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Cardiovascular Drugs Consumption – Comparison between two Croatian Regions, City of Zagreb and Lika-Senj County

Dražen Jurković[1], Danijela Štimac[2,3], Dubravko Bajramović[1], Hrvoje Tiljak[3] and Ranko Stevanović[4]

[1] Institute of Public Health of Lika-Senj County, Gospić, Croatia
[2] »Dr. Andrija Štampar« Institute of Public Health, Department of Health Promotion, Zagreb, Croatia
[3] University of Zagreb, School of Medicine, Department of Social Medicine and Organization of Health Care, Zagreb, Croatia
[4] Croatian National Institute of Public Health, Zagreb, Croatia

A B S T R A C T

The aim of this paper is to determine the differences in the outpatient consumption of cardiovascular drugs between Croatian regions: the City of Zagreb and Lika-Senj County. The data on the number of packages and the purchase price for each drug have been obtained from all pharmacies in Lika-Senj County and all pharmacies in the City of Zagreb. Defined daily doses/1000 inhabitants/day (DDD/1000/day) was calculated for every drug in accordance with its code name and Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) index of the World Health Organization (WHO) for 2007. For drug combinations without defined daily doses, equivalent doses (ED) were used. The quality of drug prescribing within the group of cardiovascular drugs was assessed using the Drug Utilization (DU90%) method and the adherence of the DU90% segment to the guidelines for prescribing individual drug groups. The statistical significance of differences in results between the City of Zagreb and Lika-Senj County was tested using the chi-square test at the level of statistical significance $p<0.05$. The comparison of the share of the five most often prescribed drug groups in Lika-Senj County has shown statistically significant differences when compared to the City of Zagreb ($\chi^2=28.93$, $df=4$, $p<0.001$). The total outpatient consumption of cardiovascular drugs in the City of Zagreb and Lika-Senj County differs significantly. The consumption, quality of prescribing drugs and cost/DDD in the City of Zagreb is higher than in Lika-Senj County; in the City of Zagreb, newer and more expensive drugs are prescribed to a higher extent.

Key words: *cardiovascular, drugs, utilisation, ATC/DDD, City of Zagreb, Lika-Senj County*

Introduction

In growing healthcare costs, costs for drugs record the fastest growth and are the subject of constant interest in every state. Drug consumption is increasing in the entire world every year, with cardiovascular drugs holding the largest share in the consumption in the majority of countries[1]. The increasing share of new drugs, which as a rule are more expensive, is affecting the cost growth[2]. Another important factor affecting the growth of costs for drugs is the prolonged life span and the increasingly dominant share of chronic diseases in pharmacotherapy and treatment costs. It is believed that the costs of treatment of chronic diseases amount to approximately 78% of all healthcare costs, and the majority are cardiovascular drugs[3,4]. Ideal, rational medicine consumption is, therefore, something to be desired as the best protection from uncontrolled increase in the costs of drugs. Rational pharmacotherapy implies the right drug in the right dose for the right patient over the necessary period of time and with the lowest possible cost for the individual and the community[2]. The basic question is how to balance the constant increase in the cost of drugs with financial capabilities of the society to achieve rational drug consumption. The answer to this question should be a part of the national medicine policy.

Zagreb, as Croatia's capital, has its specific features which separate it from the Croatian average according to political, cultural, socio-economic and health standards. As one of public health indicators, outpatient drug con-

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sumption in Zagreb has its specifics due to which it is higher than drug consumption in other Croatian counties and the Republic of Croatia[5].

According to the 2001 census, the population of Zagreb is 779.145. Some 50.000 inhabitants from the surrounding areas commute to Zagreb daily for work, education or other obligations[6]. 43% of Croatian health resources are located in Zagreb. These include five primary healthcare centres, 17 hospitals, one of which is the country's largest university hospital centre, 79 polyclinics and 100 pharmacies with 218 stores. Zagreb represents the professional and scientific medical centre of Croatia[7].

In addition to health and demographic indicators, as well as indicators of healthcare organization, drug consumption is largely influenced by economic indicators. According to the data provided by the Croatian Bureau of Statistics, GDP (Gross Domestic Product) per capita in Croatia is EUR 7.038, while GDP per capita in the City of Zagreb is almost twice as high and amounts to EUR 12.968[6]. Higher solvency and availability of drugs on the Zagreb market expectedly influence patients' demands and drug consumption in Zagreb.

The average age of the population in Zagreb is 39.7, where female inhabitants with the average age of 41.3 are somewhat older than their male counterparts, whose average age is 37.8. The majority of the population (55.6%) belongs to the working population at the age group 25–64, but the share of population older than 65 is growing annually. According to the 2001 census, this share was 14.9%[7].

The natural increase rate in the City of Zagreb is negative. The rate of live births per 1.000 people in 2005 was 9.7, the death rate per 1.000 people 10.8, and the natural increase was –1.1. The negative natural increase in Zagreb has lasted for a decade, contributing to the aging of the population in the City of Zagreb and influencing drug consumption in Zagreb.

Cardiovascular diseases cause approximately one half of the total mortality in Zagreb. Despite this fact, age-standardized mortality rate from cardiovascular diseases for all ages in Zagreb (422/100.000) is lower than the average rate for Croatia (499/100.000), but is still significantly higher than the EU average (270). Similar relations exist in comparing rates for ages up to 64. The death rate trends for the age up to 64 are decreasing for Zagreb, as well as for Croatia and the EU.

Citizens of Zagreb in all age groups are at lower risk of dying than the citizens of other regions in Croatia. Life expectancy at birth for the citizen of Zagreb is just over 77.35 years, whereas the same indicator for Croatia is 76.97. When compared to world indicators, life expectancy at birth for the citizens of Zagreb is lower than in the majority of western European countries, where it lies around 80 years, or than in Japan, where life expectancy at birth is 82 years[8].

With the total area of 5.350,50 km^2, Lika-Senj County is the largest county in the Republic of Croatia and encompasses 9.46% of the state territory. According to the 2001 census, there are 53.677 inhabitants in the territory of the Lika-Senj County[6]. Out of this number, 12.486 persons inhabit the islands and coastal areas, 30.993 persons inhabit the continental-mountainous areas and 10.198 persons inhabit areas which were occupied during the War[6]. According to the gender structure, 50.6% are female and 49.4% male[9]. The population density in Lika-Senj County is below the Croatian average, only 10/km^2. The average age in Lika-Senj County is 42.3, whereas age index is 1.45. The largest age group is over 65, particularly evident in the continental-mountainous areas[9].

Concerning economic development, Lika-Senj County falls significantly behind the rest of the Republic of Croatia. In addition to the natural, geographical landmarks, the lack of own accumulation, the shortage of highly educated professionals, bad traffic connections and bad inter-regional connections have influenced the economic lagging behind of Lika. However, due to the construction of the motorway and improved connection to urban centres, Lika-Senj County has recorded a GDP growth, which in 2007 was EUR 6.363 per capita – still lower than the Croatian average, and approximately twice as low as the GDP in the City of Zagreb.

With regard to healthcare, Lika-Senj County has the lowest number of medical teams on the primary healthcare level, records the lowest number of visits to primary healthcare doctors and has the highest number of gravitating patients on the secondary healthcare level (27%), 20% to the Clinical Hospital Centre Rijeka, and 7% to the Clinical Hospital Centre Zagreb[9].

Approximately 850 inhabitants die in the County every year, forming the general death rate of 16.26 deceased persons per 1.000 inhabitants, while the death rate at the level of Croatia is 11.32 per 1.000 inhabitants. The leading causes of death are diseases of the circulatory system, with the death rate of 838/100.000 inhabitants.

This paper will try to determine the differences in the outpatient consumption of cardiovascular drugs between one of the least inhabited and indigent Croatian regions, Lika-Senj County, and the largest and the wealthiest Croatian region, the City of Zagreb, and what causes them.

Materials and Methods

The data on the number of packages and the purchase price for each drug according to their generic names have been obtained from all pharmacies in Lika-Senj County (the total of 10) and from all pharmacies in the City of Zagreb (the total of 100). The data on the total number of pharmacies with all pharmacy stores was obtained from the Resource Register of the Croatian National Institute of Public Health. All drugs have been classified pursuant to the ATC (Anatomical Therapeutic Chemical) system of drugs classification.

The DDD/1000/day (Defined Daily Dose *per* 1000 inhabitants *per* day) was calculated for each drug in accor-

dance with its code name and ATC/DDD index of the World Health Organization (WHO) for 2007[10]. For drug combinations without defined daily doses, equivalent doses (ED) were used[11].

The quality of drug prescribing within the group of cardiovascular drugs was assessed using the Drug Utilization (DU90%) method and the adherence of the DU90% segment to the guidelines for prescribing individual drug groups. The quality of drug prescribing was further analyzed concerning morbidity and mortality indicators in Lika-Senj County and the City of Zagreb. The data on morbidity and mortality were obtained from health statistics data bases of the Institute of Public Health of Lika-Senj County and Dr. Andrija Štampar Institute of Public Health, Zagreb.

The statistical significance of differences in results between the City of Zagreb and Lika-Senj County was tested using the χ^2-test at the level of statistical significance $p<0.05$.

Results

The utilization of the five most often prescribed drug groups in Lika-Senj County has shown statistically significant differences when compared to the City of Zagreb ($\chi^2=28.93$, df=4, $p<0.001$).

The largest differences in the consumption of individual groups on the second ATC system level for group C, expressed with the standard deviation, are in the C09 group, which shows the largest consumption in both analyzed regions, and the smallest in the group with the lowest consumption, C02 (Table 1).

The differences in the quality of prescribing cardiovascular drugs between the City of Zagreb and Lika-Senj County are portrayed in the Table 2.

Within the DU90% segment in the City of Zagreb there are 22 drugs, two of which are C01 group drugs – isosorbide mononitrate and propafenone, one member of the C02 group – doxazosin and three C03 diuretics – furosemide, indapamide and chlortalidone. The C07 group within the DU90% segment is represented by two drugs – atenolol and bisoprolol, calcium channel blockers C08 have three representatives – amlodipine, lacidipine and verapamil, whereas the group with the largest consumption, C09, has eight drugs within the DU90% segment in the City of Zagreb, six of which are ACE inhibitors (three plain and three combined with a diuretic) – ramipril, lisinopril, cilazapril, lisinopril+hydrochlorothiazide (HCTZ), ramipril+hydrochlorothiazide and cilazapril +hydrochlorothiazide, as well as two angiotensin II antagonists – losartan and losartan+hydrochlorothiazide. Three lipid modifying agents are found in the DU90% segment of group C in the City of Zagreb – the second and third place in consumption respectively – atorvastatin and simvastatin, and 21st – fluvastatin.

In Lika-Senj County 20 drugs are found within the DU90% segment. Four are members of the C01 group – isosorbide mononitrate, metildigoxin, propafenone and amiodarone. The same as in the City of Zagreb, C02 group is represented by doxazosin, and the C03 group by furosemide, chlortalidone and the combination of hydrochlorothiazide+amiloride. Beta blocking agents within the DU90% segment in Lika-Senj County are represented by atenolol, whereas there are four from the C08 group – amlodipine, nifedipine, lacidipine and verapamil. Within the DU90% segment, the C09 group is the largest one with five drugs, ACE inhibitors – lisinopril, cilazapril, ramipril, enalapril and the combination lisinopril+ hydrochlorothiazide. In the DU90% segment of Lika-Senj County lipid modifying agents participate with two representatives – simvastatin and atorvastatin.

Discussion

The difference in the outpatient consumption of C group drugs, where the consumption in the City of Zagreb is three times higher than in Lika-Senj County, shows the statistical significance of the difference. The data on morbidity, i.e. the number of diagnoses set in the

TABLE 1
THE OUTPATIENT CONSUMPTION OF DRUG GROUPS WITHIN THE MAIN ATC GROUP C (DRUGS FOR CARDIOVASCULAR SYSTEM), ON THE SECOND ATC SYSTEM LEVEL, HAS BEEN PORTRAYED IN THE NUMBER DDD/1000/DAY IN THE CITY OF ZAGREB AND LIKA-SENJ COUNTY IN 2007

ATC code	City of Zagreb	Share (%)	Lika-Senj County	Share (%)	$\bar{X}$*	SD**
C01	27.44	6.68	20.33	13.74	23.89	2.25
C02	7.75	1.89	2.23	1.51	4.99	1.75
C03	38.48	9.37	30.38	20.53	34.43	2.56
C07	32.16	7.83	10.61	7.17	21.39	6.81
C08	86.95	21.16	36.14	24.42	61.55	16.07
C09	138.81	33.79	36.22	24.47	87.52	32.44
C10	79.26	19.29	12.38	8.18	45.82	21.15
Total	410.85	100.00	148.38	100.00	279.62	83.00

* arithmetic mean, ** standard deviation, ATC – Anatomical Therapeutic Chemical, C01 – cardiac therapy, C02 – antihypertensives, C03 – diuretics, C07 – beta-blockers, C08 – calcium channel blockers, C09 – agents acting on the rennin-angiotensin system, C10 – hypolipemics

TABLE 2
DRUGS WITHIN THE DU90% SEGMENT, THE SHARE OF THEIR CONSUMPTION WITHIN GROUP C (DRUGS FOR CARDIOVASCULAR SYSTEM), COST BY DEFINED DAILY DOSE (COST/DDD) EXPRESSED IN HRK (CROATIAN CURRENCY) WITHIN THE DU90% SEGMENT, OUTSIDE THE DU90% SEGMENT AND THE TOTAL COST/DDD IN THE CITY OF ZAGREB AND LIKA-SENJ COUNTY IN 2007

No	City of Zagreb		Lika-Senj County	
	Drug (generic name)	Number DDD/1000/day	Drug (generic name)	Number DDD/1000/day
1.	Amlodipine	57.68	Furosemide	24.42
2.	Atorvastatin	37.94	Amlodipine	20.94
3.	Simvastatin	35.14	Isosorbide mononitrate	10.93
4.	Ramipril	31.16	Lisinopril	10.27
5.	Lisinopril+HCTZ	26.98	Atenolol	7.94
6.	Lisinopril	24.40	Simvastatin	7.60
7.	Furosemide	23.39	Nifedipine	6.45
8.	Lacidipine	19.00	Lisinopril+HCTZ	6.11
9.	Atenolol	16.66	Cilazapril	5.86
10.	Isosorbide mononitrate	12.14	Lacidipine	4.89
11.	Bisoprolol	10.44	Metildigoxin	4.05
12.	Ramipril+HCTZ	10.38	Atorvastatin	3.86
13.	Losartan+HCTZ	8.72	Ramipril	3.78
14.	Verapamil	7.13	Verapamil	3.73
15.	Losartan	6.75	Enalapril	3.11
16.	Propafenone	6.74	Chlortalidone	2.51
17.	Doxazosin	6.61	Doxazosin	2.19
18.	Indapamide	6.63	HCTZ+amiloride	1.94
19.	Cilazapril	5.96	Propafenone	1.83
20.	Cilazapril+HCTZ	5.34	Amiodarone	1.77
21.	Fluvastatin	5.12		
22.	Chlortalidone	4.85		
Total (%)		89.85		90.43
Number of drugs within DU90% segment		22.00		20.00
Total number of drugs in group C		61.00		61.00
Total cost/DDD		1.85		2.07
Cost/DDD within the DU90% segment		1.77		1.67
Cost/DDD outside the DU90% segment		2.19		2.32

primary healthcare doctor offices in the City of Zagreb and Lika-Senj County show that the number of set diagnoses is higher in Zagreb, but by 32.23%, which by no means represents the argument for that high consumption of drugs. Furthermore, the fact that the number of set diagnoses for cardiovascular diseases is higher in Lika-Senj County than in the City of Zagreb is in discrepancy with indicators for the consumption of drugs for cardiovascular system. A partial explanation lies in the fact that the diagnoses are set in the primary healthcare doctor offices in the place of residence, whereas drugs may be picked up in any pharmacy, regardless of the place of residence. The fact that Zagreb is the Croatian health centre to which some 50.000 people migrate daily[12] and considering that approximately 50% of all hospital patients in Zagreb are gravitating patients[9], who, upon discharge from hospital and during follow-ups and check-ups pick up drugs in a nearest pharmacy, probably has a strong influence on the outpatient drug consumption in Zagreb. Furthermore, the fact that the research shows the turnover of drugs issued by pharmacies, not only of those issued on prescription, indicates the possibility of higher usage of private prescriptions and drug sales in the City of Zagreb, despite the fact that these drugs should not be issued without a prescription, which raises the question of better supervision of drug turnover in the pharmacies in the City of Zagreb.

The analysis of the DU90% segment for the group of cardiovascular drugs clearly shows differences between the City of Zagreb and Lika-Senj County. The larger number of drugs within the DU90% segment shows evidence of greater diversity and, to a larger extent, individualized approach to therapy choice in the City of Zagreb[13,14]. The differences in prescribing drugs from this

TABLE 3
GROUPS OF DIAGNOSIS ACCORDING TO INTERNATIONAL CLASSIFICATION OF DISEASES (ICD, 10TH REVISION), DETERMINED IN THE PRIMARY HEALTHCARE DOCTOR OFFICES IN LIKA-SENJ COUNTY AND THE CITY OF ZAGREB IN 2007, EXPRESSED AS RATE PER 100.000 INHABITANTS

ICD code	Diseases and conditions	City of Zagreb (rate/100.000)	Share (%)	Lika-Senj County (rate/100.000)	Share (%)
A00-B99	Infectious and parasitic diseases	682.80	3.65	185.37	1.46
C00-D48	Neoplasms	388.40	2.08	201.76	1.59
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	251.03	1.34	181.83	1.44
E00-E90	Endocrine, nutritional and metabolic diseases	935.27	5.00	742.59	5.86
F00-F99	Mental and behavioural disorders	868.37	4.65	762.34	6.02
G00-G99	Diseases of the nervous system	275.40	1.47	223.56	1.76
H00-H59	Diseases of the eye and adnexa	1.000.90	5.36	713.90	5.64
H60-H95	Diseases of the ear and mastoid process	505.35	2.70	366.26	2.89
I00-I99	Diseases of the circulatory system	2.151.59	11.51	2.228.70	17.60
J00-J99	Diseases of the respiratory system	3.884.31	20.78	2.690.72	21.24
K00-K93	Diseases of the digestive system	825.34	4.42	585.35	4.62
L00-L99	Diseases of the skin and subcutaneous tissue	892.07	4.77	663.41	5.24
M00-M99	Diseases of the musculoskeletal system and connective tissue	1.918.60	10.27	1.210.39	9.56
N00-N99	Diseases of the genitourinary system	1.325.79	7.09	621.68	4.91
O00-O99	Pregnancy, childbirth and the puerperium	105.56	0.56	71.54	0.56
P00-P96	Certain conditions originating in the perinatal period	1.40	0.01	1.12	0.01
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities	18.56	0.10	18.82	0.15
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	506.80	2.71	537.85	4.25
S00-T98	Injury, poisoning and certain other consequences of external causes	679.06	3.63	459.97	3.63
Z00-Z99	Factors influencing health status and contact with health services	1.472.32	7.88	199.34	1.57
Total		18.688.93	100.00	12.666.51	100.00

group have also been expressed. Despite the fact that both in the City of Zagreb and in Lika-Senj County the largest number of drugs in the DU90% segment comes from the C09 group, the difference in their number, as well as in the drugs most frequently prescribed from this group, is significant. Today, the group of ACE inhibitors is the first choice in the treatment of chronic heart failure and hypertension, primarily with diabetics[15–17]. Within the group of plain ACE inhibitors, the clinical effect of an individual drug is similar or identical. Due to the lowest price, the World Health Organization has placed enalapril on the List of Essential Medicines from this group[18]. Enalapril is in the DU90% segment in Lika-Senj County, but is not found among 90% of most frequently prescribed drugs in the City of Zagreb, despite the fact that some more expensive drugs from this group are. Furthermore, the consumption of plain ACE inhibitors is higher in Lika-Senj County when compared to Zagreb, whereas the consumption of ACE inhibitors and diuretics combinations, as well as the consumption of angiotensin II antagonists is higher in Zagreb. Angiotensin II antagonists have fewer side-effects and show better results than ACE inhibitors only in diabetic nephropathy[15,19–24]. These are very expensive drugs, which is why the Croatian Institute for Health Insurance has limited their application only to patients who are ACE inhibitors intolerant, upon recommendation from internal medicine specialist[13]. A higher ratio of prescribing more expensive and newer drugs from this group is evident in the City of Zagreb when compared to Lika-Senj County. To what extent is such prescribing caused by the real needs of patients, rather than the advertising influence of pharmaceutical industry is yet to be researched. Following ACE inhibitors within the DU90% segment, calcium channel blockers – C08, lipid modifying agents – C10 and diuretics – C03 are represented with three drugs respectively in the City of Zagreb. In Lika-Senj County, the group C08 and C01 – Cardiac therapy respectively

are represented with four drugs. Pursuant to European guidelines[16], calcium channel blockers are considered more efficient than diuretics and alpha blockers in the prevention of atherosclerosis development and are therefore recommended in the treatment of angina pectoris and carotid atherosclerosis. Their increased consumption in primary healthcare may be related to a significant decrease in the rate of hospitalization from ischaemic heart disease and cerebrovascular disease[13]. Due to their long-term activity and the possibility of adapting baroreceptors, amlodipine and lacidipine show significant advantage over short-activity nifedipine, which, due to reflex tachycardia, is no longer recommended, even in hypertensive crises[25–27].

Within the DU90% segment in Lika-Senj County four C01 group drugs are found, with only two in Zagreb. Metildigoxin, 11th in consumption in Lika-Senj County, is not found within 90% of the most frequently prescribed C group drugs in the City of Zagreb. Indications for the application of this drug include acute and chronic heart failure and several supraventricular arrhythmias[15,16,28]. However, digitalis glycosides are used only as the fourth choice in the treatment of chronic heart failure today, after ACE inhibitors, beta blockers and diuretics, due to possible side-effects, primarily heart rhythm irregularities. In the treatment of acute heart failure, they are used in the presence of peripheral hypoperfusion with congestion or pulmonary oedema refractory to diuretics and coronary dilatators in optimum doses[15,16,28]. High consumption of the mentioned drug today is, therefore, not considered justified. Amiodarone, antiarrhythmic agent also found in the DU90% segment in Lika-Senj County, in addition to strong antiarrhythmic action, for which it is used today instead of lidocain during reanimation, causes a number of side-effects in long-term therapy[15]. Propafenone also shows numerous side-effects, the most severe being aggravated heart failure and proarrhythmic effects[15]. Although antiarrhythmic drugs have their place in therapy, they need to be administered carefully. It must be emphasized that not all arrhythmias need to be treated. I group drugs, to which propafenone belongs, are not advised to be used in long-term treatments, particularly with patients suffering from coronary disease. Pursuant to the stated scientific knowledge, it seems that these drugs, propafenone in particular, should not be found within the DU90% segment. The group of diuretics in Zagreb and Lika-Senj County has three representatives within the DU90% segment. Although applied in hypertension therapy, diuretics only have symptomatic effect and do not decrease mortality. However, due to their low cost, they are still used as first choice drugs in treating hypertension, primarily with older patients and moderate, noncomplicated hypertensions[15,17,29–31]. Numerous cost-effectiveness studies give this group advantage in treating hypertension[32,33]. Lipid modifying agents are a group which has a significantly higher consumption in the City of Zagreb than in Lika-Senj County and three representatives within the DU90% segment, as opposed to two in Lika-Senj County. Statins are drugs with proven efficiency in lowering high serum lipid values, particularly cholesterol, and have a positive effect on the reduction of morbidity and mortality from cardiovascular complications[15,34–38]. Due to their efficiency, these drugs are on the List of Essential Medicines[18], however, with the same set of limitations to prescribing stated in the List of Medicines of the Croatian Institute for Health Insurance. Namely, due to their very high price, the prescribing of these drugs is indicated in the secondary prevention of patients who have survived myocardial infarction, cerebro-vascular insult or have ultrasound proof of carotid plaque or a coronary disease proved by coronarography, as well as patients suffering from diabetes, with total cholesterol value higher than 5 mmol/L. In primary prevention, the prescribing of these drugs is limited to patients whose total cholesterol values lie above 7 mmol/L in two laboratory tests three months apart after dieting for three months. The trend of increased consumption of lipid modifying agents is present in the entire world, but it should be kept in mind that the basic preventive and therapy measure of treatment for the most common hyperlipidaemia is diet[15]. In analysing the quality of prescribing cardiovascular drugs and adherence to professional guidelines, it can be concluded that the quality of prescribing C group drugs is higher in the City of Zagreb than in Lika-Senj County. The higher number of drugs within the DU90% segment, higher number of lipid modifying agents, ACE inhibitors and a lower number of antiarrhythmic agents prove higher quality. Morbidity indicators (Table 3) contribute to this statement, considering the fact that the diseases of the cardiovascular system are the only group with a higher prevalence rate in the primary healthcare doctor offices in Lika-Senj County than in the City of Zagreb. Furthermore, the fact that the rate of hospitalizations for cardiovascular complications in the City of Zagreb is decreasing is caused partly by better pharmacotherapy[13]. The fact, however, remains that outpatient consumption of C group in the City of Zagreb cannot be considered rational. In the City of Zagreb, the prescribing of expensive medicines is preferred, even when a cheaper variant exists (ramipril, lisinopril, cilazapril instead of enalapril, atorvastatin instead of simvastatin). The prescribing of drugs from this group in Lika-Senj County cannot be called rational either, seeing that more expensive drugs are prescribed to a larger extent despite the fact that these are drugs from the same group. This refers mostly to the ACE inhibitors group. The prescribing of cheaper drugs which is not based on professional guidelines (nifedipine, metildigoxin, amiodarone, propafenone) is not justified either. Even though the cost/DDD (cost *per* Defined Daily Dose) within the DU90% segment in Lika-Senj County is lower, the total cost/DDD is higher than in the City of Zagreb.

Regional differences in cardiovascular drug consumption, resulting either from lack of adherence to national and international guidelines for prescribing cardiovascular drugs[39] or (in certain degree) from differences in social characteristics of monitored districts[40] have also

been noted in other European countries like Portugal and Czech Republic highlighting the need of expert drug utilisation analysis.

Higher availability of the latest scientific knowledge, new drugs and undoubtedly stronger influence of pharmaceutical industry in the City of Zagreb influence both the higher quality of drug prescribing, to a higher extent in accordance with professional guidelines, and the preferred prescribing of expensive drugs, even in case where a cheaper, equally efficient substitute exists. Whether specialists, following whose recommendations a large part of cardiovascular drugs are prescribed, are to blame, or primary healthcare doctors, is less important than introducing efficient mechanisms which would disable such practice.

Conclusion

The total outpatient consumption of cardiovascular drugs in the City of Zagreb and Lika-Senj County differs significantly. The consumption in the City of Zagreb is higher than the consumption in Lika-Senj County. The quality of prescribing drugs in the City of Zagreb, assessed using the DU90% method and adherence to professional guidelines, is higher than in Lika-Senj County. The cost/DDD is higher in the City of Zagreb. In the City of Zagreb, newer and more expensive drugs are prescribed to a higher extent. New professional and scientific knowledge, as well as advertising influence of pharmaceutical industry, exert more influence on the prescribing of drugs in the City of Zagreb than in Lika-Senj County. Unique national guidelines for prescribing all medicine groups need to be adopted as soon as possible. In addition to respecting scientific knowledge, these will need to respect the specific economic situation Croatia is in. Regulatory measures should limit the prescribing of more expensive drugs if a cheaper substitute with the same effect exists, and stimulate the prescribing of generic drugs. Regulatory measures and efficient mechanisms for their regulation must decrease the influence of pharmaceutical industry advertising on doctors. Appropriate health and social policies and public health programs and actions should promote health and prevent diseases which result from unhealthy life-styles (cardiovascular diseases) which make for the largest part of morbidity and on which the largest number of drugs is spent.

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D. Štimac

»Dr. Andrija Štampar« Institute of Public Health, Department of Health Promotion, Mirogojska cesta 16, 10000 Zagreb, Croatia
e-mail: danijela.stimac@stampar.hr

POTROŠNJA KARDIOVASKULARNIH LIJEKOVA – USPOREDBA DVIJE HRVATSKE REGIJE, GRADA ZAGREBA I LIČKO-SENJSKE ŽUPANIJE

S A Ž E T A K

Cilj ovog rada je utvrđivanje razlika u izvanbolničkoj potrošnji kardiovaskularnih lijekova između hrvatskih regija: Grada Zagreba i Ličko-senjske županije. Podaci o broju pakiranja i nabavnoj cijeni za svaki pojedini lijek dobiveni su iz svih ljekarni u Ličko-senjskoj županiji te svih ljekarni u Gradu Zagrebu. Broj DDD/1000/dan izračunat je za svaki pojedinačni lijek prema zaštićenom imenu te prema ATK/DDD indeksu Svjetske zdravstvene organizacije za 2007. godinu. Za kombinacije lijekova koje nemaju definiranih dnevnih doza korištene su ekvivalentne doze (ED). Kvaliteta propisivanja lijekova unutar skupine kardiovaskularnih lijekova ocijenjena je »Drug Utilization« (DU90%) metodom, te adherencijom DU90% segmenta sa smjernicama za propisivanje pojedinih skupina lijekova. Testiratna je statistička značajnost razlika u rezultatima između Grada Zagreba i Ličko-senjske županije hi-kvadrat testom na razini statističke značajnosti $p<0,05$. Usporedbom udjela pet najpropisivanijih skupina lijekova u Ličko-senjskoj županiji utvrđene su statistički značajne razlike u odnosu na Grad Zagreb ($\chi^2=28,93$, df=4, $p<0,001$). Ukupna izvanbolnička potrošnja kardiovaskularnih lijekova u Gradu Zagrebu i Ličko-senjskoj županiji značajno se razlikuju. Potrošnja lijekova, kvaliteta propisivanja lijekova i trošak/DDD veći je u Gradu Zagrebu nego u Ličko-Senjskoj županiji; u Gradu Zagrebu se u većoj mjeri propisuju noviji i skuplji lijekovi.