Ivanova A, Lakic D, Andric V, Petrova G. Cost of outpatient hypertension pharmacotherapy - comparative study between Bulgaria and Serbia. Pharmacy Practice (Internet) 2009 Apr-Jun;7(2):108-112.

Original Research

Cost of outpatient hypertension pharmacotherapy: comparative study between Bulgaria and Serbia

Anna IVANOVA, Dragana LAKIC, Vesna ANDRIC, Guenka PETROVA.

Received (first version): 13-Jan-2009 Accepted: 3-Apr-2009

ABSTRACT*

Objective: To compare the prescribing practice and pharmacotherapy outpatient cost of hypertension and its common complications between two neighboring countries, Bulgaria and Serbia. The study questions focus on consistency of the prescribing practice with the treatment guidelines; comparability of the treatment patterns among both countries, and burden of hypertension cost to the population and third party payer in the countries under consideration.

Methods: Retrospective study, one year time horizon is for outpatient therapy.

Results: Patients with arterial hypertension in Bulgaria are most often on monotherapy (61% vs 6% in Serbia), as well as those with complications (66% vs 0% Serbia). In both countries the first choice of therapy are the ACE inhibitors (37.01% in Serbia and 41% in Bulgaria) and then follows the calcium antagonists, beta-blockers, and diuretics. The weighed monthly cost of hypertension and complicated hypertension is almost doubled in Serbia (12.56 vs 8.23 EUR for hypertension, and 13.39 vs 8.23 EUR) and prevailing part is reimbursed (88% vs 44% in Bulgaria).

Conclusion: Our study confirms that hypertension and its complications therapy consumes a huge amount of financial resources. In both countries under consideration the therapy is corresponding with the European treatment guidelines. The international cost comparisons are possible but they depend on many external factors as the regulatory measures, prescribing habits and reimbursement policy and should be analysed within this framework.

Keywords: Hypertension. Drug Costs. Health Expenditures. Serbia. Bulgaria.

COSTE DE LA FARMACOTERAPIA ANTIHIPERTENSIVA AMBULATORIA: ESTUDIO COMPARATIVO ENTRE BULGARIA Y SERBIA

RESUMEN

Objetivo: Comparar las prácticas de prescripción y el coste del tratamiento ambulatorio de la hipertensión y sus complicaciones comunes en dos países vecinos, Bulgaria y Serbia. Las preguntas de investigación se centran en la consistencia de las prácticas de prescripción con las guías de tratamiento; la comparabilidad de los patrones de prescripción entre los dos países, y el peso del coste de la hipertensión para la población y las aseguradoras en los países en estudio.

Métodos: Estudio retrospectivo con un horizonte temporal de un año para el tratamiento ambulatorio.

Resultados: Los pacientes con hipertensión arterial en Bulgaria están más frecuentemente en monoterapia (61% vs 6% en Serbia). En ambos países la primera elección de tratamiento son los IECA (37,01% en Serbia y 41% en Bulgaria) seguidos de los calcio-antagonistas, betabloqueantes y diuréticos. El coste mensual ponderado de la hipertensión complicada es casi el doble en Serbia (12,56 vs 8,23 EUR para hipertensión y 13,39 vs 8,23 EUR) y la parte principal es reembolsada (88% vs 44% en Bulgaria).

Conclusión: Nuestro estudio confirma que la hipertensión y sus complicaciones consumen una enorme cantidad de recursos financieros. En ambos países estudiados el tratamiento se corresponde con las guías europeas de tratamiento. Las comparaciones internacionales de costes son factibles pero dependen de muchos factores externos como las medidas regulatorias, los hábitos de prescripción y las políticas de reembolso, y deberían analizarse en estos marcos.

Palabras clave: Hipertensión. Coste de medicamentos. Gastos en salud. Serbia. Bulgaria.

INTRODUCTION

Arterial hypertension is one of the leading risk factors for ischemic heart disease, cerebrovascular diseases, peripheral arterial diseases, stroke and acute myocardial infarction that are among the most health care cost consuming diseases.

* Anna IVANOVA. Faculty of Pharmacy, Medical University. Sofia (Bulgaria).
Dragana LAKIC. Institute for Social Pharmacy and Pharmacy Legislation. Faculty of Pharmacy, Belgrade University. Belgrade (Serbia).
Vesna ANDRIC. Republic Institute for Health Insurance. Belgrade (Serbia).
Guenka PETROVA. Faculty of Pharmacy, Medical University. Sofia (Bulgaria).

Cardiovascular diseases were the leading cause of mortality in Serbia in 2006, with 57.6% of all deaths, and women (53.9%) died more often than men.[1] Age-standardized mortality rate for cardiovascular diseases is 554.0 per 100,000 Bulgarian population[2] and hypertension is also among the leading causes for death (108.1 per 100,000).[3] Hypertension complication leads to age-standardized annual event rate from 915 to 30 per 100,000 people all over the world.[4,5] Premature death and disability due to cardiovascular diseases represent significant economic and social burden to any country, which is recognized by European Society of Hypertension.[6]

Studying the hypertension prescribing practice is important not only from the therapeutic point of view but also from the economic point, especially when it is connected with the cost of the complications.

The aim of this study is to compare the prescribing practice and pharmacotherapy outpatient cost of hypertension and its common complications between two neighbouring countries Bulgaria and Serbia.

Study questions:

- Is the hypertension prescribing practice in both countries consistent with the treatment guidelines?
- Are the treatment patterns comparable among both countries?
- What is the burden of hypertension cost to the population and third party payer in the countries under consideration?

The studies are the retrospective ones, the point of view is that of the outpatient therapy and time horizon is for one year.

In Serbia the total number of patient with hypertension, codes I10-I11 was 2764 while in Bulgaria the whole sample is including 3240 patients. Patients without complications of hypertension were 1856 in Serbia and 2106 in Bulgaria that represent 67.15% and 65% respectively. Patients with complicated hypertension were 908, or 32.85% in Serbia and 1134 (35%) in Bulgaria.

METHODS

The studies in the two countries were organized consecutively and independently following the same methodological approach and then the results were compared.

A one year retrospective study from the point of view of health care systems in Bulgaria and Serbia was performed in 2006.

A prescription sample size was determined to satisfy the values for alpha 0.05 and a study power of 0.80. The size of 250 prescriptions per diagnosis satisfies the stated criteria.

Prescribing practice analysis

In Bulgaria on a retrospective random basis were collected 3240 reimbursable prescriptions in 2006 year from the pharmacies databases working under National health insurance fund (NHIF) conditions. In Serbia the information database of the Republic Institute of Health Insurance (RIHI) was used as a source of the analysis. The list of all insured persons according, that betake medications on 12 or more prescriptions per year (depict on chronic disease and regular therapy) was created and out of this list the random sample of patients was collected for the following conditions defined by the International classification of diseases (ICD)[7]: hypertension (I10-I11) and for its complications - heart failure (I.50); sequelae of cerebrovascular disease (I.69); angina pectoris (I.20). In Bulgaria according to NHIF rules 1 patient can receive only 1 prescription for one health condition per month including no more than 3 medicines while in Serbia there is no such a limitation.

The medicines in the collected samples were systematized and analyzed according to the following criteria:

- complexity of the therapy – mono-, di-, three-, etc.);
- frequency of the prescribed medicines as therapeutic class; international nonproprietary names; and brand name.

Prescription cost calculation

In the prescribing cost calculation were considered the following outcome indicators.

- total number of patients (n) by ICD diagnosis of arterial hypertension or with complicated hypertension;
- number of patients with ICD codes I10-I11(n) that except the I10-I11 possess and one or more of hypertension complications: angina pectoris (I20), myocardial infarct (I21), ischemic hard disease (I25), cardiac insufficiency (I50), insult (I69); In Bulgaria only angina pectoris, cardiac insufficiency and insult were considered for the analysis.
- frequency of patients (p) with hypertension out of all collected patients and frequency of patients with complications (p) complicated hypertension out of all patients with hypertension;
- number of patients (n) on mono-, di-, three- or poly therapy out of all patients with hypertension and out of all patients with complicated hypertension;
- frequency of monthly prescribing of trade names of medicines (p) in the groups of patients on mono-, di-, three- and poly therapy for hypertension and complicated hypertension, calculated as a number of dispensed packages of medicines per patient on mono- ; di-; three- etc- therapy;
- weighed monthly cost of pharmacotherapy (Σ) per patient on mono-, di-, three- and poly-therapy for hypertension and simple hypertension, calculated using the following formula:

$$WMC = (\Sigma_1 \times p_1 + \Sigma_2 \times p_2 + \ldots + \Sigma_i \times p_i),$$

where:

$\Sigma_{1, 2 \ldots i}$ is in Bulgaria the officially published retail price negotiated with NHIF[8] while in Serbia is an average monthly price of package of prescribed dosage form[9];

$p_{1, 2 \ldots i}$ is a frequency of monthly prescribing of the same trade name.

There are a variety of the co-payment in the reimbursement drug list in Bulgaria for the medicines for hypertension therapy and its complications that impose a separated calculation for the reimbursed part of the cost and co-payment contribution.[8] The same was also completed for the complicated hypertension.

The total cost of yearly therapy is calculated as a sum of the cost of all hypertension patients for 12 months (AHU), calculated as 12 monthly therapy costs multiplied by the number of patients with hypertension:

$$\Sigma_{AHU} = (\Sigma_{SAH} \text{ x } p_{SAH} + \Sigma_{AH} \text{ x } p_{AH}) \text{ x } 12 \text{ x number of patients.}$$

Statistical analysis

Differences in proportions between the prescribing practice and cost of hypertension and complicated hypertension therapy in Bulgaria and Serbia were compared with the two-sided z-test for two proportions. We estimated 95% confidence intervals (CI) assuming a normal distribution. The z value and 95% confidence interval z value were analyzed using Excel.

RESULTS

In Serbia the total number of patient with hypertension, codes I10-I11 was 2764 while in Bulgaria the whole sample is including 3240 patients. Patients without complications of hypertension were 1856 in Serbia and 2106 in Bulgaria that represent 67.15% and 65% respectively. Patients with complicated hypertension were 908, or 32.85% in Serbia and 1134 (35%) in Bulgaria.

Table 1.

	Serbia		Bulgaria		Z value
indicator	**N**	**%**	**N**	**%**	
Total sample	**2764**		**3240**		
Prescriptions for AH	**1856**	**67.15**	**2106**	**65**	1.602
Monotherapy	118	06.36	1296	61.54	36.13*
Ditherapy	552	29.74	647	30.72	0.647
Three therapy	653	35.18	162	7.69	20.912*
Polytherapy	533	28.72	0	0	5.347*
Prescriptions for complicated AH(CAH)	**908**	**32.85**	**1134**	**35**	1.602
Monotherapy	0	0	745	65.70	9.474*
Ditherapy	90	9.91	285	25.13	8.642*
Three therapy	255	28.08	104	9.17	11.187*
Polytherapy	563	62.00	0	0	9.133*
AH therapy by pharmacological groups					
ACE inhibitors		37.01		41	0.435
ACE inhibitors with diuretics		2.67		0	0.505
calcium antagonist		21.6		16	0.901
beta blockers		12.88		19	0.964
diuretics		10.03		15	0.855
other		15.81		9	0.461
Expenditures €	**value**		**value**		
waged monthly cost for AH (Euro)	12.56		6.9		
waged monthly cost of hypertension considering the chance of having complications (Euro) CAH	13.39		8.23		
RIHI participation of total expenditures in monthly therapy of AH per patient	10.70	88.44	3.04	44.06	6.419*
RIHI participation of total expenditures in monthly therapy of CAH per patient	13.36	83.45	3.96	36.77	6.628*
Distribution of complications from CAH					
angina pectoris		70		42	3.846*
heart failure		7		26	3.429*
ischemic heart disease		6		0	1.539
sequelae of cerebrovascular disease		0. 33		32	5.715*
other diagnoses in combination with AH		16.67		0	3.706*

*p < 0.05
AH, arterial hypertension; CAH, complicated arterial hypertension; ACE, Angiotensin-Converting Enzyme; RIHI, Republic Institute of Health Insurance

Distribution of patients according to available complications is following. Angina pectoris is leading complication with 70% in Serbian sample and 42% in Bulgarian, then follows heart insufficiency (7% and 26%), ischemic heart disease (6% for Serbia no information for Bulgaria), sequelae of cerebrovascular disease (0.33% and 0.32 %), and other diagnoses 16.7% in Serbia. In

complicated hypertension prevails the mono-therapy in Bulgaria for 66%, while in Serbia 62% of patients are using more than three medicines (Table 1).

Patients with hypertension in Bulgaria are most often on mono-therapy (61% vs 6% in Serbia), as well as those with complications (66% vs 0% Serbia). The mono-therapy in hypertension treatment prevails in Bulgaria in 1296 patients while in Serbia only 118 patients are on mono therapy. Two medicines were prescribed in 30% and 29% respectively, while the three therapies prevail in Serbia with 35%. More than three medicines have been prescribed in 28% of the observed patient sample in Serbia.

In spite of the differences in the complexity of the therapy it was not observed statistically significant differences among the prescribed therapeutic classes of medicines (Table 1). In both countries the first choice of therapy are the ACE inhibitors (37.01% in Serbia and 41% in Bulgaria) and then follows the calcium antagonists, beta-blockers, and diuretics.

The weighed monthly cost of hypertension and complicated hypertension is almost doubled in Serbia (12.56 vs 8.23 Euro for hypertension, and 13.39 vs 8.23 Euro) and prevailing part is reimbursed (88% vs 44% in Bulgaria).

DISCUSSION

There are some estimation that the total number of patients with hypertension in Serbia is around 1 400 000, which correspond to 17.97% prevalence (7.4 million population).[10] For Bulgaria the corresponding figure is 1.5 million hypertensive patients (7.2 million inhabitants).[11] The number of patients with hypertension and complicated hypertension is similar in both country samples and this similarity is statistically significant (Table 1). The structure of the patients with complications differs because in Bulgaria only the 3 main complications were included in the sample, while in Serbia was considered also and other complications. The fact that there were no patients on poly therapy in Bulgaria could be explained with the health insurance fund limits to prescribe no more that 3 medicines per prescription, per diagnosis per month for a particular patient. This rule affects all the prescribing structure. The fact that patients in Bulgaria are most often on mono-therapy could be explained with the same regulation because patients receive a medicines for particular diagnoses and for the main disease as is the hypertension on the same prescription. We recognize that the marginal use of combination therapy in Bulgaria contrasts with the 2007 ESH/ESC guideline's recommendations for hypertension therapy. There was a thorough debate among the health practitioners and NHIF in Bulgaria about the possible negative impact that this limitation could have on a proper handling with the high blood pressure and now a day are going changes in the positive drug list. There were included a combination products within it. We could not comment the final results because the process of medicines selections is still in process but we believe that it will be beneficial for the patients. In Serbia patients receive prescriptions for all diagnoses together.

The fact that there is a similar structure of the prescribing by the main therapeutic classless means that professionals' in both countries follows the contemporary treatment guidelines. Further researches are necessary not only on cost control measures but also there on the need of physician education on rational drug therapy, and risk screening among the population. The fact that there are patients using more than 4 medicines per diagnoses in Serbia requires careful analysis.

Study results show that 55.5% of all health insurance expenditures for reimbursed medicines in Serbia are allocated on antihypertensive drugs; that was significantly higher than in the other countries.[12] This fact underlines the significance of the cost analysis of hypertension pharmacotherapy and necessity of the strict control on antihypertensive medicines. Antihypertensive drugs accounted for more than half of the prescription drug expenditures, although only 18% of population had hypertension, according to the data. This could be commented as lack of precise epidemiological statistic for the hypertension burden and confirms the importance of the cost control measures.[13] Further analysis should be done in depth about the adequate control on the blood pressure and introduction of measures for patient's education and compliance improvement, as well as study on the commitment of health care professionals. It could be kept in mind that the introduction of cost control measures could significantly increase the misuse of the medicines and therapy could failed but in any case clear evidences about the correspondence among the medicines usage and hypertension control are necessary for making any policy changes.

The prevalence of the ACE inhibitors (37%) and calcium antagonist (22%) prescribing while the diuretics usage is only 10% and 3% as mono-therapy and fix combination respectively could be explained with the existing marketing differences in terms of authorised for sale medicines as well as with the producers' policy on the local markets.[14,15]

High percentage of patients with complicated hypertension indicates late beginning of therapy, irregular general practitioner visits and low compliance.

It is authors' opinion that better cooperation between physicians and patients would lead to arterial hypertension morbidity and mortality reduction, reduction in expenditures for patient and society, which will finally affect patient's quality of life. Further analysis is needed.

CONCLUSIONS

Our study confirms that hypertension and its complications therapy consumes a huge amount of financial resources.

In both countries under consideration the therapy is corresponding with the European treatment guidelines.

We also could conclude that the international cost comparisons are possible but they depend on many external factors as the regulatory measures, prescribing habits and reimbursement policy and should be analysed within this framework.

CONFLICT OF INTEREST

None declared.

References

1. Knežević T, Health care statistical yearbook in Serbia (Zdravstveno-statistički godišnjak Republike Srbije) 2006. Beograd: Institute for public health in Serbia (Institut za javno zdravlje Srbije "Dr Milan Jovanović Batut"), 2006:253-61
2. WHO. Core health indicators. Avail. at: http://www.who.int/whosis/database/ core_core_select_process.cfm Accessed (accessed October 08, 2008).
3. National Statistic Institute of Bulgaria. Reasons for death 2007. [In Bulgarian] Available at: http://www.nsi.bg/SocialActivities/Health.htm. (accessed July 30, 2008).
4. Sans S, Kesteloot H, Kromhout D; Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. The burden of cardiovascular diseases mortality in Europe. Eur Heart J. 1997;18:1231-1248
5. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas A.M., Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA project: Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. Circulation. 1994;90:583-612
6. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens. 2003;21:1011-1053.
7. International classification of diseases. ICD 10. Available at: www.who.int/classifications/apps/icd/icd10online (accessed June 11, 2007).
8. National health insurance fund. Amendment 2 to " Instruction for usage of drug list of NHIF (Amendment 11 of National Agreement 2006, State Gazette 106/2005) in force from 01 September 2006-work version for-pharmacy. Available at: http://www.nhif.bg/bg/default.phtml?w=800&h=570 (accessed September 15, 2006).
9. RHIF. Ordinance on Drug Price List. RHIF, 2007 http://nn01.statserb.sr.gov.yu/axd/pxweb2004/Dialog/Saveshow.asp (accessed/ 09.04.2008).
10. WHO health data basis. Available at: http://data.euro.who.int/hfadb/ (accessed May 4, 2006).
11. http://www.heartstats.org/datapage.asp?id=4541(accessed/poslednji pristup: 06.06.2008).
12. Liu JL, Maniadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. Heart. 2002;88:597-603.
13. Marković Bergman B, Kranjčević K, Reiner Ž, Blažeković Milanković S, Špehar Stojanović S. Drug Therapy of Cardiovascular Risk Factors: Guidelines versus Reality in Primary Health Care Service. Croat Med J. 2005;46(6):984-989.
14. Marques-Vidal P, Montaye M, Ruidavets JB, Amouyel P, Ferrieres J. Evolution and Cost Trends of Antihypertensive and Hypolipidaemic Drug Treatment in France. Cardiovas Drugs Ther. 2003;17:175-189.
15. Petrova GI, Ivanova AD. Study of the cost of outpatient hypertension therapy in Bulgaria. Value Health. 2007;10(6):A417-A418.