

Antihypertensive Drugs in Croatia: What Changes the Drug Usage Patterns?

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ABSTRACT

Purpose: Possible factors that could influence changes in patterns of prescribing antihypertensives could be identified by monitoring national trends in hypertension treatment. The choice of pharmacologic treatment in people with hypertension has important therapeutic and financial implications, due to the fact that the financial costs associated with hypertension continue to increase. The aims of our study were to identify and analyze changes in the usage of antihypertensive drugs in Croatia from 2000 to 2016 and to identify the changes in prescribing patterns as well as mean prices per defined daily dose (DDD).

Methods: Data on consumption in Croatia were obtained from the International Medical Statistics database. According to the World Health Organization's Collaborating Center for Drugs Statistics Methodology, per-annum volumes of drugs are presented in DDD per 1000 population per day (DDD/1000), while data on financial expenditure are presented in euros.

Findings: The consumption of drugs for cardiovascular disease in Croatia during the period from 2000 to 2016 increased 150.81%, while financial expenditure in the same period increased 47.32%. The most frequently prescribed subgroup was agents acting on the renin-angiotensin system (RAS). Their share among antihypertensives increased from 39.13% (2000) to 53.39% (2016). The share of diuretics in the same period decreased from 20.16% in 2000 to 12.73% in 2016.

Implications: The prescribing patterns of antihypertensive drugs in Croatia have changed, which could be a result of a combination of different factors, such as changes in laws, pharmaceutical marketing, and guidelines on hypertension therapy. The most prescribed subgroup in all of the investigated years was agents acting on the RAS, mainly because of the increased

prescribing of combinations of RAS agents plus diuretics. The financial implications of legal changes and the introduction of new generic drugs led to decreased cost per DDD of antihypertensives during the investigated period, but the total expenditure on antihypertensives in Croatia increased due to increased consumption. (*Clin Ther.* 2018;■:1–11) © 2018 Elsevier Inc. All rights reserved.

Key words: antihypertensive drugs, drug usage, prescription patterns, price.

INTRODUCTION

Cardiovascular diseases (CVDs) are a major health problem in contemporary world, particularly in developing countries. CVDs are the number 1 cause of death globally: more people die each year from CVDs than from any other cause.¹ According to statistics from the World Health Organization (WHO), an estimated 17.5 million people died from CVDs in 2012, representing 31% of all deaths worldwide. WHO announced that at least three fourths of the world's deaths from CVDs occur in low- and middle-income countries.¹ Worldwide, ischemic heart disease and stroke remain the leading causes of premature death,² and CV and cerebrovascular diseases were the cause of over 50% of deaths in Croatia in 2004.

Adequate therapy for CVD leads to reductions in CVD-related morbidity and mortality. Arterial hypertension is a significant health care problem in today's world as well as in Croatia. In a study performed in 2003, the prevalence of hypertension in Croatia in men

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was 40.5%; in women, 34.9%.³ Noncontrolled arterial hypertension is an important public health problem in all monitored regions of Croatia.⁴

WHO has identified hypertension as the leading cause of CVD-related mortality. The World Hypertension League, an umbrella organization of 85 national hypertension societies and leagues, recognized that >50% of the hypertensive population worldwide is unaware of their condition.⁵ Studies in hypertensive populations have demonstrated a significant decrease in CV events obtained by antihypertensive drug treatment.⁶ Adequate antihypertensive therapy prevents the complications of high blood pressure, such as stroke and myocardial infarction. A reduction in blood pressure by 5 mm Hg can decrease the risk for stroke by 34%; ischemic heart disease by 21%; and dementia, heart failure, and mortality from CVD.⁷

The effectiveness of treating hypertension and preventing CV events with thiazide diuretics, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), and β -blockers is well documented.^{8–10} The aim of our study was to identify and analyze changes in the usage of antihypertensive drugs, the most prescribed drug subgroup, the trends in usage of each subgroup, and financial changes (presented as mean price in each subgroup).

MATERIALS AND METHODS

Data on consumption in Croatia were obtained from the International Medical Statistics database from 2000 to 2016. According to WHO's Collaborating Center for Drugs Statistics Methodology, annual volumes of drugs are presented as defined daily doses per 1000 population per day (DDD/1000).¹¹ The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use. This methodology could provide a rough estimate of the percentage of the population within a defined area treated daily with certain drugs. For example, 10 DDD/1000 indicates that 1% of the population on average gets a certain treatment daily.

According to the Croatian Bureau of Statistics' Census of Population, Households and Dwellings in the Republic of Croatia from 2011, the total population of Croatia in 2011 was 4,284,889, and this number is included in calculation of the DDD/1000 value in all investigated years (2000–2016).¹²

Data on financial expenditures are presented in euros. There have been some changes in DDDs in the CV drug group that happened during investigated period. In such cases, we recalculated volumes of drugs spent in each previous year according to the last approved DDD value.

The total financial consumption is presented in euros, and the analyzed prices of each subgroup are presented in euros per DDD.

Changes in prescribing patterns are measured with *index of change*, a statistical measure of changes in a representative group of individual data points. It reflects changes in prescribing in DDDs/1000 or in expenses in euros in 2016 compared with 2000.

RESULTS

The total usage of CV drugs consistently increased, from 190.18 DDD/1000 in 2000 to 484.23 DDD/1000 in 2014, and then started a slow decrease to 476.98 DDD/1000 in 2016. In this 17-year period, consumption in DDD/1000 increased 150.81%, while the financial expenditure in the same period increased 47.32% (from €70.59 million in 2000 to €103.98 million in 2016), but achieved its maximum in 2006 (€149.1 million) (Figure 1).

The total usage of CV drugs increased at higher rates from 2000 until 2008 (range of rate changes per year, +6.54% to +12.73%). The changes in rate of increase per year in prescribing CV drugs were lower from 2009 until 2013 (range, +2.45% to +6.50%), and the first year-decreases in prescribing were observed in 2015 and 2016 (rate changes vs previous years: 2015, -0.92%; 2016, -0.59%).

Per-annum growth rates in financial expenditures in the same period were not proportional to per-annum growth rates in consumption in DDDs. Financial expenditures consistently increased from 2000 until 2006, at a mean growth rate of +13.48% per year, with a peak in 2006 at €149,100,878, which is the maximal amount of financial spending during the investigated period. After the per-annum decrease of -7.73% in financial spending in 2007 (compared with 2006), the total expenditure on CV drugs peaked a second time in 2010, with €148,086,999 spent. After 2011, total spending started to decrease, with a mean per-annum decrease of -5.48%, and a small increase of +3.79% was observed only in 2016 (total spending, €103,984,862) compared with 2015.

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