

The prevalence of resistant and undercontrolled hypertension among patients of a Hypertension Outpatient Clinic

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Abstract

Introduction. Around 57% of Hungarian hypertensive patients did not reach the goal blood pressure. According to an ESH Newsletter published in 2011, the prevalence of resistant hypertension is 2.9–43%.

Objective. Analysing only the therapy of hypertensive patients of the Hypertension Outpatient Clinic of the University of Szeged, the authors wanted to answer following main questions: How many patients were therapeutically resistant according to the definition of resistant hypertension? How many patients were taking 3 or more antihypertensive drugs? How many of these patients reached target SBP values? How many drugs were usually used in combination therapy?

Material and methods. Data were retrospectively collected from 01/01/2011 to 31/08/2011 from the electronic files of the hypertensive patients. Altogether 310 patients' data were analysed, of all cases only one visit was taken into account. For those patients who visited the Clinic more than once during this period, only the first visit was considered. Means of two measurements were calculated. The goal SBP was 140 mmHg.

Results. In this population, 234/310 (76%) patients had resistant hypertension according to the definition ($158 \pm 17/97 \pm 8$ mmHg). Three or more antihypertensive drugs were taken by 257/310 (83%) patients (136 ± 20 mmHg) and 134 of them (52% of 257 patients) reached the therapeutic goal. A fourfold combination of antihypertensive agents was the most frequent in this population.

Conclusion. It is advised to use multiple drug combinations and it is recommended to spend enough time but not longer than necessary to find the most effective combination in every case.

key words: resistant, hypertension, combination

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Background

In Hungary, the number of adult hypertensive patients (age > 19 year) registered in General Practitioner system had been doubled between 1999 and 2011 from 1 608 202 to 3 482 000 [1]. Hyperten-

sion (HT) is poorly controlled not only in Hungary, but also in Europe and worldwide. As reported in a paper based on data from 2005 to 2009, around 57% of Hungarian hypertensive patients did not reach the goal blood pressure (BP) [2].

According to the 2013 definition by the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC), HT is considered as therapeutically resistant (RHT) when an appropriate lifestyle modification with a triple antihypertensive drug combination (a diuretic and two other antihypertensive drugs belonging to different classes, but

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not necessarily including a mineralocorticoid receptor antagonist) at adequate doses fail to lower systolic blood pressure (SBP) and diastolic blood pressure (DBP) values to < 140 and 90 mmHg [3]. Patients whose BP is controlled, but with 4 or more medications, are considered to have RHT [4, 5]. In 2007, hypertension was defined as resistant or refractory to treatment when implementing lifestyle measures and at least three drugs (including a diuretic) in adequate doses has failed to lower SBP and DBP to goal values [6].

The real prevalence of RHT is not known; it varies over a wide range depending on the definition of RHT and goal BP values used at different data collection locations, the population examined and the level of medical screening (etc. work place, general practitioner [GP] office, hospital, clinic, HT centre, and so on). The prevalence of RHT in GP offices is suggested to be less than 5% of the overall HT population, while in clinical trials 10–20% and in HT centres it may be much more higher [7]. According to an ESH Newsletter published in 2011, the prevalence of RHT is 2.9–43% [8].

In 2009, the reappraisal of European guidelines recommended that SBP should be lowered to < 140/mmHg in both low to moderate and high risk HT patients [9].

Material and methods

The authors analysed data of HT patients registered in one of the Hypertension Outpatient Clinics of the 1st Department of Medicine Nephrology-Hypertension Centre, University of Szeged, Hungary. Analysing only the therapy of HT patients, the authors wanted to answer following main questions: How many patients were taking 3 or more antihypertensive drugs? How many of these patients reached the goal SBP values? How many patients were therapeutically resistant according to the definition of RHT? How many drugs were usually used in combination therapy? In this work, the authors did not investigate the possible causes of RHT or any correlations between the number of drugs and BP values.

Data were retrospectively collected from 01/01/2011 to 31/08/2011 from the electronic files of the HT patients. Altogether 310 patients' data were analysed; for all cases only one visit was taken into account. For those patients who visited the Clinic more than once during this period, only the first visit was considered. Blood pressure measurements were performed by an OMRON 705IT automatic BP monitor. Means of two measurements were cal-

culated. The goal SBP was 140 mmHg, as it was recommended in the 2009 reappraisal of European guidelines [9].

The authors used only descriptive statistics and means \pm SD are reported.

Results

The mean age of HT patients was 61.4 ± 14.3 years. The mean duration of HT was 14.2 ± 12.0 years. Among these 310 HT patients, 115 (37%) were men (age 58.2 ± 15.6 years) and 195 (63%) were women (age 63.4 ± 13.1 years). By office BP readings the BP of 186/310 (60%) patients were in the goal range (SBP 124 ± 9 mmHg) and 124/310 (40%) were not (SBP 155 ± 17 mmHg).

Among the 310 patients, 45 (15%) had only diabetes mellitus (DM) as additional risk factor, type 1 and type 2 together. Twenty-one (17%) of 124 HT patients with undercontrolled BP ($149 \pm 15/89 \pm 8$ mmHg) had DM.

According to the definition of RHT, altogether 234/310 (76%) patients had RHT in this population. The mean BP of these patients was $158 \pm 17/97 \pm 8$ mmHg. However 257/310 (83%) patients were taking 3 or more antihypertensive drugs, and their SBP was 136 ± 20 mmHg. The difference ($n = 23$) between 257 and 234 were the patients who were prescribed 3 drugs and reached the goal SBP. Altogether 174 patients were taking 4 or more drugs and 111 of them (47% of 234 RHT patients) had SBP < 140/mmHg and 63 (27% of 234 RHT patients) of them didn't reach the goal SBP.

Among the multiple-drug combinations, 83/310 (27%) patients were taking 3 antihypertensive drugs, 65/310 (21%) were taking 4 drugs, 48/310 (15%) were taking 5 drugs, 34/310 (11%) were taking 6 drugs, 20/310 (6%) were taking 7 drugs and 7/310 (2%) were taking 8 drugs.

Table I summarizes the different drug combinations and respective SBP values.

Fifteen patients were on monotherapy; their BP was $124 \pm 12/79 \pm 9$ mmHg, and only 1 of them was undercontrolled (BP 154/100 mmHg). All the patients taking 2 drugs (38/310) were in the goal range.

Table II summarizes the distribution of different antihypertensive agents in this population. Forty-one patients were not taking any renin-angiotensin system inhibitor. Nobody was taking direct renin inhibitor.

Altogether in 123/310 (40%) patients BP was undercontrolled; 60% of all the patients were in the goal BP range.

Table I. The different antihypertensive drug combinations and systolic blood pressure values (mean \pm SD)

Number of drugs combined	Patients by goal	SBP [mmHg]	
3	All	136 \pm 18	n = 83
	Resistant	155 \pm 13	n = 60
	Controlled	124 \pm 9	n = 23
4	All	135 \pm 21	n = 65
	Resistant	157 \pm 19	n = 22
	Controlled	124 \pm 10	n = 43
5	All	131 \pm 14	n = 48
	Resistant	150 \pm 8	n = 13
	Controlled	124 \pm 8	n = 35
6	All	145 \pm 26	n = 34
	Resistant	167 \pm 19	n = 16
	Controlled	126 \pm 11	n = 18
7	All	139 \pm 20	n = 20
	Resistant	156 \pm 17	n = 9
	Controlled	126 \pm 7	n = 11
8	All	147 \pm 21	n = 7
	Resistant	161 \pm 15	n = 3
	Controlled	129 \pm 8	n = 4

Discussion

The prevalence of target organ damages such as left ventricular hypertrophy, retinopathy, microalbuminuria and increased arterial intima-media thickness are 50–100% higher in true RHT compared to well-controlled hypertensives. The risk of cardiovascular diseases is also 2.5–5 times higher [10, 11].

In Hungary in 2007 the BP of 46% of the non-diabetic HT population and only 8.5% of the diabetic HT population was in the goal range [12]. During the follow-up in the program “Live Under 140/90” the proportion of patients reaching the goal BP range had been continuously improved: in 2004 it was 27%, in 2005 — 39%, in 2007 — 44% and in 2010 — 48–58% [13]. In a Hungarian pilot study enrolling 46 000 HT patients, BP over the goal range most frequently was observed in the age groups of 50–59 (25.4%) and 60–69 (28.7%) years. In this study the mean BP over the goal range was 160–179/100–109 mmHg in 45.6% and 140–159/90–99 mmHg in 43.8% [14].

In this observational study the proportion of HT patients with BP in the goal range was quite high (60%), but obviously the percentage of patients prescribed a combination of three or more

Table II. The distribution of different antihypertensive agents (ACEI = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor 1 blocker, BB = beta-blocker, DHP-CCB = dihydropyridine calcium-channel blocker, I-agonist = imidazoline-receptor agonist)

Antihypertensive agents	Number of patients
ACEI	179
ARB	90
ACEI + ARB	13
Thiazide diuretics	212
Other diuretics	104
Thiazide + other diuretics	77
Other BB	116
Vasodilator BB	106
DHP-CCB	206
I-agonist	87
Central acting	53
Alpha-blocker	98
Direct vasodilator	5
non-DHP-CCB	5

drugs was also very high (83%). Monotherapy was sufficient to reach the goal BP only in 4.8%. On the other hand, the prevalence of RHT by definition (and not the prevalence of true RHT) was also quite high (76%). These data accords with the observations that in specific HT centres the prevalence of RHT is higher. Of course not all the HTs diagnosed as RHT are true ones. The very first thing that is recommended in patients with RHT suspicion is to exclude the white coat HT and/or white coat effect with a 24-hour ambulatory blood pressure monitoring and exclude pseudoresistant HT by checking in hospital whether the patient is really taking the antihypertensive medications. After exclusion these, it is necessary to clear up any possible factors interfering with the therapy and find possible secondary causes of HT. Finally the therapy should be optimized. If BP is still not in the goal range after these procedures, than this BP is a true resistant one.

A fourfold combination of antihypertensive agents was the most frequent in this population. The most frequent drug classes were the ACEIs and/or ARBs, the DHP-CCBs and the thiazide diuretics.

In this population, 26 patients (8% of all HT patients and 11% of RHT patients) had a secondary cause of RHT known at the time of data collection, other than DM.

Conclusion

In patients with RHT, the prevalence of so called identifiable causes is fourfold higher than in non-RHT patients [15]. Pseudoresistant and secondary HT forms are usually tractable, and they can be converted to a controlled form of HT. It is advised to use multiple drug combinations and it is recommended to spend enough time but not longer than necessary to find the most effective combination in every case. If there is no any contraindication, a threefold combination of ACEI + DHP-CCB + thiazide diuretic is a basic treatment to reach the goal BP.

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