



Study of the Prescription and Effectiveness of Combinations of Medicines in the Treatment of Arterial Hypertension

Tetiana Nehoda*, Zhanna Polova, Andrii Tsyhanok, Maryna Marchenko, Yurii Paustovskyi, Perepelytsia Yuliia

Bogomolets National Medical University, Ukraine.

***Corresponding Author: Tetiana Nehoda**

Abstract

Almost half of the world's adult population suffers from cardiovascular diseases: arterial hypertension, coronary heart disease, arrhythmias and others. Because of timely treatment of patients life is prolonged, its quality improves, severe complications decrease: cerebral haemorrhage, myocardial infarction. An increase in blood pressure leads to a decrease in life expectancy. For people with the highest blood pressure, this becomes threatening. Purpose: Determination of the structure of prescriptions by doctors of different combinations of medicines for the treatment of arterial hypertension and their use by patients, as well as to study the effectiveness of combined medicines in the monotherapy of the treatment performed. Materials and methods: The following methods were used: content analysis of medical case-records. Data processing was performed using statistical and mathematical methods and graphical analysis. Results: There were identified some differences in the prescriptions of different groups of medicine combinations for the treatment of arterial hypertension and the most prescribed medicine combinations in monotherapy. Conclusions: As a result of the study, it was found that the most prescribed combination in the treatment of arterial hypertension is a combination of three-component medicines.

Keywords: *Arterial hypertension; Antihypertensive medicines; Pharmacoepidemiological study.*

Introduction

According to the recommendations of the Ukrainian Society of Cardiology, a treatment regimen for arterial hypertension was adopted [1, 2]. In moderate arterial hypertension, treatment begins with monotherapy with one of the first-line medicines, and in severe forms of arterial hypertension - with the combined use of two or three medicines.

The patient is prescribed an antihypertensive medicine from the first line in a medium dose. If the hypotensive effect occurs, then the treatment is continued [3, 4]. In case of insufficient hypotensive effect, if within 4 weeks of monotherapy with an antihypertensive medicine the therapeutic effect is not achieved, then a switch to pharmacotherapy with combination medicines shall be done. The advantages of combination therapy are that the combination of two or more antihypertensive medicines that affect different mechanisms of

blood pressure increase, promotes a more pronounced therapeutic effect, reduces the side effects of medicines, it is possible to conduct long-term outpatient pharmacotherapy [5]. In addition, you can reduce the number times needed to take medicine during the day.

Results of the Study

When studying the structure of combination therapy under the treatment regimen (combination of medicines), the number of groups of medicines used in the treatment of one patient during his stay in the hospital was determined. A content analysis of 1669 case-records of patients who were in the inpatient treatment in the cardiology departments of Kyiv for the period 2019-2020 was conducted. Treatment with the use of medicines of one group (monotherapy) was performed in 14.35% of patients (230 people), 442 people (27.57%) used two-component treatment regimens, 529 people (33%) three-

component treatment regimens, 323 people (20.15%) were treated with medicines of four groups, 35 people (2.18%) with medicines of

five groups, 14 people (0.87%) with medicines of six groups. 1.87% (30 people) did not receive medication therapy (Table. 1).

Table1: Options for combination antihypertensive therapy

Number of medicine groups used in the treatment of one patient	Number of treated patients, persons.	Share in the sample,%
0	30	1.8
1	230	13.78
2	508	30.43
3	529	31.69
4	323	19.35
5	35	2.1
6	14	0.84

Monotherapy in 1.3% of cases (three people) was performed with diuretics, 18.7% (43 people) were treated with medicines that affect the renin-angiotensin system (RAS), 28.25% (65 people) (β - adrenoblockers, 45.65% (105 people) blockers of slow calcium channels, 6.1% (14 people) were treated with complex composition medicines in fixed doses.

Combinations of medicines for the treatment of arterial hypertension, that were considered effective, less effective and ineffective. They are all two-component.

The following combinations are recommended as effective:

- Diuretic + β - adrenoblocker;
- Diuretic + medicine that affects the RAS;
- Blocker of slow calcium channels (dihydropyridine series) + β - adrenoblocker;
- Slow calcium channel blocker + medicine that affects RAS;
- α_1 - adrenoblocker + β - adrenoblocker;
- Medicine of central action + diuretic.

Combinations: “ α_1 - adrenoblocker + β - adrenoblocker”, “central action medicine + diuretic” in the structure of medication therapy regimens were not presented.

The combination “slow calcium channel blocker + medicine that affects RAS” was recorded in 110 people (21.65%), “slow calcium channel blocker (dihydropyridine series) + β - adrenoblocker” in 31 people (6.1%), “Diuretic + medicine that affects the RAS” in 30 people (6.1%) (three people were

prescribed sequentially), 39 people (7.67%) were treated with a combination of “diuretic + β - adrenoblocker”.

Thus, the share of combinations, that were considered effective, was 41.34 % (210 people). Less effective combinations are:

- Blocker of slow calcium channels + diuretic;
- β - adrenoblocker + medicine that affects the RAS.

Their use was registered in 140 people (27.56%): 16 people (3.15%) were treated with a combination of “slow calcium channel blocker + diuretic”, 124 people (24.5%) with a combination of β -adrenoblocker + medicine that affects RAS.

Ineffective combinations are:

- β - adrenoblocker + blocker of slow calcium channels (verapamil or diltiazem) - 0.78% (4 people);
- Blocker of slow calcium channels + α_1 - adrenoblocker was absent.
- In addition to the above, the sample included two-component treatment regimens of the following composition:
- Blocker of slow calcium channels + medicine with complex composition in fixed doses - 0.78% (4 people);
- β - adrenoblocker + medicines of complex composition in fixed doses - 0.59% (3 people);
- Medicine that affects RAS + medicine of complex composition in fixed doses - 1.37% (7 people).

- Three-component treatment regimens were presented in 12 combinations, the most common of which include the following:
 - “Diuretic + medicine that affects RAS + β - adrenoblocker” - 30.62% (162 people);
 - “Diuretic + medicine that affects the RAS + slow calcium channel blocker” - 30.06% (159 people);
 - “Medicine that affects RAS + β - adrenoblocker + blocker of slow calcium channels” - 19.28% (102 people);
 - “Diuretic + β - adrenoblocker + blocker of slow calcium channels” (10.4%) (55 people).
- In addition to the above, there were nine three-component combinations in the sample, the total share of which, in the overall structure of the regimes, was 9.64% (Table 2).
- Treatment regimens consisting of medicines of four groups were represented by 11 combinations, the most common of which was: “Diuretic + medicine that affects RAS + β - adrenoblocker” - 61.6% (table. 3).

Table 2: Three-component treatment regimens that are present in the structure of prescriptions

Components of treatment regimes	Number of treated patients, persons	Share in the sample, %
“Diuretic + medicine that affects RAS + β - adrenoblocker”	162	30.62
“Diuretic + medicine that affects the RAS + slow calcium channel blocker”	159	30.06
“Diuretic + β - adrenoblocker + blocker of slow calcium channels”	55	10.4
“Medicine that affects RAS + β - adrenoblocker + blocker of slow calcium channels”	102	19.28
Diuretic + medicine that affects RAS + medicine of complex composition in fixed doses	8	1.51
Medicine that affects RAS + slow calcium channel blocker + medicine of complex composition in fixed doses	7	1.32
Medicine that affects RAS + β - adrenoblocker + central action medicine	11	2.08
Medicine that affects the RAS + slow calcium channel blocker + central action medicine	4	0.75
β - adrenoblocker + blocker of slow calcium channels + central action medicine	2	0.38
Diuretic + β - adrenoblocker + central action medicine	2	0.38
Medicine that affects RAS + β - adrenoblocker + medicine of complex composition in fixed doses	12	2.27
β - adrenoblocker + slow calcium channel blocker + medicine of complex composition in fixed doses	3	0.57
Medicine that affects RAS + central action medicine + medicine of complex composition in fixed doses	2	0.38

Table 3: Four-component treatment regimens that are present in the structure of prescriptions

Components of treatment regimes	Number of treated patients, persons	Share in the sample, %
Diuretic + medicine that affects RAS + (β - adrenoblocker + blocker of slow calcium channels	199	61.6
Diuretics + medicine that affects RAS + β - adrenoblocker + α 1 - adrenoblocker”	13	4.02
Diuretics + medicine that affects RAS + slow calcium channel blocker + medicine of complex composition in fixed doses	18	5.57
Diuretics + β - adrenoblocker + slow calcium channel blocker + medicine of complex composition in fixed doses	12	3.72
Diuretics + medicine that affects the RAS + slow calcium channel blocker + central action medicine	16	4.95
Medicine that affects the RAS + (β - adrenoblocker + slow calcium channel blocker + central action medicine	15	4.64
Diuretics + medicine that affects RAS + (β - adrenoblocker + medicine of complex composition in fixed doses	9	2.79
Medicine that affects RAS + β - adrenoblocker + blocker of slow calcium channels + α -adrenoblocker	2	0.62

Medicine that affects RAS + (β - adrenoblocker + slow calcium channel blocker + medicine of complex composition in fixed doses	26	8.05
Diuretic medicine that affects RAS + (β - adrenoblocker + central action medicine	9	2.79
Medicine that affects RAS + β - adrenoblocker + central action medicine + medicine of complex composition in fixed doses	4	1.24

Five-component treatment regimens were used for 35 people, the number of

combinations - five, six-component regimens for 14 people, the number of combinations - two (Table 4, 5).

Table 4: Five-component treatment regimens that are present in the structure of prescriptions

Components of treatment regimens	Number of treated patients,	Share in the sample, %
Diuretic + medicine that affects RAS + (β - adrenoblocker + blocker of slow calcium channels + a -adrenoblocker	4	11.4
Diuretic + medicine that affects RAS + (β - adrenoblocker + slow calcium channel blocker + medicine of complex composition in fixed doses	15	42.9
Diuretic + medicine that affects the RAS + (β - adrenoblocker + slow calcium channel blocker + central action medicine	9	25.7
Diuretic + medicine that affects the RAS + slow calcium channel blocker + vasodilating agent + central action medicine	3	8.6
Diuretic + medicine that affects RAS + (β - adrenoblocker + medicine of complex composition in fixed doses + central action medicine	4	11.4

Table 5: Six-component treatment regimens that are present in the structure of prescriptions

Components of treatment regimens	Number of treated patients,	Share in the sample, %
Diuretic. Medicine that affects the RAS + β - adrenoblocker + slow calcium channel blocker + central action medicine + a - adrenoblocker	8	57.1
Diuretic + medicine that affects RAS + β - adrenoblocker + slow calcium channel blocker + central action medicine + medicine of complex composition in fixed doses	6	42.9

Thus, different approaches to antihypertensive therapy have been registered. There are absent prescriptions in 30 case of the analyzed 1669 case-records; there were registered 45 combinations by medicine groups in 1639 case-records.

The number of groups of medicines used in the treatment of one patient ranged from one to six. The most common were three-component treatment regimens - 31.7%.

A comparison of the prescriptions of combination medicines, as a combination medicine prescribed in monotherapy, was conducted. The study of the prescription of combination medicines in antihypertensive monotherapy revealed the dominance of reserpine-containing medicine with the commercial name Adelphane-Esidrex. Capozid, Enap H, Andipal, Viscaldix and Crystepin were next in declining prevalence.

The study of baseline blood pressure of patients of these groups using analysis of variance revealed the heterogeneity of the compared indicators. Multiple group comparisons showed a lower baseline systolic blood pressure (SBP) in patients receiving Andipal. This difference was significant ($p < 0.05$) in relation to the subgroup of patients treated with Viscaldix, for whom the mean value of SBP was maximum in the group of combination medicines (Table 6). Baseline levels of diastolic blood pressure (DBP) in all compared subgroups had no significant differences.

The achieved levels of SBP and DBP in the subgroups of patients who were in monotherapy with combination medicines also did not differ significantly. However, statistically significant differences were found when comparing the percentages of antihypertensive activity of these medicines.

The lowest rate was in the group with the prescription of Andipal. However, due to the large values of the standard error of the

mean value calculated for the relative values, this difference was not significant.

Table 6: Structure and efficacy of combination medicines prescribed as antihypertensive therapy

The name of the medicine	Share of prescriptions %	Baseline BP (mm Hg)		Achieved BP (mm Hg)		Decreased BP	
		SBP	DBP	SBP	DBP	SBP	DBP
		173±3.1	96±2.3	149±1.4	88±1.3	24±3.2	8±2.5
Adelphane	53.4	174±3.4	93±3.3	154±3.7	89.5±1.1	20±4.1	3.5±1.7
Capozid	12.1	174±5.7	100±1.7	142±1.2	88±1.4	32±1.7	12±2.0
Enap H	10.3	170±6.8	93±4.9	148±1.3	88±3.1	22±1.1	5±1.8
Andipal	8.6	146±5.1*	94±1.6	144±1.7	92.0±1.0	2±1.9	2±4.8
Viscaldix	8.6	197±7.2	107±1.7	132±1.8	82±2.0	65±2.7	25±3.1
Crystepin	6.9	170±9.6	110±1.3	142±2.5	90±1.0	28±2.9	20±2.6

- p<0.05 according to the Newman–Keuls criteria

Conclusions

Thus, as a result of the study, it was emphasized that in the treatment of arterial hypertension, patients are more often

prescribed combinations of medicines. The study of combination medicines used in the case of monotherapy revealed the dominance of reserpine-containing medicines with the commercial name Adelphane-Esidx.

References

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