



Trends in Antihypertensive Drug Use in Spanish Primary Health Care (1990-2012)

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Abstract

Objective: This study aimed to describe the use of antihypertensive in Extremadura (Spain) from 1990 to 2012 and its economic impact.

Method: Information on antihypertensive drug (ATC C02, C03, C07, C08, C09) utilization was obtained from the community pharmacy sales figures reimbursed by the Health System of Extremadura (Spain). Data were expressed in Defined Daily Dose (DDD) and DDD per 1000 inhabitants per day (DHD).

Results: Antihypertensive consumption in Extremadura increased from 67.1 DHD in 1990 to 315.2 in 2012 (an increase of 3.7 times). Agents acting on the Renin-Angiotensin System (C09) are responsible for 75% of the total increase. Since 2007 the use of Angiotensin II antagonist increased over ACE inhibitors.

Conclusions: The consumption of antihypertensive drugs in Extremadura increased remarkably in the last 23 years. In the last years the use of angiotensin II antagonist drugs is having a significant economic impact.

Keywords: Antihypertensives; Drug use; Pharmacoepidemiology; Primary care

Introduction

Hypertension is currently considered a major public health problem because of its importance as a cardiovascular risk factor. Worldwide, high blood pressure is estimated to cause 7.5 million deaths, about 12.8% of the total of all annual deaths [1]. Blood pressure levels have been shown to be positively and progressively related to the risk for stroke and coronary heart disease [2]. In addition to coronary heart diseases and stroke, complications of high blood pressure include heart failure, peripheral vascular disease, renal impairment, retinal haemorrhage and visual impairment [3].

The 33.3% of adult population in Spain suffer from hypertension [4]. Moreover, 1 out of every 4 deaths and 1 out of every 2.5 deaths caused by cardiovascular disease is related to high blood pressure [5].

A great number of national and international guidelines for hypertension treatment have been published. The JNC 7 guideline recommended diuretics as first-line treatment in hypertension [6]. Therefore the current Guidelines advise that diuretics (including thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, Angiotensin-Converting Enzyme (ACE) inhibitors and angiotensin receptor blockers are all suitable for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations [7].

The European guideline, on the other hand, suggests that unless a special indication exists, any of the five antihypertensive classes can be used as first-line treatment [8]. Although the number of prescriptions for Diuretics (Ds) and B-Blockers (BBs) is increasing, and for Calcium-Channel Blockers (CCBs) is decreasing, in most countries the most frequently antihypertensive classes prescribed are still Angiotensin-Converting Enzyme Inhibitors (ACEIs) or CCBs [9-15]. However, there is a considerable variation in the antihypertensive drug classes used in different countries [9-20].

The present study aimed to analyze the overall use and changes in

the prescribing pattern of antihypertensive drugs by Family Medicine physicians in the Spanish region of Extremadura from 1990 to 2012, its compliance with guidelines, and its economic impact.

Method

In order to study the use of antihypertensive drugs in Extremadura, annual data from 1 January 1990 to 31 December 2012 about the prescribing of antihypertensive drugs were collected from the community pharmacy sales figures reimbursed by the Spanish Extremadura Health System (SES), which covers almost 100% of the Extremadura population (1.100.000 inhabitants).

All the antihypertensive drugs marketed in Spain and listed in the Anatomic Therapeutic Chemical (ATC) classification system were studied. The ATC studied groups studied are the followings: C02 [Antihypertensives]; C03 [Diuretics]; C07 [Beta blocking agents]; C08 [Calcium channel blockers]; C09 [Renin angiotensin system], including: C09A (Angiotensin-converting enzyme inhibitors (ACE inhibitors), C09B (ACE inhibitors, combinations), C09C (Angiotensin II antagonists), C09D (Angiotensin II antagonists, combinations).

Drug consumption figures were expressed as the number of Defined Daily Doses (DDD) per 1000 inhabitants per Day of Treatment (DHD), using the DDD values proposed by WHO [21].

Total costs were estimated by multiplying the number of sold

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Received November 05, 2014; **Accepted** January 05, 2015; **Published** January 06, 2015

Citation: Cáceres MC, Moyano P, Fariñas H, Cobaleda J, Pijierro A, Darado P, LLerena A (2015) Trends in Antihypertensive Drug Use in Spanish Primary Health Care (1990-2012). Adv Pharmacoepidemiol Drug Saf 3: 172. doi:10.4172/2167-1052.1000172

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packages of each product by the price of each one. Cost per day was calculated by dividing the total cost by the total DDD consumed for the active ingredient or subgroup considered.

Study limitations: firstly, data were collected by auditing drug sales in all the pharmacies of Extremadura, which allowed us to estimate the prescription of antihypertensive drugs but not their real use; [22] second, the DDD methodology allows the possibility of analyzing trends of consumption over the years, but does not allow individual level analyses regarding the real DDD received by a patient daily.

Results

Antihypertensive consumption in Extremadura increased fivefold between 1990 and 2012 (Figure 1). It is estimated that in 1990 there were 73,781 people in treatment with an antihypertensive drug, increasing to 346,726 people in 2012.

Subgroup C09 (agents acting on the renin-angiotensin system) is responsible for 75% of the total increase (Figure 1).

Since 2007 the use of ARBs (C09C+C09D) increased over ACE inhibitors (C09A+C09B) (Figure 2).

The ranking of the most frequently prescribed renine-angiotensinase drugs (C09) in the study period is shown in Table 1.

Total spending on antihypertensives (C02, C03, C07, C08 and C09)

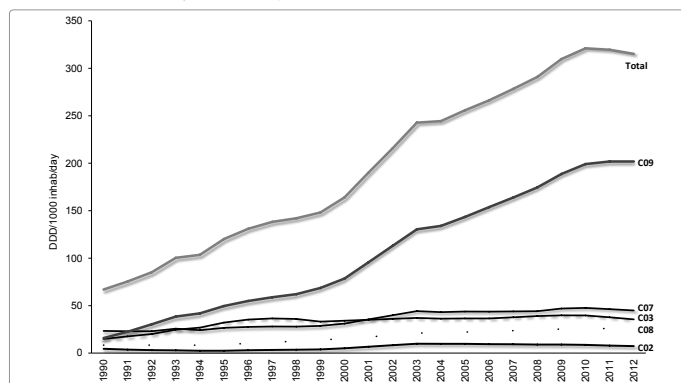


Figure 1: Antihypertensive drugs consumption in Extremadura, Spain (1990-2012). (C02 Antihypertensives; C03 Diuretics; C07 Beta-blockers; C08 Calcium channel blockers; C09 Agents acting on the renin-angiotensin system).

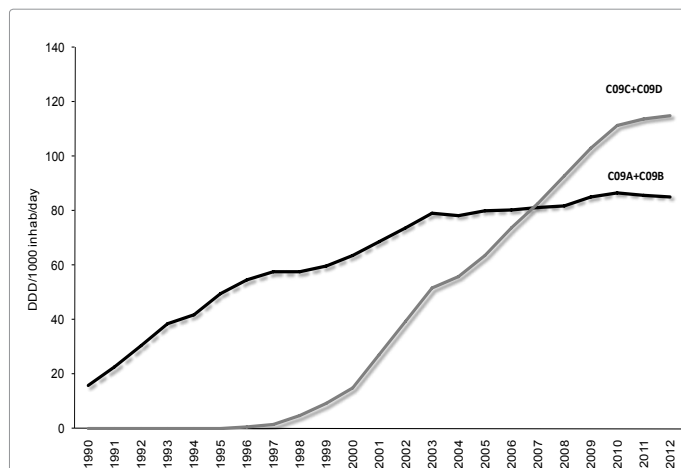


Figure 2: Angiotensin II antagonist (ARBs) and ACE inhibitors consumption in Extremadura, Spain (1990-2012).

1990		2000		2012	
Drug	%	Drug	%	Drug	%
Captopril	49.6	Enalapril	31.3	Enalapril	18.3
Enalapril	47.9	Candesartan	11.5	Candesartan	14.1
Captopril+diuretics	2.4	Ramipril	7.0	Ramipril	12.2
		Valsartan	6.6	Valsartan	8.2
		Olmesartan	5.3	Valsartan+diuretics	4.8

Table 1: Active ingredients most frequently prescribed in selected years, expressed in percentage of the total of the renin-angiotensin system drugs (C09). Combinations are fixed.

in 2012 was 42.5 million euros, of which 75.9% corresponds to the drug spending of the renin-angiotensin system (C09). Within this group, during the 2003-2012 spending on ACE inhibitors (C09A+C09B) decreased from 9.8 to 4.5 million euros, while in ARBs (C09C+C09D) increased from 22.1 to 27.0 million euros.

Discussion

There was an increase in the use of antihypertensive drugs in the study period, the same result was observed in similar studies performed in Spain [23-27]. This increase could be due to an increase in the number of people on antihypertensive treatment. It should be noted that antihypertensive drugs, except the C02 group, are not only used in hypertension, but also for treatment of other diseases such as diabetes, nephropathy, ischemic heart disease, peripheral arterial disease or stroke. Furthermore, the criteria for blood pressure control throughout the study period became more restrictive, considering as normal blood pressure values ever lower [6]. Therefore, it is increasingly common to find patients taking more than one drug, and also patients that at the beginning of the study period would be considered normotensive, at period end would not be [6]. Other possible causes for the increase in the prescription of antihypertensives may be the aging population, changes in lifestyle, a better knowledge of the condition by the population, the implementation of Health Programmes at Primary Care. Furthermore must be taking into account the important role that have the implementation on recent years of the ambulatory blood pressure monitoring and home blood pressure monitoring, these measures have facilitated the diagnosis and the management of hypertension, and have strengthened its prognostic value.

Study data shows that the total use of antihypertensives in Extremadura is higher than in other studies performed in Spain [25-27]. Extremadura is among the regions with higher rates of cardiovascular morbidity and mortality [28] and a high incidence of diabetic nephropathy and microalbuminuria [29,30] diseases that are related with the level of control of cardiovascular risk factors, particularly with high blood pressure. However, control of blood pressure in Extremadura is similar to the rest of Spain, 36.7% [31,32].

This rising use of antihypertensive over the past 20 years is not exclusive to Spain, also occurred in other European countries [33,34].

The increase in total use of antihypertensive drugs is mainly due to increased consumption of C09 group. The dramatic increase could be due to greater efficiency and tolerability of this group, although up today, clinical trials have failed to demonstrate greater efficacy and lower mortality of this group respect to others. Furthermore, it must be taken into account the possible influence of pharmaceutical companies. The C09 group is the most widely group used also in Europe, as it is shown in different European studies [33,34,38-40]. Within this group, the ACE inhibitors were the antihypertensive drugs most commonly used until 2007, at that moment they started to be replaced by ARBs. In a similar study published, in Murcia region the same fact is observed

since 2005 [27]. However Spanish data released shows that until 2006 the ACE inhibitors were the antihypertensive most prescribed [24].

Captopril was the active ingredient most widely used in 1990; from 1991 to the end of the study period, enalapril remained as the most active ingredient prescribed, even after the marketing of ACE inhibitor. This trend is also observed in other studies published [25,26]. Considering the causes of high consumption of enalapril, it should be noted that enalapril has a good tolerability and a long half-life which allows an adequate blood pressure control with a single daily dose; it is also worth noting that as its action mechanism was better known, enalapril began to be used in the treatment of other diseases such as heart failure in normotensive patients and the prevention of diabetic nephropathy in diabetic patients.

From the point of view of therapeutic recommendations, therapeutic guidelines agree on D₅ as first line treatment followed by BB₂. Since the commercialization of ACE inhibitors and CCBs, they became part of the first-line treatment. Since 1997, the JNC VI, recommended by the first time ARBs only when the ACE inhibitor is not tolerated, but in 2003, both the JNC VII and the ESH-ESC 1, added ARBs as first-line treatment [6-8,35-37].

Despite all the measures that were taken in recent years to reduce drug spending, the significant increase in the use of antihypertensive drugs in the study period generated a major economic impact on the healthcare system, being due largely to the high cost of ARBs. This fact has been observed in other studies [24,27,33,40].

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