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Antidiabetic medications use trends in an Andalusian region from 2001 to 2014

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ABSTRACT

Purpose: There is a widening range of antidiabetic medications available; however changes in consumption patterns remain poorly documented. The aim of this study is to analyze the evolution of consumption of antidiabetic medications during the period 2001–2014 in an Andalusian region.

Methods: All antidiabetic medicines on the market were selected for analysis. Consumption data were obtained for the 15-year period and were expressed in defined daily doses (DDD) per 1000 inhabitants per day (DHD).

Results: During the study period consumption of insulins grew only a 2.2%, from 17.9 DHD to 18.3 DHD, while oral agents increased a 27.6%, from 41.3 DHD to 52.7 DHD. Consumption of sulfonylureas was gradually reduced from 30.1 DHD to 16.4 DHD but metformin (alone) usage increased from 4.3 DHD to 23.7 DHD, and was the most consumed agent in 2014. A rise in consumption of dipeptidyl peptidase-4 inhibitors and “other hypoglycemic agents” was also noticed. Overall expenditure in antidiabetic medications increased notably from 4.5 in 2001 to 14.4 million euros in 2014.

Conclusion: We highlight the market uptake of antidiabetic drugs commercialized during the last decade; despite further exploration is needed to clarify the cost-benefit ratio of these new antidiabetic medicines.

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Abbreviations: DHD, Defined daily doses (DDD) per 1000 inhabitants per day; GLD, Glucose lowering drugs.

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1. Introduction

Diabetes mellitus (DM) is a chronic disease. Type 1 diabetes (DM1), is due to a deficient insulin production, while type 2 diabetes (DM2) is caused by both insulin deficiency and insulin resistance; over 90% of cases are represented by DM2 [1]. This trend has been associated with, among other reasons, aging populations, rising prevalence of obesity and increasingly sedentary lifestyles [2]. According to the World Health Organization (WHO), diabetes will represent the 7th leading cause of death in 2030, with an estimated prevalence of 7.8% [3].

The Di@bet.es study is a national cross-sectional, epidemiological study, designed to examine the prevalence of DM, obesity and other cardiovascular risk factors in Spain [4]. This is a nationally representative study, in which the sample corresponding to Andalusia (an autonomous region in southern Spain) was enlarged. The results showed that the prevalence rates of DM (15.3%) and obesity (37%) are higher in the region of Andalusia than in the rest of the country, with the results being concordant with higher cardiovascular disease mortality rates seen in this region [5].

Although life style changes play an important role in DM2 treatment, most patients also require pharmacotherapy targeted to glycemic management, which has become increasingly complex and somewhat controversial [6]. There are more than 30 medicines from 11 different drug classes currently approved for the treatment of hyperglycemia in diabetic patients. Additionally physicians rely on a wide range of both clinically objective and patient-focused factors when managing hyperglycemia. Some of these such as overall assessment of their patients' health and comorbid conditions and the patient's glycated hemoglobin level, adherence, and motivation to improve and/or avoid insulin [7].

Given the wide array of options, it is not surprising that physicians demonstrate wide clinical practice variation in the choice and sequence of medications prescribed for diabetes management. Studies on antidiabetic prescription patterns have documented an overall increase in the use of metformin, in the USA and Europe, in the last few years. There are also large differences between-countries on the use of other classes of antidiabetics [6,8–10]. The aim of this study is to analyze the evolution of consumption of antidiabetic medications for the period 2001–2014 in Granada and its metropolitan area, in order to detect changes in consumption patterns.

2. Methods

Retrospective drug utilization study conducted using administrative databases of the Andalusian Public Health-Care System (Southern Spain). The source population included about 675,000 citizens living in Granada and its metropolitan area (thereafter, district).

Medications were prescribed by either primary care specialist or hospital specialists. The total drug consumption and expenditure data were obtained through prescriptions billed in pharmacies during the study period under the National Health System coverage. In our region (Andalusia), 99% of

prescriptions are electronically generated, and all dispensed medications are included in a prescribed medication history database. This database is accessible by primary care pharmacists for clinical purposes, using Microstrategy® software, and gives access to all information on dispensed medications. Microstrategy® software was used to analyze antidiabetic prescriptions. Hospital consumption of medicines was not included. Annual data on the size of the citizen population was obtained from the Spanish Institute of National Statistics.

At the end of 2014, eight different oral medication classes for the treatment of diabetes in Spain were available and reimbursed by the National Healthcare System. These included biguanides, sulfonylureas, alpha-glucosidase inhibitors, thiazolidinediones, meglitinides, dipeptidyl peptidase-4 inhibitors (DPP4-I), glucagon-like peptide-1 receptor agonists (GLP-1) and Sodium Glucose Co-transporter 2 Inhibitors (SGLT-2).

The following Anatomical Therapeutic and Chemical (ATC) classification pharmacological subgroups were selected for analysis: Blood glucose lowering drugs excluding insulins (GLD) were classified in biguanides (A10BA), sulfonylureas (A10BB), alpha-glucosidase inhibitors (A10BF), thiazolidinediones (A10BG), DPP4-I (A10BH), combined (A10BD) and Other blood glucose lowering drugs (A10BX). Insulins were classified in: fast-acting (A10AB), intermediate-acting (A10AC), intermediate- or long-acting combined with fast-acting (A10AD) and long-acting (A10AE). Drug consumption was described for each chemical subgroup or substance. Since DM1 and DM2 could not be accurately distinguished from the available data, the type of diabetes was not considered in this analysis.

Consumption data, for the 14-year period (2001–2014), were obtained from our database expressed in defined daily doses (DDD). The DDD is defined as the assumed average daily maintenance dose for its main indication use in adults. We calculated DDD per 1000 inhabitants per day (DHD) using the ATC/DDD system developed by World Health Organization Collaborating Centre for Drug Statistics Methodology [11]. $DHD = (DDD \times 1000) / (\text{inhabitants} \times 365)$. Total costs are in euros, based on pharmacy retail price, and costs per DDD were retrieved from our database.

3. Results

Between 2001 and 2014 new insulins have been marketed: glargine (2003), asparta, Lispro Protamine–lispro (2004), detemir (2005), and glulisine (2007). New GLD were marketed too, like sitagliptin and vildagliptin (2008), exenatide (2009), liraglutide (2011), linagliptin (2012) or lixisenatide (2013), Dapagliflozin (2013) and other of fixed-dose combinations: metformin-vildagliptin and metformin-pioglitazone (2008), or metformin-sitagliptin (2009), glimepiride-pioglitazone (2010) metformin-saxagliptin (2012) and metformin-linagliptin (2013). Some others have been removed from the market: tolbutamide (2002), buformin (2004), chlorpropamide (2011) and rosiglitazone (2010) and human long-acting insulin (2006) and inhalable insulin (2008).

The consumption of antidiabetic medications in Granada and its metropolitan area increased significantly by 20.1%, from 59.2 DHD in 2001 to 71.1 DHD in 2014. During the study

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