Supplementary material

Polaczyk M, Olszanecka A, Wojciechowska W, et al. Multiple drug intolerance in patients with arterial hypertension: prevalence and determining factors. Pol Arch Intern Med. 2023; 133: 16399. doi:10.20452/pamw.16399

Questionnaire

"Multiple drug intolerance in patients with arterial hypertension - frequency and determining factors"

Dear Sir or Madam,

We kindly ask you to fill in the questionnaire below in order to conduct a study on multiple drug intolerance in patients with hypertension.

The aim of the study is to determine the frequency of multiple drug intolerance and its relationship with age, gender, and coexisting disorders. The questionnaire will help to better understand the impact of this phenomenon on the course of the disease.

The study is conducted by the 1st Department of Cardiology and Interventional Electrocardiology and Hypertension of the Jagiellonian University Medical College.

Instruction:

In order to answer the questions, please circle the box next to the chosen answer. In open questions, the answer should be entered.

We would appreciate truthful and detailed answers.

We inform you about the confidentiality and protection of your personal data. In accordance with the applicable regulations, only the doctors who conduct and coordinate the study and persons authorized to do so by law may have access to the completed questionnaire.

Name and surname: ……..

1. Gender:

- woman
- man

2. Age:

- ……

3. Body weight:

- ……

4. Body height:

- ……

5. Chronic diseases:

- …… ..
- …… ...
- …… ...

6. Medication currently used for chronic treatment:

- …… ..
- …… ...
- …… ...

7. History of adverse reactions to drugs, please provide the names of the drugs:

Adverse drug reaction is any unwanted, uncomfortable, or dangerous effects that a drug may have.

•. …… ..

• …… ...

• …… ...

8. If you have ever experienced any side effects or complications with medication use, please list what kind of the reaction it was:

Cough: a cough is a sudden expulsion of air through the large breathing passages that can help clear them of fluids, irritants, foreign particles and microbes. As a protective reflex, coughing can be repetitive with the cough reflex following three phases: an inhalation, a forced exhalation against a closed glottis, and a violent release of air from the lungs following opening of the glottis, usually accompanied by a distinctive sound.

Oedema: edema, also spelled oedema, and also known as fluid retention, dropsy, hydropsy and swelling, is the build-up of fluid in the body's tissue. Most commonly, the legs or arms are affected. Symptoms may include skin which feels tight, the area may feel heavy, and joint stiffness.

Weakness/hypotension: is low blood pressure. Blood pressure is the force of blood pushing against the walls of the arteries as the heart pumps out blood. Blood pressure is indicated by two numbers, the systolic blood pressure (the top number) and the diastolic blood pressure (the bottom number), which are the maximum and minimum blood pressures, respectively. A systolic blood pressure of less than 90 millimeters of mercury (mmHg) or diastolic of less than 60 mmHg is generally considered to be hypotension.

Rash: A rash is a change of the human skin which affects its color, appearance, or texture. A rash may be localized in one part of the body, or affect all the skin. Rashes may cause the skin to change color, itch, become warm, bumpy, chapped, dry, cracked or blistered, swell, and may be painful.

Bleeding: hemorrhage or blood loss, is blood escaping from the circulatory system from damaged blood vessels. Bleeding can occur internally, or externally either through a natural opening such as the mouth, nose, ear, urethra, vagina or anus, or through a wound in the skin.

Gastrointestinal problems (nausea, vomiting, dyspepsia, diarrhea, constipation): (abbrev. GI diseases or GI illnesses) refer to diseases involving the gastrointestinal tract, namely the oesophagus, stomach, small intestine, large intestine and rectum, and the accessory organs of digestion, the liver, gallbladder, and pancreas.

Disturbed lab test results – please describe: ……

A blood test is a laboratory analysis performed on a blood sample that is usually extracted from a vein in the arm using a hypodermic needle, or via fingerpick.

Other – please describe

• …… ....

• …… ...

• …… .. ……
..

9. What did you do after experiencing the drug side effect?

- Stopped the medication without contacting the doctor
- Asked for additional consultation with the doctor
- Read the medication leaflet

10. How long have you been suffering from hypertension?

• …… ..

Thank you for your time and for completing the survey

Results of the questionnaire

Specific side effects were reported by 47% of the respondents. In most cases, this concerned 1 type of side effect (20% of the group), while the maximum number of reported side effects was 9 *(Table S1)*. Patients reporting and not reporting side effects differed significantly from one another in terms of gender, age, and known duration of hypertension ($p < 0.001$ for all). People reporting adverse drug reactions compared to those declaring no adverse drug reactions were more often women (63% vs. 50%), were older (65.4 (15.2) years vs. 60.5 (14.4) years and had longer history of hypertension (median 15 years vs. median 10 years).

The study participants reporting adverse drug-induced symptoms also reported a significantly higher number of cardiovascular, non-cardiovascular or any diseases ($p < 0.001$ for all). In patients reporting versus non-reporting adverse drug reactions the following diseases were more frequent: coronary artery disease (30% vs. 19%, $p < 0.001$), previous myocardial infarction (18% vs. 11 %, $p = 0.002$), heart failure (23% vs. 13%, $p < 0.001$), atrial fibrillation (18% vs. 13%, $p = 0.03$), but also respiratory (15% vs. 9%, $p = 0.003$), digestive (16% vs. 11%, $p = 0.04$), metabolic (25% vs. 19%, $p = 0.02$) and endocrine diseases (20% vs. 15%, $p = 0.03$). No significant differences were observed between reporting and non-reporting adverse drug reactions in terms of the number of drugs taken ($p = 0.12$) and the number of antihypertensive drug tablets consumed ($p = 0.2$). On the other hand, significant disparities were noted between the groups when it came to the number of tablets of cardiovascular drugs taken without antihypertensive drugs by patients in the patients reporting adverse drug reactions consuming a higher quantity of such medications (median = 2 vs. median = 1, $p < 0.001$). With regard to specific classes of drugs, study participants reporting ADRs consumed the following drugs significantly more frequently than patients non-reporting ADRs: antiplatelet drugs (30% vs. 19%, $p < 0.001$), other cardiovascular drugs (52% vs. 44%, $p = 0.02$), respiratory drugs (6.9% vs. 3.5%, $p = 0.02$). Reporting ADRs consumed the following medications significantly less frequently than the non-reporting ADRs: ACE inhibitors (50% vs. 57%, $p = 0.034$) and calcium blockers (31% vs. 45%, $p < 0.001$) *(Table S2)*.

Table S1. Characteristics of study population

	Group as a whole	Range
N	1 000	

Sex, n (%)		
Women	560 (56.0%)	
Men	440 (44.0%)	
Age, year, mean (SD)	62.84 (14.96)	19-103
Body mass, kg, mean (SD)	78.72 (15.53)	43-170
Height, cm, mean (SD)	167.99 (8.65)	143-198
BMI, kg/m^2, mean (SD)	27.86 (4.84)	15.99-56.79
Drug intolerance, n (%)	479 (47.9%)	
1 drug	317 (31.7%)	
2 drugs	82 (8.2%)	
3 drugs or more	80 (8.0%)	
Number of untolerated drugs, median (Q1, Q3)	0.00 (0.00;1.00)	0-8
Side effects, n (%)	479 (47.9%)	
1 symptom	207 (20.7%)	
2 symptoms	87 (8.7%)	
3 symptoms	105 (10.5%)	
4 symptoms	36 (3.6%)	
5 or more	42 (4.2%)	
Number of side effects (Q1; Q3)	0.00 (0.00;2.00)	0-9

Data are presented as n (% of group), mean (SD) or median (Q1, Q3).

Abbreviations: BMI – Body Mass Index

Table S2. A comparison of patients reporting side effects with patients reporting no side effects in terms of comorbidities and classes of drug consumed

	Patients reporting no side effects after taking medications	Patients reporting side effects after taking medications	p
N	521	479	
Sex, n (%)			
Women	260 (49.9%)	300 (62.6%)	<0.001
Men	261 (50.1%)	179 (37.4%)	
Age, years, mean (SD)	60.5 (14.4)	65.4 (15.2)	<0.001
BMI, kg/m^2, mean (SD)	27.85 (4.89)	27.86 (4.78)	0.97
Known duration of hypertension, median (Q1, Q3)	10.00 (5.00;18.00)	15.00 (10.00;25.00)	<0.001
Cardiovascular diseases: median (Q1, Q3)	2.00 (1.00;2.00)	2.00 (1.00;3.00)	<0.001
Non-cardiovascular diseases: total, median (Q1, Q3)	1.00 (0.00;2.00)	2.00 (1.00;4.00)	<0.001
Diseases of any kind: total, median (Q1, Q3)	3.00 (2.00;5.00)	4.00 (2.00;7.00)	<0.001
Comorbidities, n (%)			
Coronary disease	97 (18.6%)	144 (30.1%)	<0.001
Previous myocardial infarction	58 (11.1%)	88 (18.4%)	0.002
Heart failure	68 (13.1%)	111 (23.2%)	<0.001
Arrhythmia	63 (12.1%)	58 (12.1%)	>0.1
Atrial fibrillation	67 (12.9%)	86 (18.0%)	0.03
Hypercholesterolemia	245 (47.0%)	247 (51.6%)	0.17
Other cardiovascular diseases	110 (21.1%)	157 (32.8%)	<0.001

Respiratory system	47 (9.0%)	73 (15.2%)	0.003
Digestive system	59 (11.3%)	76 (15.9%)	0.04
Nervous system	44 (8.4%)	43 (9.0%)	0.85
Skin diseases	9 (1.7%)	14 (2.9%)	0.29
Rheumatoid diseases	44 (8.4%)	58 (12.1%)	0.07
Metabolic disorders	98 (18.8%)	121 (25.3%)	0.02
Diabetes	144 (27.6%)	130 (27.1%)	0.92
Mental disorders	14 (2.7%)	22 (4.6%)	0.15
Endocrine disorders	76 (14.6%)	96 (20.0%)	0.03
Oncological diseases	25 (4.8%)	38 (7.9%)	0.06
Other diseases	151 (29.0%)	210 (43.8%)	<0.001
Non-cardiovascular diseases	370 (71.0%)	387 (80.8%)	<0.001
Number of drug classes, median (Q1, Q3)	5.00 (3.00;7.00)	5.00 (3.00;7.00)	0.12
Class of drug, n (%)			
ACE-inhibitors	298 (57.2%)	241 (50.3%)	0.034
Beta blockers	323 (62.0%)	290 (60.5%)	0.68
Angiotensin II receptor blockers	87 (16.7%)	96 (20.0%)	0.11
Calcium channel blockers	235 (45.1%)	147 (30.7%)	<0.001
Diuretics	277 (53.2%)	235 (49.1%)	0.22
Other antihypertensive drugs	106 (20.3%)	78 (16.3%)	0.11
Antiplatelet drugs	101 (19.4%)	142 (29.6%)	<0.001
Anticoagulants	71 (13.6%)	87 (18.2%)	0.06
Statins	260 (49.9%)	238 (49.7%)	0.1
Other cardiovascular drugs	230 (44.1%)	248 (51.8%)	0.02

Cardiovascular drugs in total	496 (95.2%)	447 (93.3%)	0.25
Antihypertensive drugs	485 (93.1%)	433 (90.4%)	0.15
Cardiovascular drugs other than antihypertensive drugs	356 (68.3%)	349 (72.9%)	0.13
Number of cardiovascular drugs taken in tablet form without antihypertensive drugs	1.00 (0.00;2.00)	2.00 (0.00;3.00)	<0.001
Antihypertensive drugs taken – number of tablets, median (Q1, Q3)	2.00 (1.00;3.00)	2.00 (1.00;3.00)	0.20
Respiratory system	18 (3.5%)	33 (6.9%)	0.02
Nervous system	16 (3.1%)	18 (3.8%)	0.67
Psychotropic	15 (2.9%)	19 (4.0%)	0.44
Dermatological	2 (0.4%)	2 (0.4%)	>0.1
Metabolic group	143 (27.4%)	117 (24.4%)	0.31
Rheumatology	7 (1.3%)	8 (1.7%)	0.87
Other non-cardiovascular	142 (27.3%)	170 (35.5%)	0.006
Non-cardiovascular drugs	257 (49.3%)	260 (54.3%)	0.13
Any drugs taken	501 (96.2%)	455 (95.0%)	0.45

Data are presented as n (% of group), mean (SD) or median (Q1, Q3). Groups were compared using the chi-square test or Fisher's exact test and t-test as well as Mann-Whitney's test for interval and nominal variables, respectively.

Abbreviations: BMI – Body Mass Index