Some approaches to improving patients' compliance with antihypertensive pharmacotherapy

Vdovichenko V.,[1]* Snezhitskiy V.,[2] Kazakiewicz D.[1]

1 Pharmacology Department, Grodno State Medical University, Grodno, Belarus
2 Department of Internal Diseases, Grodno State Medical University, Grodno, Belarus

ABSTRACT

Purpose: The purpose of this work was to investigate the impact of usage of a computer program PharmCalculation in the polyclinic on the patients' compliance.
Material and methods: Study group was made of 73 AH outpatients whose physicians have been provided with the computer program PharmCalculation. Treatment patterns were observed during two-month period. Afterwards patients were surveyed in order to investigate compliance. Control group consisted of 100 randomly chosen customers of drugstores who were buying antihypertensives. Survey was performed in order to investigate their compliance.
Results: 80.8% of patients in the study group were taking antihypertensive drugs regularly. In the control group, there were 60% of patients who took antihypertensives regularly. Odds' ratio of adherence to treatment was 2.8 in the favor of the study group (95% interval –1.4-5.8). There was an evidence, that usage of antihypertensive drugs in median therapeutic doses raised adherence of patients in the study group to the prescribed pharmacotherapy (p=0.019). Odds' ratio was 4.4 in the favor of usage of median therapeutic doses with 95% confidence interval 1.1-21.8.
Conclusion: There is evidence that usage of software PharmCalculation in the polyclinic may improve compliance among hypertensive outpatients.
Keywords: hypertension, out-patient, compliance, pharmacotherapy

* **Corresponding author:**
Pharmacology Department
80 Gorky str., Grodno
230009 Belarus
Tel. +375 29 7846910
E-mail: vmariposa60@yahoo.com
(Vdovichenko Vladimir)

Received: 1.04.2011
Accepted: 7.06.2011
Progress in Health Sciences
Vol. 1(1) · 2011 · pp 27- 33.

INTRODUCTION

The arterial hypertension (AH) is the most widespread cardiovascular pathology in the world which demands lifelong medical supervision and treatment [1]. Non compliance is a major obstacle to achieve target blood pressure values [1]. Financial constrains may be a serious limiting factor for some patients and generics became drugs of choice. So, the question arises, how doctor can make an optimal choice in the situation when innovative drugs are not available to everyone. It would seem reasonable if doctor could roughly estimate the cost of intended treatment, then discuss with a patient if given cost is affordable and seek some other options among cheap generic in some cases. Therefore, it would be useful to have a simple tool which could help to actually estimate the cost of treatment. Then, another question arises, which doses can be used as a starting point for such calculations while dosage regimens for individuals may vary significantly. The idea of this work is that most commonly used doses (median therapeutic doses) can be used for estimation of the cost of future antihypertensive treatment for given patient as a proper starting point. It is obvious, that the factual cost would differ from these calculations in the majority of cases. The main point of such calculations, however, is a rough estimation, not precise prediction. Such approach might be useful for improving compliance with antihypertensive treatment.

We have designed original software named PharmCalculation, which counts cost of monotherapy within one month for various antihypertensive generics, using the median therapeutic dose as a starting point for each drug and mean price on the pharmaceutical market. The aim of this work is studying of impact of usage of the program PharmCalculation in out-patient settings on patients' compliance with prescribed pharmacotherapy.

METHODS

PharmCalculation is a very simple computer program without specific hardware requirements which can be used on virtually any contemporary version of OS Windows. Market data for each available generic should be manually entered before starting usage of PharmCalculation, in particular, settings. For instance, to perform this study, we had to input data about available generics on Belarusian market, including international nonproprietary name, brand name, dose of one tablet, number of tablets in a pack, mean market price, name of company, country of production. It is really a time consuming job, but afterwards the software can be used on any computer in given settings and requires only minor revisions, such as adding a new drug or changing a price. There are five main categories in the PharmCalculation according to main five antihypertensive classes.

Doctor can choose antihypertensive class and input maximum desired cost of monthly treatment (with one drug of chosen class). The software simply provides information about drugs of chosen class, which fit in chosen monthly cost range. This information includes the international and brand name of the drug, company name, country of production and cost of monthly treatment. So doctor can freely choose a drug according to his preferences among all available generics which are affordable for a patient.

Study of impact of the program on the AH treatment was performed based on the Grodno central polyclinic during the last quarter of 2010. Nine local primary care physicians that prescribed treatment by the patient with AH took part in this investigation. It was offered to doctors to use program PharmCalculation for a choice of prescriptions (i.e. to make the decision on a choice of drug with respect to cost of treatment comprehensible to the given patient). All calculations were based on the most commonly used doses (median therapeutic doses) [2]. The program was represented as a tool for the additional help in a choice of optimum pharmacotherapy AH and doctors were not "obliged" to strictly follow all suggestions of the program. In the absence of effect from drug (drugs) prescription in a median therapeutic dose to the treatment scheme the next drug from other pharmacological classes was added.

There were 73 persons with AH in the study group. The appointed scheme of pharmacotherapy, including doses of drugs was fixed for each patient. Patients' sex, age, an educational level, the experience and degree AH were marked also. After 2 months of the pharmacotherapy survey of patients was performed concerning regularity of prescribed drug usage, frequency of hypertensive crises and ways of coping with them. General information regarding age, diagnosis, duration of disease, treatment was taken from medical records. Patients themselves were asked about regularity of taking antihypertensives (see more information below). Then they were asked about frequency of elevations of blood pressure and the way of coping with them. Patients were also asked to define, whether they like Belarusian generics, and whether they prefer state or private drugstores.

Control group included 100 patients with AH who was buying antihypertensive drugs in drugstores of Grodno (regional center). The method of questioning was used in the control group. Selection of a participant was made in random order. During questioning in drugstores it was specified whether person was buying antihypertensive drugs for own usage. If the answer was positive, patient was asked

to take part in the survey. Firstly, every responder was asked to provide information about age, sex, diagnosis. Next, patients were asked to recall what they have bought in drugstore and what other antihypertensive drugs they were taking. Question regarding compliance was exactly the same in both control and study groups. Responders were asked if they take antihypertensives on regular basis. There were three possible options of answer to that question: yes, no, according to indications. The answer "according to indications" in the subsequent analysis was regarded as irregular usage. At the analysis of the collected information in investigated group those cases when the dose of an appointed drug for treatment AH was below median therapeutic were marked. The exception has been made for the fixed combinations (some medical products which are a part of one drug). Statistical processing of the information was performed with the use of methods of logistic regression (with the purpose of obtaining odds ratios), exact logistic regression at the small size of subgroups, Poisson's regression [3, 4]. Data in this work were analyzed using R, a free software environment for statistical computing and graphics (www.r-project.org).

RESULTS

Patients

The age of patients in the study group varied from 31 to 90 years with mean age 68 years and standard deviation 13,6 years (Fig. 1). Women prevailed (78.1%) in that group. 4.2% of patients had AH stage, I, 60.6% of patients – AH stage II, 34.2% – AH stage III. Minimal duration of disease in that group was 2 years, maximal – 31 years with meaning 14.1 years and standard deviation 7.8 years. The number of acute elevations of blood pressure during the period of study varied from 0 to 4 (mean – 0.9) for each patient. More often (52.1%) patients preferred to cope with hypertensive crises by themselves. Frequency of occurrence of hypertensive crises in the study group was increasing with age (p=0.019) and with an increase of severity of AH (p=0.012). The age of patients in the control group varied from 23 to 90 years with a mean 65 ±14.1.

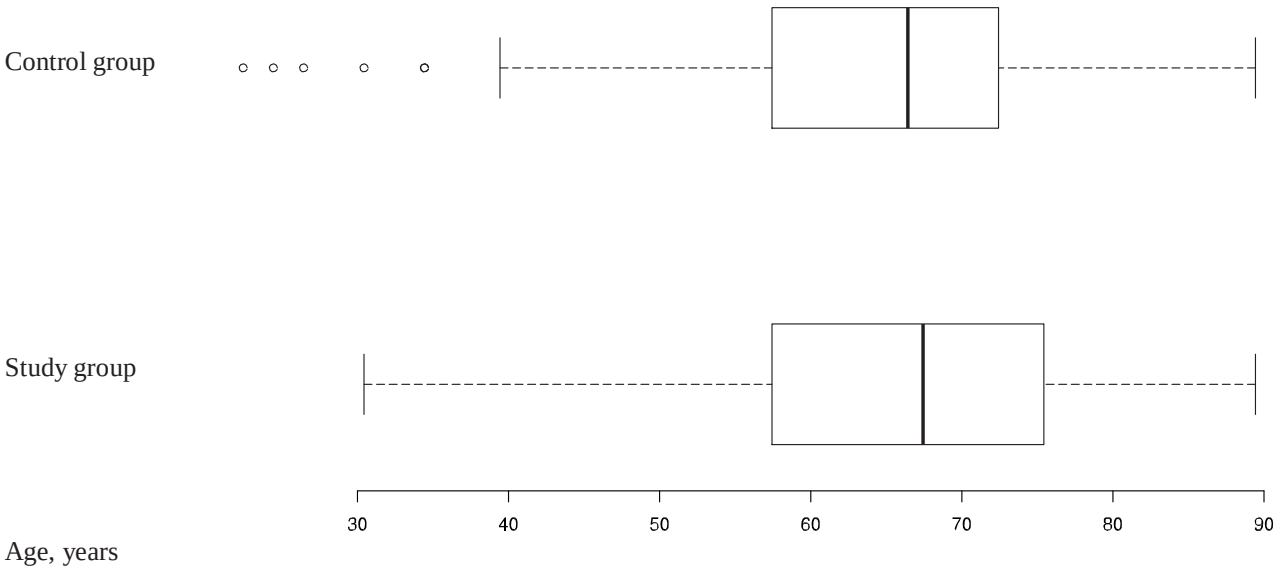

Figure 1. Age distribution in the study and control groups (box-and-whisker plot).

There were 52 (71%) women in the study group. Mean duration of AH in the control group was 12.4±9.3 years, minimum – less than 1 year, maximum – 49 years. 37% of responders were not sure about their current stage of AH, while 63% did answer that question. Only 5 (5%) patients from control had AH stage, I, 28 patients – AH stage II, 30 patients – AH stage III.

Pharmacology

The following antihypertensive drugs were used for the treatment of AH in the study group (listed in alphabetic order): amlodipine, atenolol, bisoprolol, carvedilol, chlortalidon, diltiazem, enalapril, hydrochlorothiazide, indapamide, lisinopril, meto-prolol, ramipril. Each patient received from one to four antihypertensive drugs. The standard deviation in the number of drugs received by one patient was 0.82, a median – 2. Thus, 43 (58.9%) patients received either 1 or 2 antihypertensive drugs, and 30 (41.1%) patients received either 3 or 4 antihypertensive drugs. The number of drugs received by one patient increased with an increase of severity of AH ($p<0.001$). 57.5% of patients in the study group were prescribed antihypertensives in median therapeutic doses (with the exception of fixed combinations), and (42.5%) of patients received one or more anti-hypertensive drugs in lower doses, then the median therapeutic ones. There were no cases when prescription doses exceeded median therapeutic ones. According to data obtained, men were prescribed antihypertensive drugs in lower doses than women ($p=0.044$). There was an evidence that ($p <0.001$) median therapeutic doses were used more frequently in patients with more severe AH. In the control group, ACE inhibitors were used by 52% patients. Among ACE inhibitors enalapril was 65% and lisinopril were chosen in 65% and 21% cases respectively. β- blockers were chosen by 17% patients (mainly metoprolol – 65%). Diuretics were used in 12% of cases (indapamide– 58%, hydrohlorothiazide – 33%), a calcium antagonist. – in 11% of cases (among which amlodipine was chosen in 64%). Nobody has among 100 randomly chosen patients had bought angiotensin II blockers.

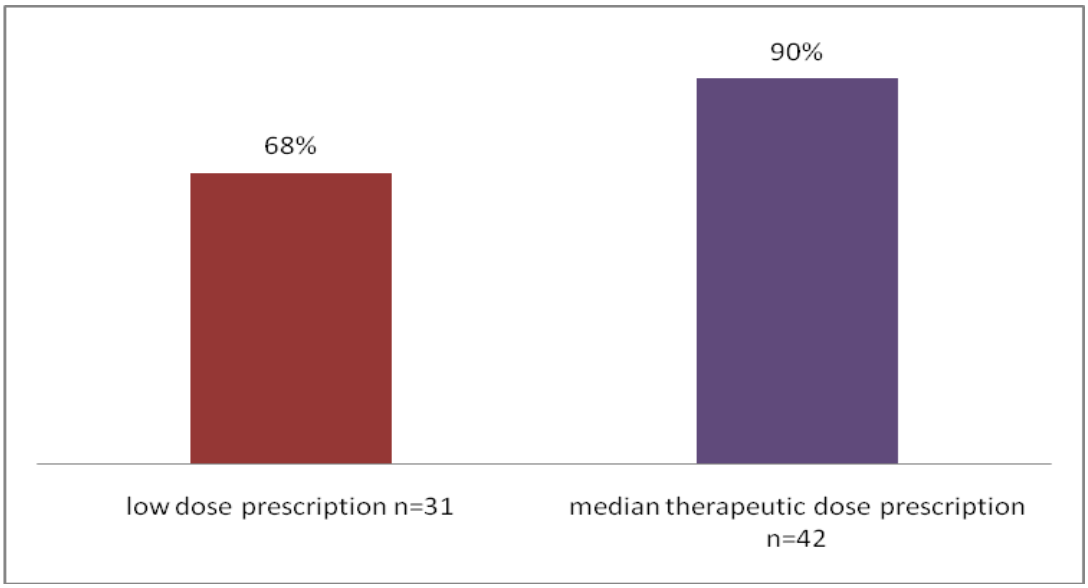

Figure 2. Percentage of patients from study group with perfect compliance with respect to prescription dosage n – number of patients in each subgroup.

Compliance

Survey was performed in study group after two months period. Patients were asked about regularity of antihypertensive drugs usage. Nearly 68% of patients who were prescribed antihypertensives in low doses took drugs on regular basis (Fig.2). Perfect compliance was reported by 90% of the patients to whom all antihypertensives (with exceptions mentioned in methods section) were given in median therapeutic doses. Thus, there is median therapeutic doses raises adherence of patients to the prescribed pharmacotherapy ($p=0.019$). Odd ratio was 4.4 in the favor of usage of median therapeutic doses with 95% confidence interval 1.1-21.8. Overall, 80.8% of patients in the study group were taking antihypertensive drugs regularly. In the control group, there were 60% of patients who took antihypertensives regularly according to prescriptions. (Fig. 3)

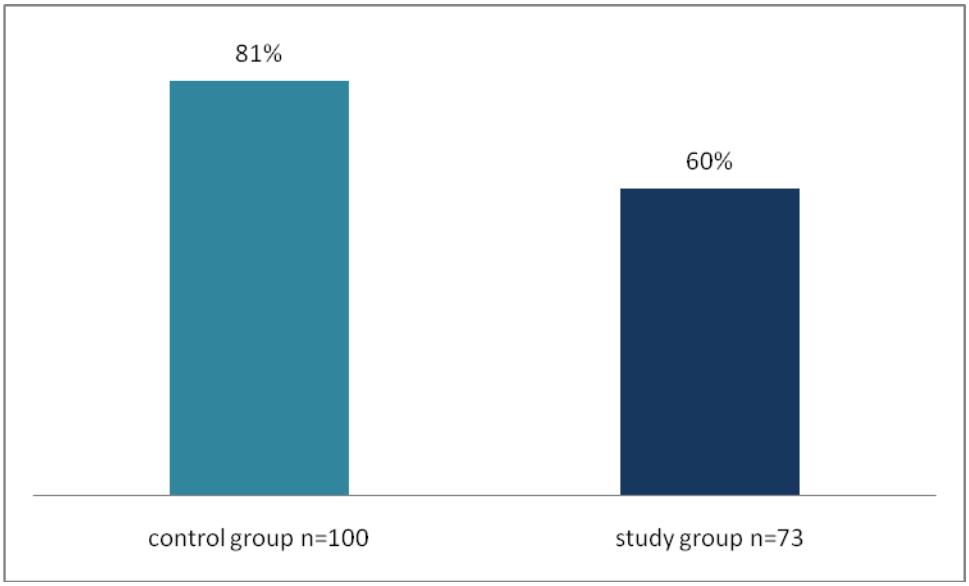

Figure 3. Percentage of patients with perfect compliance in study and control group n – number of patients in each group.

Thus, adherence of patients to the prescribed treatment was better in the study group in comparison to adherence in the control group (p=0.006). Odd ratio of adherence to treatment was 2.8 in the favour of the study group (95% interval – 1.4-5.8).

DISCUSSION

The data obtained suggest that use of software PharmCalculation improves adherence of patients to prescribed treatment AH (Fig. 3). PharmCalculation helps a physician to choose from different options depending on financial matters of a patient. That, in turn, seems to improve adherence of patients with the limited budget to prescribed treatment. Our findings emphasize well known importance of economic factors in the treatment of AH. According to the data obtained, usage of antihypertensive drugs in median therapeutic doses by itself improves compliance of patients with AH with prescribed treatment (Figure 2). For instance, Marvin Moser gives the following important statement: "At a dosage of 50 mg of hydrochlorothiazide or its equivalent, pressure decrease, possibly, in 80-90% of patients. The dosage of 100 mg can increase quantity of patients at which has decreased the blood pressure or to make figures of decrease the blood pressure more considerable, but for the account of additional adverse effects" [5]. In multicenter double blind randomized trial the efficiency of three various antihypertensive drugs was com- pared: small doses (1.25 and 2.5 mg a day) of thiazide diuretics bendroflumethiazide (its median therapeutic dose – 7.5 mg a day), 10 mg of enalapril (its median therapeutic dose – 20 mg a day) and amlodipine in an median therapeutic dose (5 mg). Obtained results suggested, that maximum antihypertensive effect was provided by amlodipine [6]. In other words, indeed, antihypertensive drugs optimally realize the therapeutic potential in doses close to median therapeutics ones. In multicenter double blind randomized trial at patients with AH where within 12 weeks patients were prescribed median therapeutic doses of lisinopril (20 mg) and nebivolol
(5 mg), the conclusion was made about the similarity of antihypertensive effect of both drugs [7].

Furthermore, controlled trial where propranolol was studied in the wide range of recommended day dosages, i.e., 60 mg, 120 mg and 240 mg was extremely indicative [8]. Results are rather eloquent, because the antihypertensive activity of propranolol at daily dose 60 mg did not differ from placebo, and dosages of 120 mg (a middle therapeutic dose) and 240 mg (the maximum day dose) revealed a similar effect. It is also can be noticed, that frequency of side effects is increasing with an increase of a dosage of antihypertensive drugs [9–12]. In cases when various options are possible, median therapeutic dose seems to be a reasonable reference point, some kind of "beacon" in the ocean of generics. It is necessary to emphasize, however, that the given approach does not by any means contradict to individual dosage consideration, including dose titration and selection of a dose

according to comorbidity.

The main limitation of the study is a study design when compliance in two groups of a patient was investigated in different settings. Therefore, our results should be considered as preliminary and should be confirmed by further research. Other limitations include small sample size and lack of clinical data. Unfortunately, there is no possibility neither to compare mean blood pressure in the control and study group, no to verify the answers in the control group.

CONCLUSIONS

1. Differentiating prescriptions of antihypertensives with respect to the financial possibilities of each patient improve patients' compliance with prescribed treatment.
2. Software PharmCalculation is a useful tool to gain the improvement by such means.
3. Usage of antihypertensive drugs in median therapeutic doses may also improve patients' compliance with prescribed treatment.

REFERENCES

1. Mansia G, Backer GD, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Boudier HAS, Zanchetti A. 2007 ESH-ESC Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Blood Press. 2007; 16(3): 135–232.
2. Cooper DH, Krainik AJ, Lubner SJ, Reno H. The Washington Manual of Medical Therapeutics. 32 ed. Lippincott Williams & Wilkins; 2007. p. 780.
3. Mehta CR, Patel NR. Exact logistic regression: theory and examples. Stat Med. 1995 Oct 15; 14(19): 2143–60.
4. Belle van G, Fisher LD, Heagerty PJ, Lumley T. Biostatistics. A Methodology for the Health Sciences. 2nd ed. Wiley series in probability and statistics, Wiley-Interscience; 2004. p. 871.
5. Moser M. Clinical Management of Hypertension. 2nd ed. PCI; 1997. p.336.
6. Rasmussen S, Borrild N, Andersen JV. Efficacy and safety of 24 weeks of therapy with bendro-flumethiazide 1.25 mg/day or 2.5 mg/day and potassium chloride compared with enalapril 10 mg/day and amlodipine 5 mg/day in patients with mild to moderate primary hypertension : a multicentre, randomised, open study. Clin Drug Investig. 2006; 26(2): 91–101.
7. Rosei EA, Rizzoni D, Comini S, Boari G, Group NLS. Evaluation of the efficacy and tolerability of nebivolol versus lisinopril in the treatment professential arterial hypertension: a randomized, multicentre, double-blind study. Blood Press. 2003; 12 Suppl 1: 30-5.
8. Galloway DB, Glover SC, Hendry WG, Logie AW, Petrie JC, Smith MC, Lewis JA, Simpson WT. Propranolol in hypertension: a dose-response study. BMJ. 1976 Jul 17; 2(6028): 140–2.
9. Trafford JA, Latta D, Little PS, Parsley J, Ankier SI, Quail D. A multi-centre, placebo controlled compa-rative study between 200 mg and 400 mg celiprolol in patients with mild to moderate essential hypertension. Curr Med Res Opin. 1989; 11(9): 550–6.
10. Williams RL, Goyle KK, Herman TS, Rofman BA, Ruoff GE, Hogan LB. Dose-dependent effects of betaxolol in hypertension: a double-blind, multi-center study. J Clin Pharmacol. 1992 Apr; 32(4): 360–7.
11. Bergstrand R, Herlitz H, Johansson S, Berglund G, Vedin A, Wilhelmsson C, Gomez HJ, Cirillo VJ, Bolognese JA. Effective dose range of enalapril in mild to moderate essential hypertension. Br J Clin Pharmacol. 1985 May; 19(5): 605–11.
12. Frick MH, McGibney D, Tyler HM. Amlodipine: a double-blind evaluation of the dose-response relationship in mild to moderate hypertension. J Cardiovasc Pharmacol. 1988; 12 Suppl 7: S76-8.