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ARTICLE

Utilisation of antihyperglycaemic drugs in ten European countries: different developments and different levels

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Abstract
Aims/hypothesis The aim of this study was to compare developments in the utilisation of antihyperglycaemic drugs (AHGDs) in ten European countries.
Subjects and methods Data on the yearly utilisation of insulin and oral AHGDs were collected from public registers in Denmark, Finland, Norway, Sweden, Belgium, England, Germany, Italy, Portugal and Spain, and were expressed as defined daily doses per 1,000 inhabitants per day.
Results Total AGHD utilisation increased everywhere, but at different rates and levels. Insulin utilisation doubled in England and Germany, but hardly changed in Belgium, Portugal or Italy. Sulfonylurea utilisation doubled in Spain, England and Denmark but was reduced in Germany and Sweden. Metformin utilisation increased greatly everywhere. There were two- to three-fold differences in AHGD utilisation even between neighbouring countries. In Finland, there were more users of both insulin (+120%) and oral AHGDs (+80%) than in Den-

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mark, and the daily oral AHGD doses were higher. In Denmark and Sweden, AHGD utilisation was equal in subjects aged <45 years, but in those ≥45 years of age, both insulin and oral AHGD utilisation were twice as high in Sweden.
Conclusions/interpretation The ubiquitous increase in AHGD utilisation, particularly metformin, seems logical, considering the increasing prevalence of type 2 diabetes and the results of the UK Prospective Diabetes Study. However, the large differences even between neighbouring countries are more difficult to explain, and suggest different habits and attitudes in terms of screening and management of type 2 diabetes.

Keywords Antidiabetic drug utilisation · Antihyperglycaemic drug utilisation · Diabetes mellitus · Insulin · International comparison · International variation in drug utilisation · Metformin (Biguanides) · Sulfonylurea · Treatment of diabetes

Abbreviations
AHGD Antihyperglycaemic drug
UKPDS United Kingdom Prospective Diabetes Study

Introduction

The United Kingdom Prospective Diabetes Study (UKPDS) [1, 2] showed that, in patients with type 2 diabetes, addition of antihyperglycaemic drugs (AHGDs), such as insulin, sulfonylurea or metformin, promotes better glucose control and fewer diabetes-related events than attempts at lifestyle changes alone. However, many subjects with type 2 diabetes may be undetected, and many detected subjects may be undertreated [3, 4]. Moreover, several earlier studies indicate that the utilisation of AHGDs varies pronouncedly, both between and within countries, and even within counties [5–15]. A comparison of the Nordic countries in 1985 suggested that greater utilisation was associated with a higher degree of obesity and a higher prevalence of diabetes [8]. In addition, the countries with the highest utilisation also appeared to use higher mean doses of AHGDs. A later comparison of the diabetes populations in two Swedish neighbouring towns indicated that glucose control was better in the town in which AHGD use was more extensive [15]. Based on these findings, and as recent studies have revealed very large differences between European countries in terms of the utilisation of other drugs, such as antibiotics [16] and statins [17], the aim of the present study was to update and compare the utilisation of insulin and oral AHGDs in a number of European countries where such data were available.

Subjects and methods

Data on utilisation of AHGDs

Ten European countries were studied: four northern (Denmark, Finland, Norway, Sweden), two western (Belgium, England), one central (Germany) and three southern (Italy, Portugal, Spain). In these ten countries, patient costs of insulin and oral AHGDs are reimbursed via the tax systems, allowing registration of national drug sales data. From such registers, yearly data on the utilisation (pharmacy sales, except in Norway where whole sales data were obtained) of AHGDs, expressed as defined daily doses per 1,000 inhabitants per day, were obtained. Ten-year data (1994–2003) were obtained for all countries except for Belgium (1997–2003), Italy and Portugal (2000–2003).

Data on the proportion of AHGD-treated individuals and data on average purchased doses

In Denmark and Finland, the drug registers allow the proportion of individuals treated with AHGDs to be recorded, as well as the average purchased doses of insulin and oral AHGDs. This enables determination of possible differences between these two countries in terms of these two parameters, based on data from 2000.

AHGD use in type 1 and type 2 diabetes, as suggested by patient age

A previous comparison of drug utilisation (in 2000) in the southernmost region in Sweden (Skåne) and its close neighbouring region in Denmark (Østdanmark) included data on insulin and oral AHGDs stratified according to age, and this was used in the present study to assess whether an inter-regional difference was due to different use among younger (<45 years, i.e. mainly type 1 diabetes) or older (≥45 years, i.e. predominantly type 2 diabetes) patients.

Results

Secular increase in AHGD utilisation

With time, total AHGD utilisation increased in each country, but at different rates and levels. For example, insulin utilisation doubled in England and Germany, but hardly changed in Belgium, Portugal or Italy (Fig. 1a), whereas sulfonylurea utilisation doubled in Spain, but decreased in Sweden and Germany (Fig. 1b). Biguanide (metformin) utilisation increased everywhere, particularly in Finland (Fig. 1c).

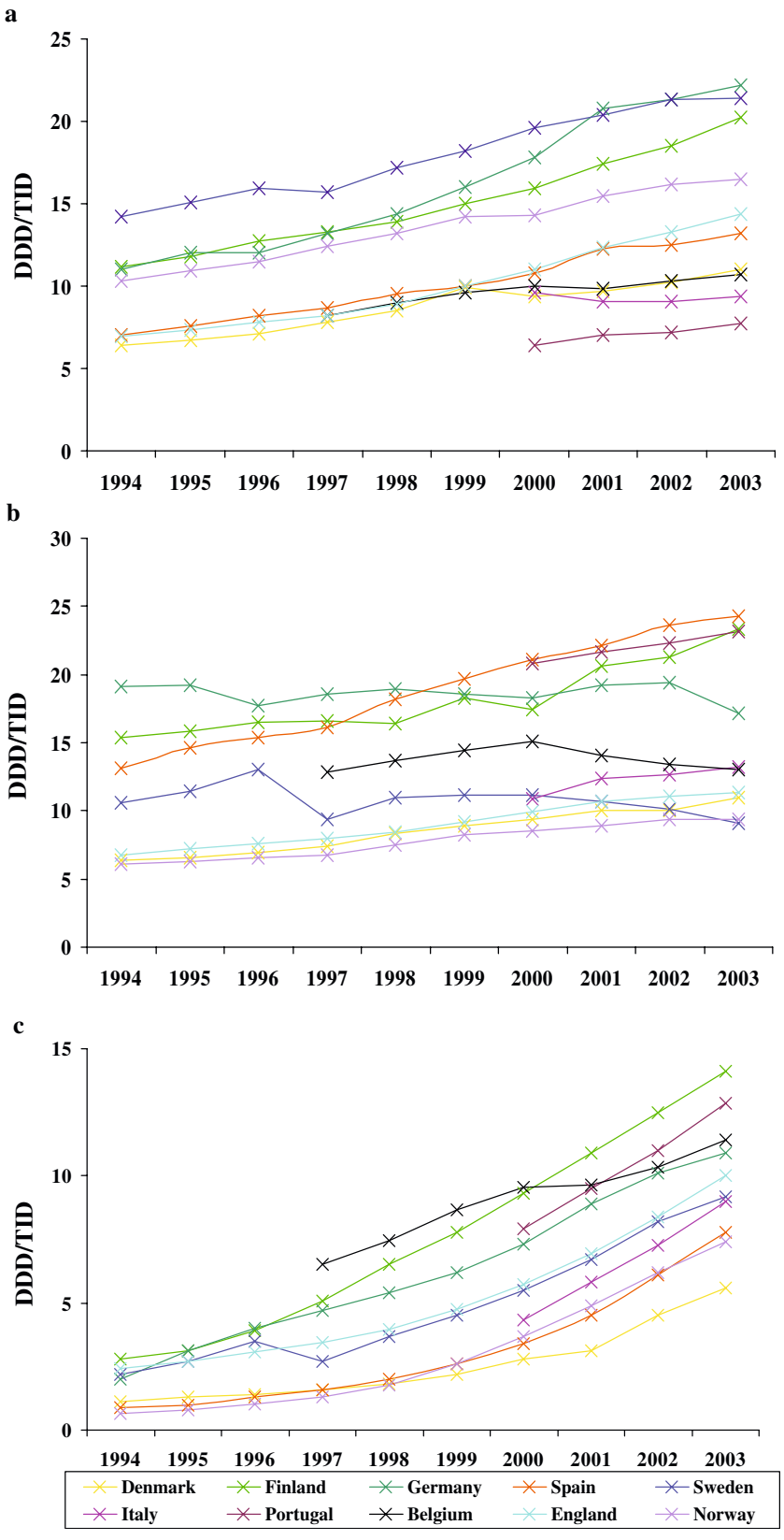

Fig. 1a–c Secular development of the utilisation of the AHGDs insulin (**a**) sulfonylureas (**b**) and biguanides/metformin (**c**) in ten European countries, expressed as defined daily doses per 1,000 inhabitants per day (DDD/TID)

Large between-country differences in AHGD utilisation levels

Insulin

Up to 2000, insulin utilisation was highest in Sweden (Fig. 1a). Utilisation in Germany, Sweden and Finland subsequently approached similar levels. In 2003, these countries were followed, in descending order, by Norway, England, Spain, Belgium, Denmark, Italy and Portugal, with insulin utilisation in Portugal only one-third that in Germany.

Oral AHGDs

Sulfonylurea and metformin made up the bulk of oral AGHD utilisation; utilisation of acarbose, glinides and thiazolidenediones (glitazones) was low or nil in most countries; therefore, no data on the latter drug groups are presented.

Sulfonylureas

Germany had the highest sulfonylurea utilisation up to 1998 (Fig. 1b), after which time it was surpassed by Spain, Portugal and Finland. These four countries were followed by Belgium, Italy, Denmark, England, Norway and Sweden; the 2003 levels in the latter two countries were less than half those in Spain, Portugal and Finland.

Biguanides (metformin)

Metformin was the sole biguanide in use, apart from in Italy, where buformin and phenformin were also available. In 2003, the highest level of metformin (biguanide) utilisation (Fig. 1c) was recorded in Finland and the lowest in Denmark, with levels in Portugal, Belgium, Germany, England, Italy, Sweden, Spain and Norway in between these two.

Large difference in utilised proportions of insulin and oral AHGDs

When the utilisation of each AHGD was calculated as a proportion of the total for each country (Fig. 2), Sweden had the highest (>50%) and Portugal the lowest (<20%) utilisation of insulin; Spain and Portugal the highest (>50%) and Sweden and Norway the lowest (<30%) sulfonylurea utilisation, and Belgium and Portugal the highest (>30%) and Spain the lowest (<20%) utilisation of metformin.

Large difference in the proportion of users and in mean purchased daily doses

Among the Finnish population, there were about 60, 120 and 80% more users of AHGDs (all), insulin and oral AHGDs, respectively, than in Denmark (Table 1). In addition, the mean purchased daily doses of glibenclamide and metformin were ≥20% higher in Finland, whereas the mean purchased daily doses of insulin hardly differed (Table 1).

Differences mainly related to subjects >45 years of age

In Sweden and Denmark (Table 2), among younger subjects (<45 years), insulin utilisation was similar and oral AHGD utilisation was very low. In those aged ≥45 years; however, both insulin and oral AHGD utilisation were twice as high in Sweden as in Denmark.

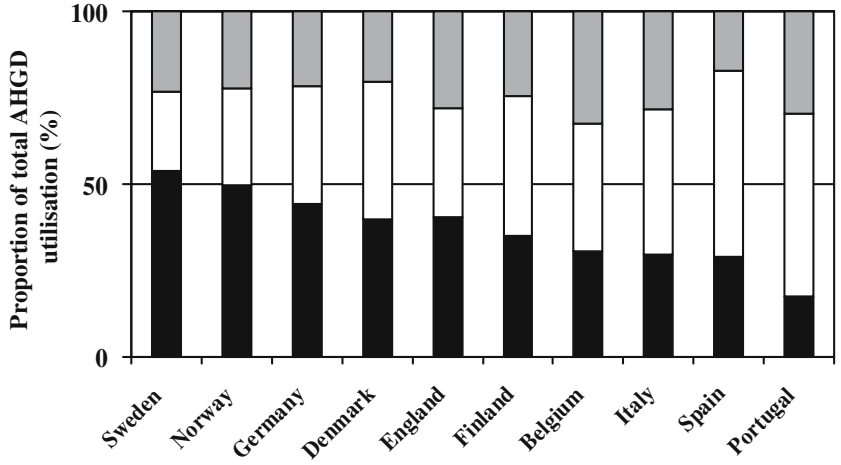

Fig. 2 Utilisation (2003) of insulin (*black bars*), sulfonylureas (*white bars*) and biguanides/metformin (*grey bars*) in ten European countries expressed as proportions of total AHGD utilisation for each country

Table 1 Differences in the proportion of users and in mean purchased doses of AHGDs between the total populations of Denmark and Finland in 2000

	Denmark	Finland
Users of AHGDs (percentage of entire population)		
All AHGDs	1.96	3.15
Insulin	0.79	1.76
Oral AHGDs	1.31	2.40
Mean purchased dose		
Insulin	47.4 IU	48.8 IU
Glibenclamide	6.13 mg	7.43 mg
Metformin	1.15 mg	1.43 mg

In 2000, Denmark and Finland were the only two countries with individual-based drug registers, allowing calculation of number and proportion of users

Discussion

The ubiquitous increase in AHGD utilisation, especially of metformin, seems a rational consequence of the increasing prevalence of type 2 diabetes and the results of the UKPDS [1, 2]. On the other hand, the levels and rates of increase differed greatly even between neighbouring countries. Differences in diabetes prevalence might explain some of these differences, and a previous comparison between eight municipalities in Sweden indicated a close correlation between total AHGD utilisation and detected diabetes prevalence [10]. However, it is uncertain whether the observation that the proportion of the population using AHGDs is 50% higher in Finland than in neighbouring Denmark (Table 3) reflects a difference in true or detected diabetes prevalence, or in therapeutic traditions. The fact that the mean doses of oral AHGDs were higher in Finland infers that different habits and attitudes concerning the management of type 2 diabetes may contribute.

Effective in 1997, Sweden changed the reimbursement of AHGDs; while reimbursement of insulin remained at 100%, that of oral AHGDs was reduced. This probably explains why, in Sweden, the 1997 utilisation of total AHGDs, oral AHGDs, sulfonylurea and biguanides, but not that of insulin, was reduced. This also emphasises that differences in reimbursement systems may help explain some of the between-country differences.

The assumption that most of the differences in AHGD utilisation relate to type 2 diabetes is strengthened by the comparison between Denmark and Sweden, which revealed no differences in the utilisation of insulin or oral AHGDs in those aged <45 years (i.e. predominantly type 1 diabetes) but differences of 100% among those aged ≥45 years (i.e. predominantly type 2 diabetes), with the higher rates seen in Sweden.

As the prevalence of type 2 diabetes increases with age, part of the between-country differences in AHGD utilisation might result from differences in mean life expectancy. However, if this were a predominant reason, total AHGD utilisation in Sweden should have been among the highest, which was not the case.

The large differences in utilisation, both in terms of the amounts and proportions of the various AHGDs, even between neighbouring countries are more difficult to explain than the general increase and suggest considerable variations in attitudes and habits with regard to the management of type 2 diabetes. A most important issue to be investigated in future studies is whether the recorded differences in AHGD utilisation have consequences in terms of differences in glucose control and in diabetes complications.

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Duality of interest None of the authors know of any duality of interest relating to this study.

Table 2 Age-related differences in utilisation of insulin and oral AHGDs between the neighbouring regions of East Denmark and Scania, south Sweden

Age group (years)	Insulin use (DDD/TID)		Oral AHGD use (DDD/TID)	
	Denmark	Sweden	Denmark	Sweden
0–14	2	3	0	0
15–44	8	9	0.5	2
45–64	16	30	28	48
≥65	7	22	20	42

DDD/TID: defined daily doses per 1,000 inhabitants per day

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