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The Use of Antihypertensive Therapy in Spain (1986–1994)

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We aimed to analyze the trends in antihypertensive therapy in Spain during the period 1986 to 1994, as well as the change in the pattern of different drugs, in relation to different national/international recommendations for hypertension treatment. Antihypertensive consumption was studied using the defined daily dose (DDD) and the DHD (DDD/1000 inhabitants/day) of each drug, as defined by the Drug Utilization Research Group of the European Office of the World Health Organization. The anatomical classification of hypotensive drugs has been made according to EPhMRA (European Pharmaceutical Market Association) guidelines.

A significant increase of 117.4% (41.39/90 DHD) in antihypertensive drug consumption was observed in the period 1986 to 1994. In 1986 diuretics were the most consumed (30.27 DHD), followed by calcium antagonists (5.37), β-blockers (3.93), and the angiotensin-converting enzyme (ACE) inhibitor (1.37). In 1994 ACE inhibitors, calcium antagonists, and β-blockers increased significantly ($P < .0001$), whereas diuretics were still the most commonly prescribed. Nifedipine and captopril were the most used among calcium antagonists and ACE inhibitors. National and international recommendations had no effect on prescription patterns.

Antihypertensive therapy of all types is increasing in Spain. Diuretics remain the most popular, β-blockers stay stable, whereas the newer types are rising rapidly. National and international recommendations had no effect on prescription patterns. Am J Hypertens 2000;13:607–610 © 2000 American Journal of Hypertension, Ltd.

KEY WORDS: **Hypertension, hypotensive drug consumption, prescription pattern.**

Over the last 20 years[1–5] an increase of the use of antihypertensive drugs has been observed in the developed countries. In Spain, an increase of more than 100% was described between 1981 and 1990.[1] These facts can be explained by an improved awareness and treatment of hypertensive disease[6,7]; great public health demand, as almost 100% of the Spanish population are covered by the National Health Service; changing recommendations on the detection, evaluation, and treatment of high blood pressure[7–10]; and the discovery that treatment of hypertension reduces cardiovascular risks.[11] In the 1970s, changes in hypertensive drugs were recorded, β-blockers, diuretics, and central sympatholitic being the most prescribed drug treatments.[2,5] In the last decade, the consumption of diuretics and β-blockers has not declined, while there has been a spectacular increase with respect to angiotensin-converting enzyme (ACE) inhibitors and calcium antagonists, and an almost total disappearance of central sympatholitic drugs.[2–4,12,13] In the opinion of some writers, these changes have no correlation with national or international recommendations for hypertensive treatment,[4,13] whereas others take the view that

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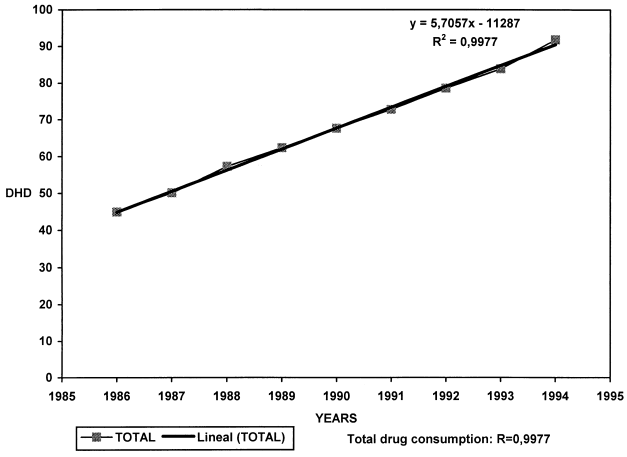

FIGURE 1. *Trends in antihypertensive drug use (in DHD), 1986 to 1994 (lineal regression).*

temporal patterns in the use of hypotensive drugs are related to increased clinical trials[14] and the effectiveness of pharmaceutical promotional practices.[15–17]

The objective of this study was to describe the trends in antihypertensive drug use in Spain from 1986 through 1994, as well as their changing patterns, and their correlation with national/international recommendations on hypertensive treatment.

MATERIALS AND METHODS

In carrying out this study on the use of antihypertensive drugs in Spain, we have used the anatomical classification of the European Pharmaceutical Market Research Association (EPhMRA). The study includes all hypotensives dispensed through the Spanish National Health Service from 1986 to 1994, on the basis of the ECOM data base, which has been in operation since 1981. This database includes complete information with regard to the dispensing of pharmaceuticals in pharmacies. Such information is available in automated form, taking into account the bills of all the prescriptions issued by the National Health Service, which covers almost 100% of the Spanish population. The data was provided by the Subdirección General de Ordenacion y Asistencia Farmacéutica, of the Dirección General de Farmacia y Productos Sanitarios of the Ministerio de Sanidad y Consumo, in the form of numbers of units sold, pharmaceutical form (capsules or pills), and composition. We have calculated the DHD (see below) on the basis of these data. It should be stressed that many of these pharmacologic subgroups, and in particular diuretics and β-blockers, are used in other pathologies such as ischemic heart disease or congestive heart failure, given that the Spanish database does not take into account diagnostic indications.

The DHD expresses antihypertensive consumption (DDD [defined daily dose]/1000 inhabitant/day) and is used to quantify drug consumption. The DDD of each drug is defined by The Drug Utilisation Research Group of the European Office of the World Health Organization (WHO), which publishes a list of the different DDD drugs including hypotensives.[18] The DDD is very useful as an international comparative unit, as it allows comparisons between different countries and periods of time without taking into account prices or unit doses.[19]

The DHD is calculated according to the formula:

$$\frac{\mathrm{UV} \times {}^{\mathrm{FF}}/_{\mathrm{E}} \times {}^{\mathrm{C}}/_{\mathrm{FF}} \times 1000\mathrm{inh}}{\mathrm{DDD} \times \mathrm{inh.\ no.} \times 365\ \mathrm{days}}$$

where UV is the unit of drugs sold, FE/E is the number of tablets for each box, C/FF is the composition of each drug, and Inh is the inhabitant.

We used SPSS-PC for data analysis. All data are expressed as means ± SEM; linear regression analysis was used to express the differences in the use of drugs between different periods; r = correlation coefficient and $P < .05$ was considered statistically significant.

RESULTS

Our results show a 117.4% (41.39/90 DHD) increase in the consumption of antihypertensive drugs between 1986 and 1994 (Figure 1). In 1986, diuretics were the most consumed antihypertensive drugs (30.27 DHD),

TABLE 1. TRENDS IN ANTIHYPERTENSIVE DRUG USE (IN DHD), 1986 TO 1994

Drug	1986	1987	1988	1989	1990	1991	1992	1993	1994	r	*P*
ACEI	1.3	2.4	4.5	7.6	11.2	14.6	18.6	21.9	24.7	0.9871	.0001
CA	5.3	7.5	8.9	10.8	13	15.2	17	19.3	22.3	0.9947	.0001
D	30.2	32.5	35.6	35.6	35.4	35	34.9	34.6	35.5	0.4024	.66
βB	3.9	4.4	5	5.6	5.9	6.1	6.3	6.3	6.6	0.9178	.0001
αB	0.4	0.4	0.39	0.3	0.3	0.31	0.48	0.6	0.7	0.3316	.10
$\alpha\beta$B	0.01	0.01	0.01	0.0	0.0	0.008	0.009	0.009	0.01	0.7306	.003

ACEI = angiotensin-converting enzyme inhibitor, CA = calcium antagonist, D = diuretics, βB = β-blockers, $\alpha\beta$ = α-blockers, $\alpha\beta$B = $\alpha\beta$-blockers. r = correlation coefficient; P *= statistically significant.*

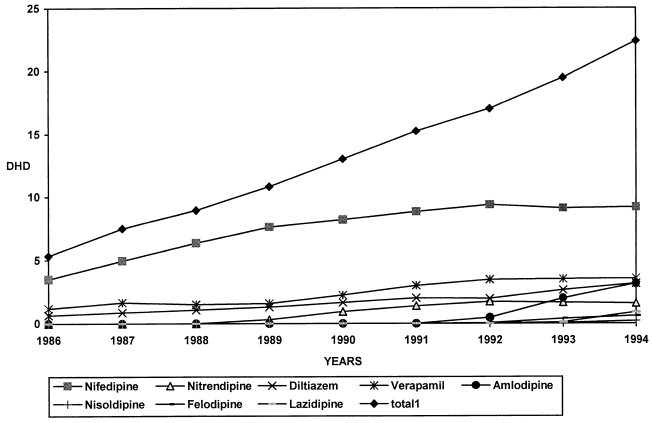

FIGURE 2. *Trends in calcium antagonist use (in DHD), 1986 to 1994*

followed by calcium antagonist (5.37 DHD), β-blockers (3.93 DHD), and ACE inhibitors (1.37 DHD) (Table 1).

Over a 9-year period, use of ACE inhibitors, calcium antagonists, and β-blockers increased significantly ($P < .0001$) (24.76, 22.36, 6.64 DHD), while diuretics were still the most commonly prescribed and experienced a small but not significant increase (Table 1). The remaining group (α- and αβ-blockers) did not show a significant change over the same period.

Within the calcium antagonist group, nifedipine was the most used, followed by verapamil, with a spectacular increase for amlodipine (Figure 2). Captopril remained the most-used ACE inhibitor, followed by enalapril, another ACE inhibitor group still far behind captopril (Figure 3).

DISCUSSION

Our results show a very high increase in the use of antihypertensive agents in Spain, which has doubled in the last decade. We noted a change in the use of the different hypotensive groups, with an increased use of new ones such as ACE inhibitors and calcium antagonists, which became the most commonly prescribed after diuretics.[2–4] Our results are important because they cover the consumption of antihypertensive drugs within the total Spanish population. However, it is not possible to establish whether these drugs are used for hypertension or for other diseases, such as cardiac failure, ischemic heart disease, or diabetic nephropathy, as the Spanish data do not include diagnostic indications. Nevertheless, we remain convinced of the importance of these data, as in most cases the most frequent indication is hypertension.

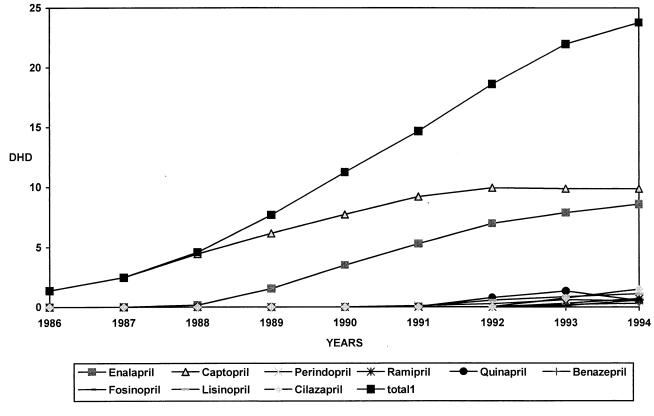

FIGURE 3. *Trends in ACE inhibitor use (in DHD), 1986 to 1994*

The use of DDD not only allows for the definition of drug consumption, but also for its comparison with other countries. In 1984 the use of prazosin in Norway was 5.5 DDD/1000 inhabitants/day,[20] whereas in Spain it was 0.28 DDD/1000 inhabitants/day.[1] Our study covers a long time period compared with others,[4,12,13] which are of shorter periods, work with smaller populations,[3,21,22] or study some, but not all, antihypertensive drugs.[22]

We consider that the increase in antihypertensive consumption is related to a major health demand, to the fact that the Spanish National Health Service is free, and to an improved awareness and treatment of the Spanish hypertensive population.[6]

Psaty et al[14] report a temporal increase in diuretics and β-blockers and decrease in use of ACE inhibitors and calcium antagonists related to major clinical trials on hypertension treatment,[23–25] which show that the use of low doses of diuretics reduces cardiovascular risk. We have not found this temporal relation, as the consumption of diuretics was the same between 1989 and 1992 (35 DHD).

National and international recommendations for treatment of high blood pressure had little effect on prescribing patterns,[4,13] as we have seen in our results. There are several possible reasons for this: the attractiveness of using new therapies so that practitioners are considered up-to-date; the fact that clinicians may be disappointed with the results of clinical trials; the fact that many hypertensive patients also suffer from other diseases (diabetes mellitus, ischemic heart diseases, gout, etc.) where the new drugs have specific indications, and finally the effectiveness of pharmaceutical promotional practices.[15–17]

The cost implications of these practice patterns are enormous. The estimated wholesale cost for antihypertensive drugs in 1996 in Spain is $106 million, representing 2% of all drug consumption.[26] In 1995 consumption of calcium antagonists in the US was $2.67 billion and $1.67 for ACE inhibitors, whereas the cost of diuretics and β-blockers was $168 million and $433 million, respectively.[27] Given that in 1995 cal-

cium antagonist use represented 38% of prescriptions for cardiovascular disease in community retail pharmacies, compared with 8% for diuretics, the potential savings from a change in hypertensive prescribing patterns could amount to hundreds of millions of dollars.

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