ORIGINAL ARTICLE

Assessment of adherence to treatment in patients with resistant hypertension using toxicological serum analysis

A subgroup evaluation of the RESIST-POL study

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KEY WORDS

adherence to treatment, resistant hypertension

ABSTRACT

INTRODUCTION Nonadherence to antihypertensive therapy is one of the main causes of resistant hypertension.

OBJECTIVES The aim of our study was to evaluate adherence to therapy in patients with resistant hypertension by determining serum antihypertensive drug levels with the use of liquid chromatography– –tandem mass spectrometry (LC-MS/MS).

PATIENTS AND METHODS The study included 36 patients with primary resistant hypertension selected from the RESIST-POL study (23 men and 13 women; mean age, 52.5 ±9.1 years; range, 22–67 years; mean number of antihypertensive drugs, 5.3 ±1.4), who met all 3 inclusion criteria: use of ≥4 antihypertensive drugs; average daytime ambulatory systolic blood pressure ≥140 mmHg; one of the clinical features suggesting nonadherence. All patients had their serum drug levels assessed using LC-MS/MS. Patients in whom the serum level of at least 1 drug was below the limit of quantification for the method used were regarded as nonadherent.

RESULTS Of all study patients, nonadherence was observed in 31 patients (86.1%), and none of the prescribed drugs was detected (complete nonadherence) in 5 patients (13.9%). In 26 patients (72.2%), at least 1 of the prescribed drugs could not be detected (partial nonadherence).

CONCLUSIONS In our study, we documented a surprisingly low adherence to antihypertensive treatment in patients with resistant hypertension. Our results suggest that, particularly in those patients, the analysis of serum antihypertensive drug levels using LC-MS/MS might allow to avoid a comprehensive and costly diagnostic work-up including biochemical and imaging studies.

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INTRODUCTION Resistant hypertension (RHT) is defined as a failure to lower systolic blood pressure and diastolic blood pressure to the values of less than 140 mmHg and 90 mmHg, respectively,[1] in patients receiving a therapeutic regimen including a diuretic and 2 other antihypertensive drugs belonging to different classes at adequate doses. Patients with RHT have a higher prevalence of target organ damage, secondary hypertension (HT), and a higher risk of future cardiovascular and renal events requiring greater health care expenditures compared with patients with well-controlled HT.[1-9]

The prevalence of RHT has been reported to range from 5% to 30% of the overall population receiving antihypertensive treatment, but

uncontrolled HT despite a multidrug antihypertensive regimen is not necessarily resistant.[1-5] One of the major causes of pseudoresistance, apart from the white-coat effect, is poor medication adherence.[1,2,8,10]

Patients with unrecognized nonadherence frequently undergo several additional, often expensive, diagnostic steps at specialized centers to identify the causes of poor response to antihypertensive treatment. Therefore, the evaluation of patients with RHT should be directed towards confirming treatment resistance, which should include the assessment of adherence.[1] Such assessment is difficult in clinical practice owing to a generally low awareness of the problem among physicians and a tendency to overestimate patients' adherence. Relatively few studies have been conducted so far indicating that clinicians' estimates of poor adherence are very low, with the predictive value of approximately 30%.[1,11-14]

One of the reasons for this inconsistency is the lack of objective and direct methods to screen for nonadherence to antihypertensive treatment among patients. There are several ways to monitor compliance, including counting pills, self-reported compliance, rate of prescription refills, and electronic monitoring systems, which may provide some information about long-term adherence to therapy, particularly suggesting accurate timing of drug administration.[12,15-17]

The first study to assess serum antihypertensive drug levels in patients with difficult-to-control arterial HT was conducted by Ceral et al.,[15] and since then, a few subsequent reports have been published.[11,18,19] So far, 2 methods have been implemented for the assessment of adherence in patients with RHT: evaluation of serum drug levels and toxicological urine analysis for the drug or the corresponding metabolites, using liquid chromatography–tandem mass spectrometry (LC-MS/MS).[11,15,18-20]

In the present paper, we used a toxicological analysis to assess adherence to therapy in patients with RHT, who participated in the RESIST-POL study.[6] In contrast to other studies, we identified a subgroup of patients with the most pronounced clinical characteristics of RHT and meeting the following criteria: receiving an antihypertensive regimen of at least 4 drugs, having the highest blood pressure (BP), and showing clinical characteristics that may suggest nonadherence during the study.

PATIENTS AND METHODS

Patients and study design

Patients were selected from the population of the RESIST-POL study,[6] conducted at the Department of Hypertension, Institute of Cardiology, Warsaw, Poland, from 2009 to 2011. In the RESIST-POL study, 204 patients with RHT (confirmed by 24-hour ambulatory BP monitoring), preserved renal function (estimated glomerular filtration rate, ≥60 ml/min/1.73 m^2), and no history of diabetes were evaluated.

All patients underwent a detailed examination, including the evaluation of target organ damage, screening for coexisting conditions (obstructive sleep apnea, impaired glucose metabolism, depression, insomnia, and excessive sodium excretion), and screening for secondary causes of HT, including primary aldosteronism, renal artery stenosis, pheochromocytoma, Cushing syndrome, and hyperthyroidism.

Patients who met predefined criteria for admission to the RESIST-POL study reported good adherence to treatment, as assessed by a referring family doctor before hospitalization. After admission to the Department of Hypertension, ambulatory BP monitoring was repeated in all referred subjects to confirm RHT, and all patients were interviewed again to evaluate treatment adherence. Since all patients required to be treated with at least 3 drugs at optimal doses, including a diuretic, no treatment modification was made at this stage of the study.

Among 204 patients included in the RESIST-POL study,[6] secondary causes of HT were found in 49 subjects and essential HT was diagnosed in 155 patients. For the purpose of the study, we selected 36 patients who met the following 3 criteria: antihypertensive regimen of at least 4 drugs, average daytime ambulatory systolic BP of 140 mmHg or higher, and one of the clinical features that may suggest nonadherence during the study (eg, tachycardia while using an adequate dose of β-blocker or lower potassium plasma levels when taking spironolactone).

In 36 patients (23 men and 13 women; mean age, 52.5 ±9.1 years) who fulfilled the inclusion criteria, serum antihypertensive drug levels were assessed using LC-MS/MS.

The 36 patients selected for the evaluation of adherence using LC-MS/MS had higher daytime systolic BP values compared with the remaining patients included in the RESIST-POL study.[6] There was no difference between the groups with regard to other characteristics such as age, sex distribution, prevalence of smoking, obesity, metabolic syndrome, or obstructive sleep apnea. There was also no difference between the groups with regard to the prevalence of depression and insomnia.

Serum antihypertensive drug levels were assessed by means of LC-MS/MS. A 10-ml sample of serum was collected from each patient. Nonadherence was diagnosed if at least 1 drug was below the limit of quantification (LOQ) for the method used. Complete nonadherence was defined as the absence of all measured antihypertensive drugs, while partial nonadherence was defined as the absence of at least 1 but not all antihypertensive drugs.

The study was approved by the Ethics Committee of the Institute of Cardiology, Warsaw, Poland. All patients provided written informed consent to participate in the study.

TABLE 1 Antihypertensive drugs identified by liquid chromatography–tandem mass spectrometry (LC-MS/MS): their therapeutic and toxic concentration ranges and limit of quantification of the LC-MS/MS method

Antihypertensive drug	Concentration ranges[b], ng/ml		LOQ
	therapeutic	toxic	
amlodipine	3–9	>40	0.6
atenolol	50–600	1000–1500	0.6
bisoprolol	10–60	NA	3.5
carvedilol	20–300	NA	2
clonidine	1–2	(5)[a] 15–25	1.5
diltiazem	3–200	400	0.7
enalapryl	10–50	NA	4
furosemide	2–5 (10)[a] × 10^3	25–30 × 10^3	5
hydrochlorothiazide	70–450	NA	10
indapamide	40–260	NA	2
lacidypine	3–6	NA	4
lisinopril	1–35	250	2
losartan	150–1000	NA	2.5
metoprolol	20–340	75–1000	2.5
perindopril	50–150	NA	0.6
propranolol	20–300	500–3000	1
quinapril	90–200	NA	1.5
ramipril	1–10	NA	1
telmisartan	10–260	NA	1

a some authors reported this value
b based on Uges[24]

Abbreviations: LC-MS/MS, liquid chromatography–tandem mass spectrometry; LOQ, limit of quantification; NA, not available

Analysis of serum antihypertensive drug levels using liquid chromatography–tandem mass spectrometry

The analysis of serum antihypertensive drug levels was performed at the Department of Forensic Toxicology, Institute of Forensic Research, Kraków, Poland, where the LC-MS/MS method was implemented for the purpose of the study. After the solid-phase extraction (using Oasis MCX columns and acetonitrile/ammonia eluent) of 0.5 ml of serum, the antihypertensive drugs were separated on a Superspher RP-select B (125-2 mm) column using gradient elution of 0.1% (v/v formic acid in water and acetonitrile). The target drugs were screened for, identified, and quantified using a multiple-reaction monitoring mode. The assay was found to be selective for all tested compounds. No interfering peaks were observed in the extracts of 10 different blank serum samples. We assessed interferences with common drugs typically taken in combination. The assay was linear from therapeutic to overdose concentrations. In the processed samples, the analytes were stable for a period of more than 48 hours frozen.[20]

LC-MS/MS enabled to evaluate the serum concentration of 19 different antihypertensive drugs (TABLE 1).[20] This precise method allowed to detect, identify, and quantify the listed drugs at concentrations ranging from therapeutic to toxic, with an accuracy and precision not exceeding 15% of the LOQs.

The detection limits, determined by a signal-to-noise ratio of 3 or higher, ranged from 0.1 to 6 ng/ml. The LOQs (signal-to-noise ratio, ≥10) ranged from 0.7 ng/ml (for amlodipine, atenolol, and perindopril) to 10 ng/ml (for hydrochlorothiazide). The degree of adherence to medical recommendations was assessed on the basis of therapeutic concentrations of a given antihypertensive drug.

Statistical analysis Data were analyzed using the statistical software, PASW Statistics 18 (SPSS Inc., Chicago, Illinois, United States). The results were presented as mean ± 1 standard deviation or median and interquartile range. The values of variables were compared between groups. For continuous and discrete variables, *t* test and Mann–Whitney test were used; for categorical variables, the χ^2 test or Fischer exact test. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

The assessment of the serum concentration was possible for 3.7 ±1.2 (4 ±1) out of 5.3 ±1.4 (5 ±1) antihypertensive drugs prescribed for each patient. Using LC-MS/MS, we determined the presence of 19 different antihypertensive drugs prescribed (TABLE 1).

The clinical characteristics of the patients are shown in TABLE 2, and the recommended antihypertensive therapy at the time of the assessment is presented in TABLE 3.

Nonadherence criteria were met in 31 patients (86.1%; at least 1 of the prescribed medications below the LOQ). Moreover, in 5 patients (13.9%), none of the prescribed drugs could be detected, and those patients were considered as completely nonadherent. In 26 patients (72.2%), at least 1 of the prescribed drugs (but not all drugs) could not be detected, and those patients were considered as partially nonadherent (FIGURE 1).

In our study group, only 5 patients (13.9%) were recognized as compliant. The degree of adherence to medical recommendations was also assessed by the number of drugs with serum concentrations within the therapeutic range. Among the 5 compliant patients, serum drug concentrations of all prescribed drugs were determined to be within the therapeutic range in 2 patients (5.6%; FIGURE 1).

When comparing adherence to treatment between different classes of antihypertensive drugs, we found that the rates of adherence ranged from 19.4% (angiotensin-converting enzyme inhibitors, ACEIs) to 61.3% (calcium channel blockers, CCBs) (FIGURE 2).

A toxicological analysis revealed that 14% of the patients showing nonadherence were completely nonadherent and 72%—partially nonadherent. Having been confronted with the results of the toxicological analysis, only 13% of the patients admitted to not having taken their medication, at least not regularly. The clinical characteristics of adherent and nonadherent patients are shown

TABLE 2 Characteristics of patients

Characteristics	Value
men	23 (63.9)
age, y	52.5 ±9.1
daytime[a] systolic BP, mmHg	150.8 ±18.1
daytime diastolic BP, mmHg	93.2 ±13.9
daytime heart rate, bpm	75.4 ±11.5
obesity (BMI >30 kg/m^2)	21 (58.3)
smokers	8(22.6)
metabolic syndrome	27 (75)
newly diagnosed diabetes	4 (11.1)
obstructive sleep apnea	28 (77.8)
depression	14 (38.8)
insomnia	16 (44.4)
microalbuminuria	9 (25)
left ventricular hypertrophy[b]	19 (54.3)
statins	21 (58.3)

Data are presented as mean ± standard deviation or number (percentage).

a differentiation between sleep and activity periods was made based on data from patients' diaries
b in echocardiography, left ventricular hypertrophy was defined according to the ESH/ESC 2007 criteria (left ventricular mass index of ≥110 g/m^2 for women and ≥125 g/m^2 for men)

Abbreviations: BMI, body mass index; BP, blood pressure; ESH/ESC, European Society of Hypertension/European Society of Cardiology

TABLE 3 Antihypertensive therapy in the study group

Antihypertensive therapy		Value
No. of ADs per patient		5.3 ±1.4
No. of serum AD concentration measurements per patient		3.7 ±1.2
No. of ADs prescribed	4	14 (38.9)
	5	8 (22.2)
	6	6 (16.7)
	≥7	8 (22.2)
fixed-dose combination tablet[a]		2 (5.6)
β-blockers		32 (88.9)
calcium channel blockers		32 (88.9)
thiazides		32 (88.9)
angiotensin II receptor blockers		27 (75)
ACEIs		26 (72.2)
α-blockers		17 (47.2)
loop diuretics		9 (25)
centrally acting drugs[b]		9 (25)

Data are presented as mean ± standard deviation or number (percentage).

a angiotensin II receptor blocker and thiazide diuretic in both cases
b clonidine in all cases

Abbreviations: ACEIs, angiotensin-converting enzyme inhibitors; ADs, antihypertensive drugs

in TABLE 4 and FIGURE 3. They did not differ in terms of the education level and socioeconomic status.

DISCUSSION In our study, we used LC-MS/MS to determine the serum concentrations of antihypertensive drugs and showed a high prevalence of overall noncompliance (86%) with pharmacological BP-lowering therapy among patients with RHT. Of nonadherent patients, 14% showed complete nonadherence and 72% showed partial adherence to antihypertensive therapy.

It should be noted that we used LC-MS/MS to report the prevalence of nonadherence to antihypertensive therapy in a group of patients with RHT who were meticulously examined and showed the clinical characteristics suggesting nonadherence during the RESIST-POL study.[6] Our data suggest that a detailed and costly diagnostic workup could be minimized or even avoided if the analysis of serum drug levels by means of LC-MC/MS was used first to screen for nonadherence.

Of note, there is a notable difference in the prevalence of overall nonadherence to antihypertensive treatment between our study and those of other investigators, which may be partially explained by the different inclusion criteria.[11,15,18,19]

In our study, all patients with RHT were hospitalized. In addition, most of them were obese and showed a high rate of comorbidities such as metabolic syndrome, newly diagnosed diabetes, or obstructive sleep apnea. In all subjects, blood samples were obtained within a maximum of 3 to 5 hours after the expected time for their regular morning doses of medication to be taken. Therefore, sufficient levels of all antihypertensive drugs should have been present in serum, making it possible to detect them using a screening procedure.

Based on a similar methodology, a recent survey including patients with RHT who were hospitalized or had been referred by an outpatient clinic showed nonadherence to BP-lowering therapy at a level of 47%.[18] Moreover, using the toxicological analysis of patients' serum, Ceral et al.[15] assessed noncompliance with antihypertensive therapy in 84 outpatients with RHT and showed nonadherence (both partial and complete) in 66% of the subjects.

Another newly published study, performed at an outpatient nephrology center, evaluated patients with HT who were not achieving the BP goal despite the concurrent use of at least 4 antihypertensive agents and in whom the secondary cause of HT was excluded. Among 108 patients who met the criteria for RHT, 53% were found to be nonadherent based on the toxicological analysis of patients' urine.[11]

Recent data from a study by Tomaszewski et al.,[19] who conducted a urine analysis using LC-MS/MS, were based on a clinically more diverse sample of hypertensive patients referred to the clinic for a wider range of reasons. Nonadherence was observed in 25% of the subjects. However, it should be noted that most of the patients in this study were nonselected referrals

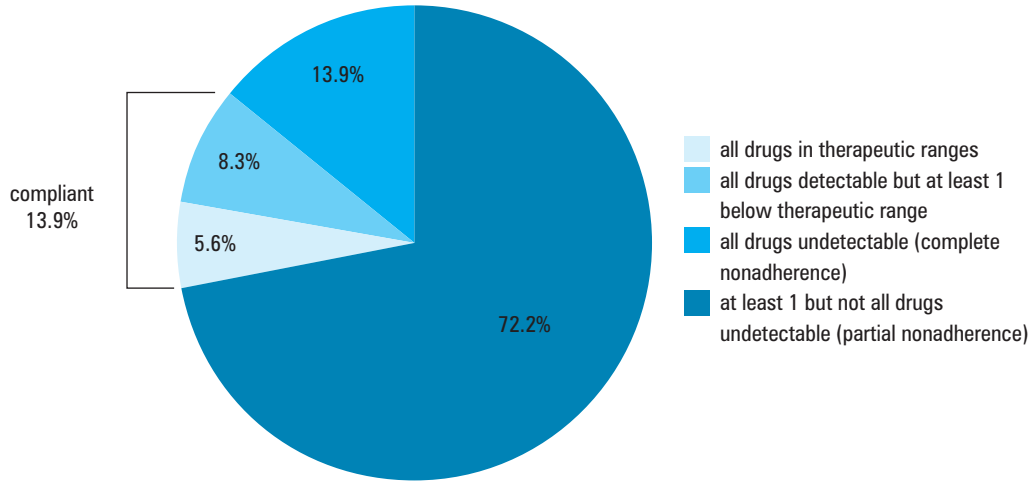

FIGURE 1 Presence of drugs in serum

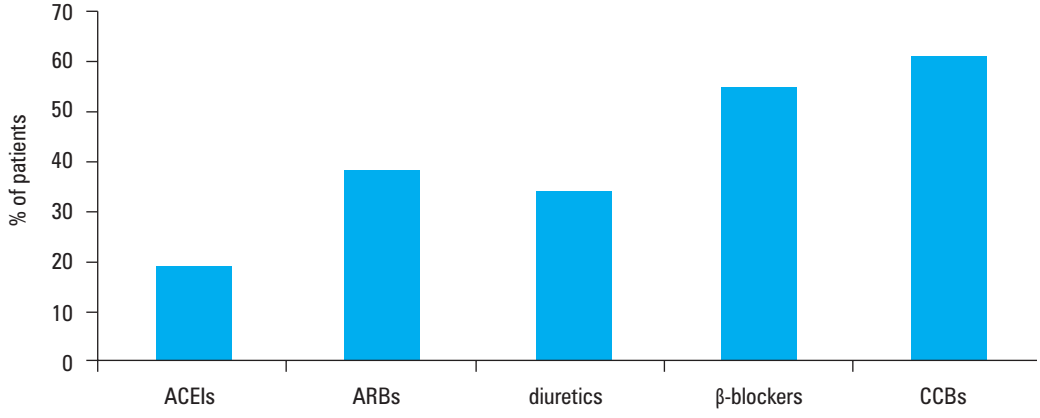

FIGURE 2 Adherence to therapy depending on a drug class
Abbreviations: ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; others, see **TABLE 3**

from primary care doctors, not all of whom met the criteria for RHT.

In contrast to our study (in which only 4 of 31 nonadherent patients reported not having taken their medication, at least not regularly), a study by Jung et al.,[11] based on a toxicological analysis of patients' urine, revealed nonadherence to a prescribed drug regimen in more than 50% of the patients. After being confronted with the results, 87.5% of those patients admitted not to have taken their recommended medication. This difference is difficult to explain and may reflect a higher motivation of patients to communicate with the physician to further improve adherence in the Jung study.[11] Both studies showed that, except for higher BP levels and heart rate, there were no significant differences between adherent and nonadherent patients in terms of clinical characteristics. This proves that nonadherence is generally overestimated in clinical practice, where either physicians' subjective assessments or patients' self-reports provide unreliable data because they do not allow to ultimately confirm that a medication has been taken.

In our study, complete nonadherence was significantly less common than partial nonadherence, which confirms the findings ofJung et al.[11] (30% vs 70%, respectively), but not necessarily the results of 2 other studies assessing serum antihypertensive drug levels, in which the rates of complete nonadherence among nonadherent patients were 51%[18] and 52.8%,[15] respectively. This discrepancy may be due to a higher number of drugs analyzed in our study (3.7 ±1.2), as compared to 3.1 ±1.2 drugs assessed by Ceral et al.[15] and 3.5 ±1.2 (outpatients) or 2.2 ±1.0 (inpatients) drugs assessed by Strauch et al.[18]

We found that 72% of nonadherent patients showed partial nonadherence, taking at least some of the drugs prescribed. Hence, the approach to measure drug intake for 1 specific drug within a multiple regimen as an indicator of adherence may substantially underestimate adherence to therapy, irrespective of the technique used.

An interesting fact revealed by the studies conducted by Jung et al.[11] and Strauch et al.[18] is that nonadherence was shown to be almost evenly distributed when comparing different classes of antihypertensive drugs. This finding stands in contrast to numerous reports and meta-analyses in the literature describing the effect of antihypertensive drugs on adherence and showing that adherence was lower for diuretics and β-blockers than for angiotensin II receptor blockers and ACEIs.[21]

Of note, our study showed that adherence to different antihypertensive drugs varied significantly from 19.1% for ACEIs to 61.3% for CCBs. Although we confirmed the higher rate

TABLE 4 Characteristics of adherent and nonadherent patients

Characteristics	Adherent (n = 5)	Nonadherent (n = 31)	Partially nonadherent (n = 26)	Completely nonadherent (n = 5)
men	5 (100)	18 (58.1)	14 (53.8)	4 (80)
age, y	51.2 ±9.2	49.8 ±9.2	49.4 ±9.9	52.0 ±4.0
daytime[a] systolic BP, mmHg	151.0 ±13.8	150.8 ±18.9	149.2 ±19.1	159.2 ±17.0
daytime diastolic BP, mmHg	92.4 ±15.1	93.3 ±14.0	91.4 ±13.8.1	102.8 ±12.1
obesity (BMI >30 kg/m^2)	2 (40.0)	26 (83.9)	21 (80.8)	5 (100)
smokers	2 (40.0)	6 (19.4)	4 (15.4)	2 (40.0)
metabolic syndrome	3 (60)	24 (77.4)	20 (76.9)	4 (80)
newly diagnosed diabetes	0 (0)	4 (12.9)	3 (11.5)	1 (20)
obstructive sleep apnea	5 (100)	23 (74.2)	19 (73.1)	4 (80)
depression	1 (20)	13 (41.9)	20 (34.6)	4 (80)
insomnia	0 (0)	16 (51.6)	13 (50)	3 (60)
microalbuminuria	1 (20)	8 (25.8)	5 (19.2)	3 (60)
left ventricular hypertrophy[b]	4 (80)	26 (86.7)	23 (84.6)	4 (80)

Data are presented as mean ± standard deviation or number (percentage).

a differentiation between sleep and activity periods was made based on data from patients' diaries
b in echocardiography, left ventricular hypertrophy was defined according to the ESH/ESC 2007 criteria (left ventricular mass index of ≥110 g/m^2 for women and ≥125 g/m^2 for men)

Abbreviations: see **TABLE 2**

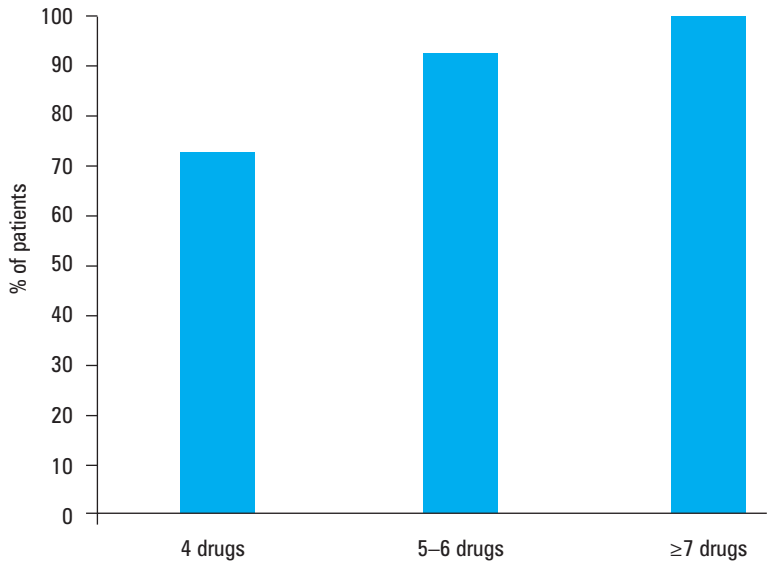

FIGURE 3 Nonadherence according to the number of antihypertensive drugs prescribed

of adherence to CCBs, we found a relatively low adherence to ACEIs compared with the previous studies, despite the fact that this antihypertensive class was prescribed to a comparable percentage of patients in those studies.[11,18]

The difference between our study and the 2 other reports[11,18] may stem from the fact that a smaller and more selected group of patients with RHT was evaluated for adherence to antihypertensive therapy. Also, several reasons apart from the high number of antihypertensive drugs prescribed and distinct side effects may affect adherence (including ACEIs), such as differences in reimbursement rates and types of drugs prescribed by physicians or patients' belief in the benefit of the medication. Differences between our study and the previous ones in terms of adherence to therapy within the various drug classes may result from the fact that, in our study, the proportion of completely nonadherent patients (eg, taking none of the prescribed drugs) was particularly high (14%).

We noted a relatively high prevalence of depressive symptoms (36.8%) in patients with RHT. The presence of depressive symptoms in patients with RHT is of considerable clinical relevance because depression may be related to poor adherence to antihypertensive medications.[22] However, the prevalence of depression in the group of patients that were nonadherent to antihypertensive therapy did not differ from that in patients with RHT who were not screened for adherence in the RESIST-POL study.[6] Therefore, it can be assumed that mood disorders may not have been directly related to patients' adherence, and further studies are needed to determine the effect of depression on adherence in large groups of patients with RHT.

Our study has several limitations. First, we included a relatively small number of patients who underwent a detailed examination and were suspected of nonadherence. Therefore, our results may not be applicable to a broader population of patients with RHT, who have a lower incidence of overall nonadherence as reported in other studies.

Secondly, similarly to a study by Strauch et al.,[18] we were not able to measure the serum concentration of all of the antihypertensive agents taken, largely because of cost. Also, a single serum analysis may not fully account for the periodicity of nonadherence to treatment. Furthermore, one might expect some patients to adhere differently to treatment during hospitalization, and thus the serum analysis may overestimate patients' adherence. Repeated tests could provide a better insight into patients' adherence to antihypertensive therapy.

However, it should be noted that toxicological screening for adherence to antihypertensive treatment using a serum sample has several advantages. First, it is a minimally invasive procedure that can be conducted by a health care assistant before routine clinical appointments. Unlike many other screening methods used before, the analysis clearly indicates the presence or absence of antihypertensive medications based on direct serum measurement. Moreover, frozen samples are stable when stored before the analysis.

Our findings also have some potential cost implications. In the Polish health care system, a price of approximately 100 Euro, regardless of the number of drugs assessed by LC-MS/MS, is not reimbursed and seems costly. In our study, the toxicological analysis of patients' serum was covered by a grant from the Ministry of Science and Higher Education. On the other hand, since nonadherence is far more common than true resistance due to secondary causes, LC-MS/MS may be cost-effective, and clinical investigations seeking the secondary cause of HT would be conducted at a minimum cost of 200 to 250 Euro. Therefore, when comparing the cost of LC-MS/MS with that of other methods used to improve adherence, LC-MS/MS shows to be within the lower-cost range.

In summary, our main finding was a surprisingly low adherence to antihypertensive treatment in patients with RHT. Our data suggest that, particularly in patients with the clinical features suggesting nonadherence, detailed diagnostic workup could potentially be avoided or minimized if the serum analysis using LC-MS/MS was employed first to screen for nonadherence.

Nonadherence to therapy is thought to be one of the major factors contributing to the development of RHT. At the same time, the assessment of patients' adherence is extremely difficult in everyday practice.[1,23] Therefore, an objective and direct method to detect BP-lowering medications in serum or urine by means of LC-MS/MS provides a unique opportunity to assess the incidence of nonadherence. Special attention should be paid to improving patients' education to minimize the potential risk of noncompliance, particularly in RHT.

Contribution statement EF, AJ, AP, MK, MK, and KN conceived the idea of the study. EWC, BT, ESP, MGP, and MK contributed to the design of the research. All authors were involved in data collection. EWC, AP, and AJ analyzed the data. AP, EF, and AJ coordinated funding of the project. All authors edited and approved the final version of the manuscript. EF and EWC equally contributed to the submitted work and may be considered as the "first" authors.

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ARTYKUŁ ORYGINALNY

Ocena przestrzegania zaleceń lekarskich dotyczących przyjmowania leków przez chorych z prawdziwie opornym nadciśnieniem tętniczym na podstawie toksykologicznej analizy surowicy krwi

Ocena podgrupy pacjentów biorących udział w badaniu RESIST-POL

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SŁOWA KLUCZOWE

oporne nadciśnienie tętnicze, stopień stosowania się do zaleceń lekarskich

STRESZCZENIE

WPROWADZENIE Jedną z głównych przyczyn opornego nadciśnienia tętniczego jest nieprzestrzeganie zaleceń lekarskich.

CELE Celem badania była ocena stopnia stosowania się do zaleceń lekarskich przez chorych z prawdziwym opornym nadciśnieniem tętniczym dokonana na podstawie badania stężenia leków hipotensyjnych w surowicy z wykorzystaniem metody chromatografii cieczowej sprzężonej z tandemową spektrometrią mas (LC-MS/MS).

PACJENCI I METODY Do badania włączono 36 chorych z pierwotnym opornym nadciśnieniem tętniczym biorących udział w badaniu RESIST-POL (23 mężczyzn, 13 kobiet; średni wiek 52,5 ±9,1 roku; zakres, 22–67; średnia liczba leków hipotensyjnych 5,3 ±1,4), którzy spełniali wszystkie trzy kryteria: przyjmowanie ≥4 leków hipotensyjnych, średnie dzienne wartości skurczowego ciśnienia tętniczego ≥140 mm Hg, jedna z cech klinicznych nasuwających podejrzenie niestosowania się do zaleceń lekarskich. U wszystkich chorych oceniono stężenie leków hipotensyjnych w surowicy za pomocą metody LC-MS/MS. Pacjentów, u których stężenie conajmniej jednego leku było poniżej progu detekcji stosowanej metody uznano za nieprzestrzagających zaleceń lekarskich.

WYNIKI Spośród wszystkich badanych pacjentów 31 chorych (86,1%) nie stosowało się do zaleceń lekarskich, a u 5 chorych (13,9%) nie stwierdzono obecności żadnego z zaleconych leków hipotensyjnych (całkowite nieprzestrzeganie zaleceń). U 26 chorych (72,2%) nie stwierdzono obecności co najmniej jednego z zaleconych leków hipotensyjnych (częściowe nieprzestrzeganie zaleceń).

WNIOSKI Nasze badanie wykazało zaskakująco niski stopień stosowania się do zaleceń lekarskich dotyczących przyjmowania leków wśród chorych z opornym nadciśnieniem tętniczym. Uzyskane wyniki sugerują, że szczególnie w tej grupie chorych ocena stężenia leków hipotensyjnych z wykorzystaniem metody LC-MS/MS może pozwolić uniknąć kosztownej diagnostyki biochemicznej i obrazowej.

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