABP ( $\leq 140/90$  mm Hg) was achieved only in 5.8% of the examined patients who continuously used antihypertensive agents (23).

Almost 85% of the patients in this study were treated with a combination of two or more antihypertensive agents. A high proportion of patients who received combined treatment may nearly explain the high level of the controlled blood pressure seen in this study. However, despite of the fact that almost all high- and very high-risk patients (90.2%) were treated with a combination of drugs, the target ABP was achieved only by 26.3% of the patients from this group. One of the possible reasons may be the lower target ABP (<135/85–125/75 mm Hg) for high- and very high-risk patients, comparing with the target ABP (<140/90 mm Hg) for lowand moderate-risk patients. According to the data obtained from similar studies performed in other

countries, monotherapy was used in 30%–60% of hypertension patients (13–19, 21, 24, 25). There are no data in Lithuania regarding the use of antihypertensive agents in publications about ABP control (22, 23). In case of monotherapy (even using maximum doses), blood pressure control is achieved in less than 50% of patients suffering from hypertension (26). Combinations of drugs are much more effective: in the hypertension treatment guidelines, low-dose combination therapy is indicated as a first-choice therapy in high- and very high-risk patients (9, 26, 27). Combinations of drugs are more effective in blood pressure control even for the patients who were unsuccessfully treated with different single drugs (28–31).

We have no information about how patients complied with instructions assigned by physicians (the continuous use of drugs, use of full prescribed doses, considering life style recommendations, etc.). The performed trials indicate that usually the patients are not strictly following treatment recommendations, and physicians indicate it as the main reason of insufficient blood pressure control (3).

Possibility of sampling errors (possibility of inclusion of patients with better controlled blood pressure) cannot be rejected when analyzing study results. To minimize sampling errors, every third patient who came for a regular visit was included into this clinical trial.

The comparison of the groups of the patients who achieved or did not achieve target ABP indicates that in the group of the patients who did not achieve target ABP, there were more patients who had several concomitant diseases or several risk factors. Patients who did not achieve target ABP were treated with a combination of two or more drugs more frequently; however, almost 12% of these patients were given monotherapy. For the patients who achieved target ABP, only nonpharmacologic measures were recommended more frequently, whereas for the patients who did not achieve target ABP, nonpharmacologic recommendations were usually combined with an increased dose of the used drugs or with administration of an additional drug. Physicians did not change the treatment for almost 16% of the patients who did not achieve target ABP.

#### Conclusions

The results of this study indicate that despite pharmacologic treatment, the level of arterial blood pressure control was not sufficient in the studied group of patients (45.4%), especially in the group of high- and very high-risk patients (26.3%). In addition, almost 12% of the patients with unachieved target arterial blood pressure were still undergoing monotherapy, whereas no modifications of antihypertensive treatment were given for 16% of the

patients. Such data indicate that the treatment administered by general practitioners does not always correspond with the treatment presented in the Lithuanian guidelines for hypertension treatment.

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## Arterinės hipertenzijos kontrolės ir gydymo įvertinimas šeimos gydytojų kasdienėje praktikoje

#### Žaneta Petrulionienė<sup>1, 2</sup>, Daiva Asta Apanavičienė<sup>3</sup>

<sup>1</sup>Vilniaus universito ligoninės Santariškių klinikų Kardiologijos ir angiologijos centras, <sup>2</sup>Vilniaus universiteto Širdies ir kraujagyslių ligų klinika, <sup>3</sup>"Sanofi-Aventis Lietuva"

Raktažodžiai: arterinė hipertenzija, kraujospūdžio kontrolė, vaistai nuo hipertenzijos.

**Santrauka**. *Tyrimo tikslas*. Nustatyti, kokia dalis sergančių pirmine arterine hipertenzija (PAH) ir vaistais nuo hipertenzijos gydomų pacientų pasiekė numatytą tikslinį arterinį kraujospūdį (AKS) bei palyginti tikslinį AKS pasiekusių ir nepasiekusių pacientų charakteristikas, jiems skirtą gydymą bei rekomenduotas gydymo koregavimo priemones.

*Tyrimo medžiaga ir metodai.* Epidemiologiniame tyrime dalyvavo 429 18–80 metų pacientai, sergantys PAH, kuri gydoma ne trumpiau kaip vienerius metus. Šeimos gydytojai surinko informaciją apie pacientų demografines ir klinikines charakteristikas, taikomą hipertenzijos gydymą bei rekomenduojamas gydymo koregavimo priemones.

Rezultatai. Gydytojų vertinimu, 45,4 proc. pacientų buvo pasiekę tikslinį AKS. Mažos ir vidutinės širdies ir kraujagyslių ligų (ŠKL) rizikos grupėje tikslinį AKS pasiekė 141 (62,9 proc.) pacientas, o didelės ir labai didelės rizikos grupėje tikslinį AKS pasiekė tik 54 (26,3 proc.) pacientai (p<0,0001). Pagal tyrimo metu išmatuoto AKS rodmenis 160 (37,3 proc.) pacientų AKS buvo <140/90 mm Hg. Daugiausia pacientų vartojo dviejų (n=153, 35,7 proc.) arba trijų (n=144, 33,6 proc.) vaistų nuo hipertenzijos derinius. Vaistų deriniais dažniau buvo gydomi tikslinio AKS nepasiekę pacientai. Gydytojai nekeitė gydymo 37,8 proc. (n=162) pacientų, dažniausiai tiems, kurie pasiekė tikslinį AKS.

*Išvado*s. AKS kontrolė tirtoje pacientų grupėje buvo nepakankama, ypač didelės ir labai didelės rizikos pacientų grupėje, kurioje nustatytas griežtesnis tikslinis AKS. Be to, beveik 12 proc. tikslinio AKS nepasiekusių pacientų buvo gydomi vienu vaistu, o 16 proc. tokių pacientų gydymas nebuvo koreguojamas.

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