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Outpatient Utilization Patterns of the Six Main ATC Drug Groups in Republic of Croatia, City of Zagreb, and Croatia Counties in 2004

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ABSTRACT

The aim of the study was to determine drug utilization according to Croatian counties, and to identify the causes of the possible between-county utilization variation. Zagreb Institute of Public Health in collaboration with the Croatian Drug Agency collected and analyzed data on outpatient utilization of the six main Anatomic-Therapeutic-Chemical (ATC) drug groups. Data on the number and size of packages, and on wholesale price were obtained from all pharmacies in Croatia. Based on these data, the number of defined daily doses (DDD) and DDD per *1000 inhabitants* per *day (DDD/1000/day) in 2004 were calculated for all drugs. County differences in the drugs utilization were calculated by use of relative standard deviation. This method revealed the outpatient drug utilization to vary among particular Croatian counties. Study results indicated the need of national guidelines for appropriate drug use to develop, along with education of the physicians and general population on their implementation.*

Key words: *outpatient, utilization, drugs, counties, Croatia*

Introduction

The utilization and appropriate use of drugs are the subject of numerous economic discussions and topic of professional and scientific papers worldwide. In 2006, the utilization of drugs in the world has increased by 6%–7% and is anticipated to rise by another 5%–6% in 2007[1]. The growing drug cost is influenced by an ever greater proportion of new drugs, which as a rule are more expensive[2]. In contrast to the world patterns, in Croatia the mean drug cost in 2005 was lower 8% as compared with 2004. However, in spite of the considerable reduction of drug prices in Croatia, which has been effective as of August 2004, financial indicators released by the Croatian Institute of Health Insurance (CIHI) show the 2005 drug utilization to exceed the 2004 one by 3%, amounting to 3.738.927.612 HRK[3]. Besides drug prices, the rise in drug costs is influenced by the extended life expectancy, entailing an ever greater share of chronic diseases in the cost of pharmacotherapy and treatment in general. The cost of treatment of chronic diseases is considered to account for 78% of overall health care costs[4,5]. In the conditions of increasing demands, appropriate use of drugs should be encouraged as the best protection from uncontrolled drug expenditure increase. Rational pharmacotherapy implies optimal drug dosage to achieve the maximum possible cure rate[6,7]. Standardized methods of drug utilization monitoring by use of the Anatomic-Therapeutic-Chemical (ATC) classification and defined daily dose (DDD), i.e. ATC/DDD methodology released by the World Health Organization (WHO) should be established as a basis of an economic approach to drug utilization[8]. Standard methodology is a precondition for the intervention measures to employ and properly evaluate[9,10]. High quality prescribing policy and practice, based on the physician's knowledge and experience, existence of quality prescribing guidelines, and implementation of the guidelines in daily practice, at primary health care level in particular, as it accounts for 80%–90% of drug utilization in Croatia as well as in the world, make

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another important factor in rational drug prescribing[7,11–13]. Determination of drug utilization by use of ATC/DDD methodology revealed great differences between different countries and regions[14]. This variation results from different morbidity indicators, differences in prescribing guidelines, and differences in the physicians' compliance with the guidelines[14].

The aim of the present study was to determine drug utilization according to counties in the Republic of Croatia, and to identify the causes of the potential between-county differences.

Methods

Based on the By-Law on the Type of Data and Mode of Reporting on Medicine Marketing[15], Zagreb Institute of Public Health in collaboration with National Drug Agency collected and analyzed data on outpatient utilization of drugs from the six main ATC groups, i.e. A – gastrointestinal and metabolic agents; C – cardiovascular drugs; J – drugs for treatment of systemic infections; M – musculoskeletal agents; N – central nervous system agents; and R – respiratory system agents.

Data on the number and size of packages, and on wholesale prices were obtained from all pharmacies in Croatia. Information on the total number of pharmacies and their units was obtained from Personnel Registry kept at Croatian Institute of Public Health. Drugs were grouped according to the ATC classification system. Based on these data, the number of defined daily doses (DDD) and DDD *per* 1000 inhabitants *per* day (DDD/1000/day) in 2004 were calculated for all drugs according to the WHO ATC/DDD index[16]. On calculating the number of DDD/1000/day for the Republic of Croatia, particular counties and the City of Zagreb, data from the 2001 census, kept at the National Bureau of Statistics, were used[17]. Equivalent dose (ED) was used in case of drug combinations where DDD was not available[18]. Between-county differences in drug utilization for the six ATC groups included in the study were calculated by use of relative standard deviation (RSD) defined as:

standard deviation of the main anatomical group of drugs at primary level of ATC system, expressed as percentage (%) of total drug utilization of

RSD= all six groups in a particular county × 100

mean utilization of the respective group of drugs in Croatia, expressed as percentage (%) of overall utilization in Croatia

A higher RSD value indicates greater between–county differences in the utilization of particular drug groups. Similar measures have also been employed in other international studies assessing variation in drug utilization between particular countries[13,19].

Morbidity indicators of diseases and states, established at primary health care in Croatia as a whole, in Croatian counties and in the City of Zagreb in 2004, were provided by the Croatian Institute of Public Health to assess the causes of the possible between-county differences in drug utilization. Based on these data, morbidity rate *per* 1000 inhabitants at primary health care level was calculated for the leading groups of states and diseases. Diseases were grouped according to the International Classification of Diseases 10th Revision (ICD X)[20].

Results

Outpatient utilization of the six main groups of prescription drugs at primary level of the ATC system in Croatia in 2004 is presented in Table 1.

Cardiovascular agents accounted for almost a half of the outpatient prescription drug utilization. In group C, a major proportion of utilization (30%) referred to agents acting on the renin-angiotensin system (C09), predominated by pure ACE inhibitors and followed by agents acting on the central nervous system. Psycholeptics (N05) accounted for more than a half of the latter group utilization (66%), with 82% referring to benzodiazepines. These were followed by gastrointestinal system agents, where antidiabetics predominated with 45% of utilization. The musculoskeletal system agents ranked fourth, with 86% of their utilization referring to anti-inflammatory agents and antitheumatics (M01), followed by respiratory system agents with the highest proportion (47%) of drugs for obstructive airway diseases (R03). The agents used in the treatment of systemic infections showed lowest utilization, with antibiotics (J01) accounting for 97% of their utilization. Outpatient utilization of the six main ATC

TABLE 1
OUTPATIENT UTILIZATION OF SIX MAIN ATC PRESCRIPTION DRUG GROUPS AT PRIMARY LEVEL OF ATC SYSTEM IN CROATIA IN 2004, EXPRESSED SA DDD/1000/DAY

ATC code	Drug group	No.of DDD/1000/day	Percentage (%)
A	Gastrointestinal and metabolic agents	80.00	13.57
C	Cardiovascular agents	283.97	48.16
J	Agents for treatment of systemic infections	24.81	4.21
M	Musculoskeletal system agents	51.16	8.68
N	Nervous system agents	108.21	18.35
R	Respiratory system agents	41.46	7.03
Total		591.88	100.00

drug groups according to counties including City of Zagreb is shown in Table 2.

The City of Zagreb led in drug utilization according to counties, followed by Šibenik-Knin County and Dubrovnik-Neretva County, whereas the lowest drug utilization was recorded in Zagreb County and Lika-Senj County. The pattern of particular drug group utilization according to counties is more conveniently presented by the share of particular drug groups expressed as DDD/1000/day in total outpatient drug utilization in a particular county (Table 3).

Variation in particular drug group utilization is presented by RSD (Figure 1).

As illustrated in Figure 1, greatest deviation from the national average, i.e. highest variation in drug utilization among particular counties was recorded in group A. Tables 2 and 3 show that the highest utilization of gastrointestinal and metabolic agents was recorded in Šibenik-Knin County, where the utilization of this drug group exceeded the respective national average by 43% (Table 1). It was mainly due to the high utilization of antidiabetic drugs (A10) amounting to 57.37 DDD/1000/day, exceeding the respective drug utilization in any other county and national mean rate of 36.01 DDD/1000/day by 38%. The second drug group according to RSD in Croatian counties was group J (Figure 1), with Zadar County showing highest utilization of this drug group, where it was by 37% greater than the national mean rate. Besides Zadar County, a high share of group J in total drug utilization was also recorded in Šibenik-Knin, Istrian, Split-Dalmatia and Dubrovnik-Neretva Counties. The high utilization of group J drugs in these counties was mainly due to the high utilization of amoxicillin+clavulanate. In the mentioned counties as well as in the City of Zagreb, Primorje-Gorski Kotar and Lika-Senj Counties, amoxicillin+clavulanate was among the first 20 drugs according to utilization, ranking tenth in Zadar County with 11.48 DDD/1000/day through twentieth with 9.63 DDD/1000/day in the City of Zagreb and with 3.76 DDD/1000/day in Lika-Senj County. According to RSD, group N followed with highest utilization in Dubrovnik-Neretva County (Table 2). The highest share of group N drugs in total drug utilization (Table 3) and second place according to group N utilization expressed in DDD/1000/day (Table 2) were recorded in Osijek-Baranya County. In Dubrovnik-Neretva County, diazepam showed highest utilization of all prescription drugs, with 38.78 DDD/1000/day, which was almost twofold diazepam utilization at the national level. Another three benzodiazepines were among the 20 leading prescription drugs in Dubrovnik-Neretva County, i.e. lorazepam with 16.21 DDD/1000/day, alprazolam with 11.02 DDD/1000/day, and oxazepam with 9.40 DDD/1000/day. In Osijek-Baranya Co-

TABLE 2
OUTPATIENT UTILIZATION OF PRESCRIPTION DRUGS EXPRESSED AS DDD/1000/DAY FOR SIX MAIN DRUG GROUPS AT PRIMARY LEVEL OF ATC SYSTEM IN CROATIAN COUNTRIES AND CITY OF ZAGREB IN 2004

County	ATC code						Total
	A	C	J	M	N	R	
City of Zagreb	115.36	390.81	31.04	65.07	126.43	57.57	786.29
Zagreb County	39.94	147.37	13.54	32.06	56.45	26.00	315.29
Dubrovnik-Neretva County	111.85	278.17	31.55	50.19	148.44	48.68	668.87
Split-Dalmatia County	82.93	228.70	25.76	43.72	101.69	36.94	519.74
Šibenik-Knin County	141.32	294.37	34.07	45.33	124.14	38.19	677.42
Zadar County	110.26	281.26	38.09	56.58	137.50	44.35	668.04
Osijek-Baranya County	64.83	276.86	27.88	60.71	140.97	36.85	608.11
Vukovar-Srijem County	73.51	230.85	19.91	43.54	104.33	30.01	502.15
Virovitica-Podravina County	61.65	255.35	20.35	47.52	108.45	39.34	532.65
Požega-Slavonia County	79.45	259.77	29.26	61.32	115.89	40.62	586.31
Brod-Posavina County	44.01	203.38	15.64	35.66	74.08	22.54	395.31
Međimurje County	60.26	286.01	23.79	44.06	108.47	42.26	564.84
Varaždin County	69.25	358.39	23.29	60.07	98.78	46.72	656.51
Bjelovar-Bilogora County	66.03	285.31	22.33	57.27	97.37	48.72	577.03
Sisak-Moslavina County	76.73	302.65	22.15	44.11	102.80	40.60	589.02
Karlovac County	91.78	320.66	23.01	52.96	86.13	45.26	619.80
Koprivnica-Križevci County	69.47	287.06	14.88	55.22	118.59	30.24	575.45
Krapina-Zagorje County	76.57	279.94	20.18	54.86	108.42	41.14	581.10
Primorje-Gorski Kotar County	64.76	273.69	22.45	49.63	106.00	42.98	559.51
Istrian County	83.34	279.18	31.20	44.40	96.80	45.91	580.82
Lika-Senj County	39.49	147.28	12.25	28.70	45.14	20.53	293.38

unty, as many as five group N drugs were among the 20 leading prescription drugs in 2004. These included four benzodiazepines: diazepam with 21.11 DDD/1000/day, alprazolam with 20.65 DDD/1000/day, oxazepam with 19.86 DDD/1000/day, and lorazepam with 10.46 DDD/1000/day. In contrast to all other counties, an analgesic, metamizole, was among the 20 leading prescription drugs with 7.19 DDD/1000/day in Osijek-Baranya County.

Group R showed a somewhat lower RSD than group N, with highest utilization in the City of Zagreb, where the highest prescribing rate was recorded for loratadine with 11.02 DDD/1000/day *vs.* 7.99 DDD/1000/day at the national level. In the City of Zagreb, the utilization of fexofenadine was threefold that recorded in Croatia at primary health care level. Besides the group of antihistaminics (R06), the City of Zagreb also had higher utilization of other drug groups for respiratory system at the secondary level of ATC system than the respective utilization at the national level.

According to RSD (Figure 1), group R was followed by group M. The City of Zagreb showed highest utilization of group M drugs as expressed in DDD/1000/day (Table 2); however, the greatest share of this drug group in total drug utilization (Table 3) was recorded in Požega-Slavonia County, primarily due to the extremely high utilization of diclofenac with 35.38 DDD/1000/day. The utilization of diclofenac was 28.84 DDD/1000/day in the City of Zagreb and 23.57 DDD/1000/day at the national level. Diclofenac was by far the most frequently prescribed group M drug in all Croatian counties. The consumption of aledronate-sodium was greatest in the City of Zagreb, where it ranked second according to group M drug utilization. The utilization of aledronate-sodium was 9.16 DDD/1000/day and 5.29 DDD/1000/day in the City of Zagreb and Croatia, respectively.

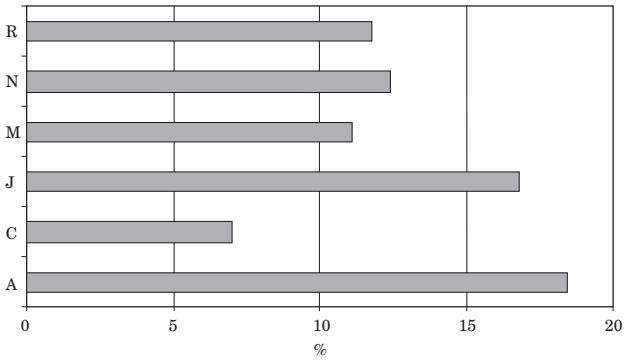

Fig 1. Relative standard deviation (RSD) for the main anatomical groups of ATC system (A, C, J, M, N and R) in Croatian counties and City of Zagreb in 2004.

TABLE 3
PERCENTAGE (%) OF SIX MAIN DRUG GROUPS AT PRIMARY LEVEL OF ATC SYSTEM IN TOTAL OUTPATIENT UTILIZATION OF THE SIX MAIN PRESCRIPTION DRUG GROUPS EXPRESSED AS DDD/1000/DAY IN CROATIAN COUNTIES AND THE CITY OF ZAGREB IN 2004

County	ATC code						Total
	A	C	J	M	N	R	
City of Zagreb	14.67	49.70	3.95	8.28	16.08	7.32	100.00
Zagreb County	12.66	46.74	4.29	10.17	17.90	8.22	100.00
Dubrovnik-Neretva County	16.72	41.59	4.72	7.50	22.19	7.28	100.00
Split-Dalmatia County	15.95	44.00	4.96	8.41	19.57	7.11	100.00
Šibenik-Knin County	20.86	43.45	5.03	6.69	18.33	5.64	100.00
Zadar County	16.62	42.39	5.74	8.53	20.04	6.68	100.00
Osijek-Baranya County	10.66	45.53	4.58	9.98	23.18	6.06	100.00
Vukovar-Srijem County	14.64	45.97	3.96	8.67	20.78	5.98	100.00
Virovitica-Podravina County	11.57	47.94	3.82	8.92	20.36	7.39	100.00
Požega-Slavonia County	13.55	44.31	4.99	10.46	19.77	6.93	100.00
Brod-Posavina County	11.13	51.45	3.96	9.02	18.74	5.70	100.00
Međimurje County	10.67	50.64	4.21	7.80	19.20	7.48	100.00
Varaždin County	10.55	54.59	3.55	9.15	15.05	7.12	100.00
Bjelovar-Bilogora County	11.44	49.44	3.87	9.92	16.87	8.44	100.00
Sisak-Moslavina County	13.03	51.38	3.76	7.49	17.45	6.89	100.00
Karlovac County	14.81	51.74	3.71	8.54	13.90	7.30	100.00
Koprivnica-Križevci County	12.07	49.88	2.59	9.60	20.61	5.26	100.00
Krapina-Zagorje County	13.18	48.17	3.47	9.44	18.66	7.08	100.00
Primorje-Gorski Kotar county	11.57	48.92	4.01	8.87	18.95	7.68	100.00
Istrian County	14.35	48.07	5.37	7.64	16.67	7.90	100.00
Lika-Senj County	13.46	50.20	4.18	9.78	15.39	7.00	100.00

Group C with highest utilization in all Croatian counties showed least between-county variation (RSD, Figure 1) in outpatient utilization. Although an increased consumption of this drug group was observed in the City of Zagreb (Table 2), Varaždin County accounted for the greatest share in the utilization of this drug group (Table 3). In the City of Zagreb, the consumption of group C10 drugs (hypolipidemic agents) was almost threefold that in Varaždin County (60.99 DDD/1000/day *versus* 23.85 DDD/1000/day). On the other hand, Varaždin County had a significantly greater utilization of group C09 (142.93 DDD/1000/day), predominated by lisinopril with 66.46 DDD/1000/day. The correlation of outpatient drug utilization in the City of Zagreb and Croatian counties with the morbidity at primary health care level can be perceived by comparing data on drug utilization with Table 4.

Discussion

The absolute and relative indicators of drug utilization clearly point to variation in the utilization of particular drug groups among Croatian counties. According to total drug utilization in the counties and City of Zagreb, the latter had highest outpatient drug utilization in 2004. Lowest utilization was recorded in Lika-Senj County. These data reflect the fact that 43% of the Croatian health care resources are located in Zagreb, and some 50 000 people from all parts of Croatia come daily to Zagreb for various reasons. A great deal of people residing all over Zagreb County and elsewhere come to Zagreb daily for work and shopping, probably also taking their prescription drugs in Zagreb pharmacies. The influence of pharmaceutical industry is rather strong in Zagreb, while the purchasing power of Zagreb citizens exceeds that in the rest of Croatia[21,22]. In contrast to Zagreb, Lika-Senj County as the least populated Croatian county showed lowest drug utilization, which could be explained by the lowest number of medical teams at primary health care level, lowest rate of visits to primary health care physicians, and highest catchment population referred to secondary health care level (27% in total, i.e. 20% and 7% referred to Rijeka University Hospital Center and Zagreb University Hospital Center, respectively)[23]. The pharmacy density is highest in the City of Zagreb, and consumption data are geograficalily caracterized by phar-

TABLE 4
DISEASES AND STATES* RECORDED IN PRIMARY HEALTH CARE IN THE REPUBLIC OF CROATIA, CITY OF ZAGREB AND CROATIAN COUNTIES IN 2004, EXPRESSED AS RATE *PER* 1000 INHABITANTS

County	A00-A99	E00-E90	F00-F99	G00-G99	I00-I99	J00-J99	K00-K93	L00-L99	M00-M99	N00-N99
Republic of Croatia	87.18	71.91	81.47	26.40	205.03	553.62	84.75	109.89	182.09	121.47
Zagreb	93.35	53.71	72.83	24.76	171.29	516.37	74.28	101.07	151.53	101.99
Krapina-Zagorje	81.37	58.78	82.85	27.22	200.17	517.94	84.91	114.82	193.26	111.55
Sisak-Moslavina	78.05	72.84	83.60	24.00	225.88	487.50	80.72	94.95	170.80	104.82
Karlovac	95.67	64.63	86.35	23.13	203.25	483.02	98.44	111.98	209.07	114.46
Varaždin	83.27	70.97	81.76	23.71	228.51	549.00	70.28	99.39	185.66	94.18
Koprivnica-Križevci	84.23	66.04	102.74	28.61	229.67	466.87	86.49	108.30	227.35	110.88
Bjelovar-Bilogora	95.44	81.61	112.82	30.15	284.07	536.41	90.82	123.91	231.91	144.74
Primorje-Gorski Kotar	125.09	77.60	88.61	31.74	215.27	587.93	102.26	119.32	207.31	127.80
Lika-Senj	43.89	51.18	56.97	18.29	174.32	358.68	64.11	71.54	116.79	60.40
Virovitica-Podravina	88.62	86.52	101.69	33.43	225.57	509.26	94.83	133.99	213.31	124.49
Požega-Slavonia	71.08	61.61	75.93	23.26	163.16	403.40	67.87	74.32	167.98	92.72
Brod-Posavina	64.38	73.69	83.86	25.98	214.17	431.79	74.28	97.02	167.41	125.15
Zadar	75.68	91.85	88.01	27.23	250.59	553.96	99.32	115.62	210.92	131.83
Osijek-Baranya	87.18	71.09	91.74	22.70	179.92	560.81	86.29	112.13	172.46	128.94
Šibenik-Knin	50.00	94.24	86.51	32.86	289.25	543.56	93.39	120.04	188.82	120.60
Vukovar-Srijem	61.31	53.48	76.10	17.08	157.28	406.94	59.03	78.36	128.30	83.24
Split-Dalmatia	78.46	76.94	73.99	27.60	202.80	724.18	93.13	131.19	180.17	131.89
Istria	98.47	76.60	69.47	29.29	191.09	621.84	87.35	104.64	203.54	121.51
Dubrovnik-Neretva	37.75	81.74	94.14	38.07	257.48	501.04	102.99	117.21	171.20	147.33
Međimurje	74.44	64.49	72.59	22.12	163.00	505.78	74.03	83.39	156.90	91.85
City of Zagreb	107.82	73.47	72.92	26.02	194.55	603.78	81.98	115.20	181.42	143.19

*A00-B99 Infectious and parasitic diseases; E00-E90 Endocrine diseases, alimentary disorders and metabolic disorders; F00-F99 Mental disorders and behavioral disturbances; G00-G99 Nervous system diseases; I00-I99 Circulation diseases; J00-J99 Respiratory diseases; K00-K93 Gastrointestinal diseases; L00-L99 Cutaneous and subcutaneous tissue diseases; M00-M99 Musculoskeletal and connective tissue diseases; N00-N99 Genitourinary system diseases

macy location, rather than patients home address, which also explanes the highest consumption of drugs in the City of Zagreb.

The real pattern of outpatient drug utilization according to counties is better indicated by relative values, i.e. shares of particular drug group consumption in overall drug utilization in particular counties and their variation. According to these parameters, the share of group A drug utilization showed greatest between-county differences, being highest in Šibenik-Knin County, primarily due to the very high consumption of antidiabetic agents. Comparison of these figures with morbidity data indicates the prevalence of endocrine diseases, alimentary disorders and metabolic diseases established at primary health care to be significantly higher in this county relative to the rest of Croatia, exceeding the national mean rate by 24%. Analysis of data on diabetes mellitus alone yielded a significant difference between Šibenik-Knin County and other Croatian regions. In 2004, the prevalence of diabetes mellitus in Šibenik-Knin County was 47/1000 *vs*. 29/1000 in Croatia. At the same time, the prevalence of diabetes mellitus was lowest in Zagreb County (19/1000). Accordingly, the high outpatient utilization of antidiabetics in Šibenik-Knin County was consequential to the high prevalence of the disorder in the area. As this county was exposed to direct war actions over a long period of time, the impact of prolonged war stress exposure on the high rate of diabetes in the area should be considered. However, some other Croatian counties that had also been exposed to direct war actions for a long period of time (Vukovar-Srijem and Osijek-Baranya Counties) showed no major deviation from the national mean rate. Considering the multifactorial etiology of diabetes mellitus[24–27], additional in-depth studies in the field should be conducted and appropriate public health actions launched for primary and secondary prevention of the disease in Šibenik-Knin County[28].

The share of antibiotic consumption in total drug utilization showed great between-county variation; however, the utilization of amoxicillin+clavulanate was by far highest in all counties as well as at the national level. Comparison with morbidity indicators according to counties failed to reveal any direct association with the high consumption of antibiotics in some counties, first of all Zadar County. Acute respiratory infections are the most common reason for uneconomical prescribing of antibiotics[29,30]. Although outpatient utilization of antibiotics requires additional studies and analysis of prescription drug utilization in correlation with medical diagnosis, the fact that amoxicillin+clavulanate was the most frequently prescribed antibiotic can be considered neither rational nor consistent with international research data that unanimously prefer narrow-spectrum antibiotics[31–33]. High utilization of broad-spectrum antibiotics is characteristic of south and east European countries, whereas north and west European countries give preference to narrow-spectrum antibiotics[34].

Osijek-Baranya and Dubrovnik-Neretva Counties showed highest outpatient utilization of psychopharmaceuticals, which could in part be explained by the high prevalence of mental disorders (F00-F99) in these counties, and the highest prevalence of nervous system diseases (G00-G99), including sleep disorders (G47). Unfortunately, data on isolated G47 diagnosis morbidity were not available, thus the association of the high consumption of psychopharmaceuticals, benzodiazepine in particular, in this county with the morbidity justifying such a high prescribing pattern could only be postulated. The high utilization of benzodiazepines at the national level poses a question of their rational use because these drugs are used at a considerably wider scale than the disorders they are indicated for[35–37]. The high outpatient utilization of metamizole in Osijek-Baranya County is not substantiated either by morbidity indicators or by professional and scientific data[38–40].

The highest consumption of group M drugs is in Požega-Slavonia County. The very high utilization of diclofenac as the leading non-steroidal antirheumatic on prescription in all Croatian counties is not based on evidence[41–43]. The unjustifiably high outpatient utilization of this agent should at least in part be ascribed to the impact of domestic pharmaceutical industry.

The share of cardiovascular drug utilization showed least between-county variation, being the group of drugs with highest utilization in all Croatian counties. However, there was some within-group variation. The City of Zagreb differed from all other regions according to distribution of particular group C subgroups, yielding a high consumption of hypolipidemic agents. In Zagreb, the consumption of hypolipidemic agents was twofold (Istrian, Primorje-Gorski Kotar and Osijek-Baranya Counties) to threefold (Varaždin, Brod-Posavina and Vukovar-Srijem Counties) that in the rest of Croatia. The proportion of cardiovascular drugs in total drug utilization was greatest in Varaždin County, which was in correlation with the respective morbidity indicators. The cardiovascular morbidity rate in Zagreb was below the national mean rate. The cardiovascular mortality rate in has been found to decline since 2001 in the City of Zagreb while showing a mild rise in the rest of Croatia[44]. The increased utilization of hypolipidemic agents recorded during the same period of time in the City of Zagreb[45] may have contributed to such a health pattern, as these agents have been demonstrated to be efficient in the prevention of cardiovascular complications[46–48]. ACE inhibitors were the most widely prescribed drugs in all Croatian regions, and prescribing cardiovascular agents does not appear to be rational in terms of their cost-effectiveness[49,50].

The pattern of drug utilization according to counties would be more comprehensive had all the 14 ATC drug groups been included in the study. However, as DDD has not been established for the majority of drugs from the remaining drug groups, interpretation of their utilization by use of ATC/DDD methodology would not be reliable. As the six drug groups included in the study account for the major part of outpatient drug utilization, we believe that this survey provides an insight into the main characteristics of drug utilization in all Croatian regions.

Methodologically, the interpretation of results was also limited by the fact that data on drug utilization and morbidity were collected from various sources, thus only roughly reflecting the association between drug utilization and morbidity, i.e. between justifiability and rationality of drug utilization. The quality of drug prescribing practice in Croatian counties should be evaluated on prescription samples in correlation with diagnosis associated with each individual prescription, especially for the groups of drugs outstanding for a questionable prescribing pattern such as antibiotics, benzodiazepines, ACE inhibitors and metamizole in Osijek-Baranya County. Appropriate public health monitoring of all relevant parameters would urgently require complete computerization of the health care system, in order to minimize data scattering and to reduce the possibility of erroneous interpretation of public health parameters. National guidelines on drug prescribing at the primary health care level should be urgently adopted to make drug utilization in Croatia more rational.

Conclusion

Outpatient drug utilization shows varying patterns in different Croatian counties. The high prevalence of diabetes mellitus has entailed high utilization of antidiabetic agents in Šibenik-Knin County. The high prevalence of diabetes mellitus in this county poses the need of additional studies as well as of public health actions and measures of both primary and secondary prevention. There is no correlation of the high utilization of broad-spectrum antibiotics and morbidity. The high share of benzodiazepines at the national level points to the need of proper education of both physicians and population at large in the rational use of these agents. The utilization of metamizole is unjustifiably high in Osijek-Baranya County, and so is the utilization of diclofenac, in Požega-Slavonia and Osijek-Baranya Counties in particular. The high utilization of hypolipidemic agents in Zagreb and of ACE inhibitors at the national level requires additional cost-effectiveness analysis.

In addition to morbidity, the pattern of drug prescribing appears to also be considerably influenced by the prescribers' experience and habits (antibiotics, benzodiazepines), pharmaceutical industry (diclofenac), availability of latest concepts and drugs, and purchasing power of the population (hypolipidemics). Accordingly, there is an obvious need of national guidelines on rational drug utilization, along with appropriate education of the physicians, pharmacists and population at large on their implementation.

REFERENCES

1. IMS Health Forecasts 6 to 7 Percent Growth for Global Pharmaceutical Market in 2006. Available from: URL: http://www.imshealth.com/ims/portal/front/article — 2. VUKUŠIĆ I, ČULIG J, Acta Med Croatica, 59 (2005) 277. — 3. LUKOVNJAK I, ČULIG J, ŠTIMAC D, Pharmaca, 44 (2006) 152. — 4. SMITH G, Pharm J, 271 (2003) 380. — 5. MORGAN SG, Med Care, 43 (2005) 996. — 6. VUKUŠIĆ I, Farmaceutski glasnik, 60 (2004) 98. — 7. ŠTIMAC D, ČULIG J, TOMIĆ S, ŠOSTAR Z, BUCALIĆ M, Pharmaca, 44 (2006) 96. — 8. WHO Collaborating Centre for Drug Statistics Methodology. About ATC/DDD system. Available from: URL: http://www.whocc.no/atcddd/ — 9. WERTHEIMER AI, Hosp Pharm, 21 (1986) 239. — 10. NATSCH S, HEKSTER YA, R DE JONG, HEERDINK ER, HERINGS RM, VAN DER MEER JW, Eur J Clin Microbiol Infect Dis, 17 (1998) 20. — 11. FINK KS, BYRNS PJ, Ann Fam Med, 2 (2004) 488. — 12. TAYLOR LK, KAWASUMI Y, BARTLETT G, TAMBLYN R, Health Q, 8 (2005) 81. — 13. BANTHIN JS, MILLER GE, Med Care, 44 (2006) 127. — 14. STOLK P, VAN WIJK BLG, LEUFKENS HGM, HEERDINK ER, J Hum Hypert, (2006) 1. — 15. By-law on data collection and reporting on drug marketing. Official Gazette of the Republic of Croatia, 29 (2005) 1879. — 16. Anatomical Therapeutic Chemical (ATC) Classification Index with Defined Daily Doses (DDDs) WHO Collaborating Centre for Drug Statistics Methodology, Oslo, 2004. — 17. Republic of Croatia – National Bureau of Statistics. Population distribution according to age, sex, activity, and residence, March 31, 2000. Available from: URL: http://www.dzs.hr/. — 18. Guidelines for ATC classification and DDD assignment 2006. WHO Collaborating Centre for Drug Statistics Methodology, 2006. — 19. BEGAUD, B, U. BERGMAN, H.G.EICHLER, Br J Clin Pharmacol, 54 (2002) 528. — 20. Croatian institute of Public Health: International classification of diseases and allied health problems. Tenth revision, Volume 1. (Medicinska naklada, Zagreb, 1994). — 21. ŠTIMAC D, VUKUŠIĆ I, ČULIG J, Pharm World Sci, 27 (2005) 230. — 22. ŠTIMAC, D, VUKUŠIĆ I, ČULIG J, Pharmaca, 42 (2004) 174. — 23. Croatian institute of Public Health: Croatian health statistics annals 2004. (Croatian Institute of Public Health, Zagreb, 2005). — 24. FLETCHER B, GULANICK M, LAMENDOLA C, J Cardiovasc Nurs, 16 (2002) 17. — 25. NEELON, FA, N C Med J, 64 (2003) 85. — 26. AVENEL A, BROOM J, BROWN TJ, POOBALAN A, AUCOTT L, STEARNS SC, SMITH WC, JUNG RT, CAMPBELL MK, GRANT AM, Health Technol Assess, 8 (2004) 1. — 27. WOLFORD J.K, VOZAROVA DE COURTEN B, Treat Endocrinol, 3 (2004) 257. — 28. PARK KS, Diabetes Res Clin Pract, 66 Suppl 1 (2004) 33. — 29. MANDIĆ D, OREŠKOVIĆ S, FRANCETIĆ I, Coll Antropol, 2 (2001) 459. — 30. FRANCETIĆ I, KUZMAN I, Course in antimicrobial treatment for primary health care physicians. (Ministry of Health of Republic of Croatia, Zagreb, 2001). — 31. BROOK I, GOBER AE, J Med Microbiol, 54 (2005) 553. — 32. RIFFER E, SPILLER J, PALMER R, SHORTRIDGE V, BUSMAN TA, VALDES J, Curr Med Res Opin, 21 (2005) 61. — 33. HENRY DC, Jr. SYDNOR A, SETTIPANE GA, ALLEN J, BURROUGHS S, COBB MM, Jr. HOLLEY HP, Clin Ther, 21 (1999) 1158. — 34. GOOSSENS H, FERECH M, VANDER STICHELE R, ELSEVIERS M, ESAC PROJECT GROUP, Lancet, 365 (2005) 579. — 35. MANT A, MATTICK RP, DE BURGH S, DONNELLY N, HALL W, Fam Pract, 12 (1995) 37. — 36. SRISURAPANONT M, GARNER P, CRITCHLEY J, WONGPAKARAN N, BMC Fam Pract, 23 (2005) 27. — 37. DIVAC N, VELJKOVIĆ S, NEŠIĆ Z, STOJANOVIĆ R, VASILJEVIĆ Z, PROSTRAN M, SAMARDŽIĆ R, Vojnosanit Pregl, 63 (2006) 370. — 38. IBANEZ L, VIDAL X, BALLARIN E, LAPORTE JR, Arch Intern Med, 165 (2005) 869. — 39. BACKSTROM M, HAGG S, MJORNDAL T, DAHLQVIST R, Pharmacoepidemiol Drug Saf, 11 (2002) 239. — 40. IBANEZ L, VIDAL X, BALLARIN E, LAPORTE JR, Eur J Clin Pharmacol, 60 (2005) 821. — 41. WOLFE MM, LICHTENSTEIN DR, SINGH G, N Engl J Med, 340 (1999) 1888. — 42. VOUTILAINEN M, MANTYNEN T, FARKKILA M, JUHOLA M, SIPPONEN P, Scand J Gastroenterol, 36 (2001) 817. — 43. VUKUŠIĆ I, ŠTIMAC D, ČULIG J, Coll Antropol, 29 (2005) 147. — 44. TEŠIĆ V, PAJAN LEHPANER G, ŠTIMAC D, ORBAN M, LEPPEE M, The City of Zagreb-public health database. (Zagreb Institute of Public Health, Zagreb, 2005). — 45. ŠTIMAC D, ČULIG J, Outpatient drug utilization in the City of Zagreb in 2005. (Zagreb Institute of Public health, Zagreb, 2006). — 46. EVANS M, ROBERTS A, DAVIES S, REES A, Drugs, 64 (2004) 1181. — 47. JACOBSON TA, Am J Med, 110, Suppl 6A (2001) 3. — 48. VOGEL R, SCHAEFER E, Am J Manag Care, 7, Suppl 5 (2001) 117. — 49. FISHER MA, AVORN J, JAMA, 291 (2004) 1850. — 50. MELANDER A, NILSSON LG, J Ambul Care Manag, 27 (2004) 115.

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OBILJEŽJA IZVANBOLNIČKE POTROŠNJE ŠEST GLAVNIH ATK SKUPINA LIJEKOVA U REPUBLICI HRVATSKOJ, GRADU ZAGREBU I ŽUPANIJAMA REPUBLIKE HRVATSKE U 2004. GODINI

S A Ž E T A K

Cilj ovoga rada je utvrditi potrošnju lijekova u regijama Republike Hrvatske te istražiti uzroke eventualnih razlika u potrošnji među regijama. Zavod za javno zdravstvo Grada Zagreba, u suradnji sa Agencijom za lijekove i medicinske proizvode, prikupljao je i analizirao podatke o izvanbolničkoj potrošnji lijekova iz šest glavnih Anatomsko-Terapijsko-Kemijskih (ATK) skupina. Podaci o broju i veličini pakovanja te financijskim iznosima prema veleprodajnim cijenama dobiveni su iz svih ljekarni u Hrvatskoj. Na temelju dobivenih podataka, za sve lijekove je izračunat broj definiranih dnevnih doza (DDD) i broj DDD na 1000 stanovnika na dan (DDD/1000/dan). Razlike u potrošnji lijekova među županijama, izračunate su za šest promatranih ATK skupina pomoću relativne standardne devijacije (RSD). Utvrđeno je da postoje razlike u izvanbolničkoj potrošnji lijekova među regijama Hrvatske. Iz prikazanih rezultata, nameće se potreba donošenja nacionalnih smjernica za racionalnu primjenu lijekova te edukacija liječnika, ljekarnika i šire populacije o potrebi primjene istih.