

Use of statins in patients receiving oral blood glucose-lowering drugs

Hanne Strøm, Solveig Sakshaug and Svetlana Skurtveit

Norwegian Institute of Public Health, Department of Pharmacoepidemiology, Oslo, Norway

ABSTRACT

Objectives: The aim was to study the prevalence of co-medication of statins in patients receiving oral blood glucose-lowering drugs by age and gender. **Method:** Treatment with oral antidiabetics was used as a surrogate endpoint for the presence of type 2 diabetes. Data on patients with at least one prescription of oral antidiabetics in the period 2004-2006 were retrieved from the Norwegian Prescription Database (NorPD). Information on dispensation of statins in the same calendar year was also obtained. Long-term users of oral antidiabetics were defined as patients filling a prescription of these drugs the year prior to the year of observation. **Results:** In 2006, a total of 76 288 users of oral blood glucose-lowering drugs were registered as long-term users. 57.0% men and 49.7% women of long-term users received a statin. 15 646 patients were new users of oral antidiabetics in 2006. 45.5% men and 34.9% women of new users received a statin. The proportion of statin users increased with age and was higher in men than in women in all age groups. An absolute increase of 3% from 2005 to 2006 was observed in the proportion of use of statins in both long-term users and new users of oral antidiabetics. **Conclusions:** In 2006, 54% of long-term users and 40% of new users of oral blood glucose-lowering drugs also received statins; these proportions were an increase from 2005. Men were more likely to receive statins than women which can reflect that, in the general population, the overall cardiovascular risk in men is higher than in women.

INTRODUCTION

In 2006, the one-year prevalence of drug-treated diabetes mellitus in Norway was 2.7%, representing approximately 125 000 individuals (www.norpd.no). Both type 1 and type 2 diabetes mellitus are associated with increased risk of coronary heart disease, and prevention of cardiovascular disease (CVD) is an important issue.¹ Studies have shown that type 2 diabetes patients, with no myocardial infarction, have a risk of infarction similar to that of nondiabetic patients with a prior myocardial infarction.² There is increasing evidence that statin therapy should be considered in patients with diabetes.³ International guidelines recognise the increased cardiovascular risk in patients with type 2 diabetes and endorse the use of statins in adult patients with type 2 diabetes with CVD, as well as without CVD if their total cholesterol is > 3.5 mmol/L.⁴ According to recommendations from the Norwegian Medicines Agency, all type 2 diabetes patients should receive statins.⁵ Little information is available regarding the extent of use of oral antidiabetics in combination with statins in Norway. The aim of the present study was to investigate the prevalence of co-medication of statins in patients receiving oral blood glucose-lowering drugs by age and gender in 2005 and 2006.

MATERIALS AND METHODS

Norwegian Prescription Database (NorPD)

Data were retrieved from the Norwegian Prescription Database (NorPD) covering the entire population in

Norway (4.7 million inhabitants). As of 1 January 2004, all pharmacies in Norway were obliged to submit electronic prescription data to the Norwegian Institute of Public Health. The NorPD contains information from all prescriptions dispensed from Norwegian pharmacies to individual patients living outside institutions.⁶

Study population

Treatment with oral antidiabetics was used as a surrogate endpoint for the presence of type 2 diabetes. In the period 2004-2006, data on patients with at least one prescription of oral blood glucose-lowering drugs, (i.e. drugs in ATC group A10B⁷), were retrieved from NorPD. Information on dispensation of statins (ATC group C10AA) in the same calendar year was also obtained, together with gender and age. Long-term users were defined as patients filling a prescription of oral antidiabetics the year prior to the year of observation. New users were defined as individuals who had no oral antidiabetics dispensed during a 12-month period prior to the observation year.

RESULTS

Table 1 shows the number of total users, long-term users, and new users of oral blood glucose-lowering drugs, and the proportion of patients also receiving a statin according to gender in 2005 and 2006. The number of users of oral antidiabetics <40 years of age was low, accounting for only 6% of the total number of users. In 2006, a total of 76 288 users of oral blood

Table 1. Total number of users of oral blood glucose-lowering drugs in 2005 and 2006. Number of long-term users and new users of oral blood glucose-lowering drugs and proportions (%) of patients receiving statins. Data from the Norwegian Prescription Database analyzed according to gender.

	2005			2006		
	Women	Men	Total	Women	Men	Total
Total number of users of oral blood glucose-lowering drugs	40355	44662	85017	43395	48539	91934
Number of users <40 year of age	3277	1544	4818	3564	1644	5208
Number of long-term users of oral blood glucose-lowering drugs	33150	37431	70581	35669	40619	76288
Proportion (%) of long-term users receiving statins	46.4	54.1	50.5	49.7	57.0	53.6
Number of new users of oral blood glucose-lowering drugs	7205	7231	14436	7726	7920	15646
Proportion (%) of new users receiving statins	31.8	43.1	37.4	34.9	45.5	40.3

glucose-lowering drugs were registered as long-term users and 15 646 persons were registered as new users. Among long-term users, 57.0% men and 49.7% women received a statin, while 45.5% men and 34.9% women received a statin among new users. From 2005 to 2006 there was an absolute increase of 3% in the use of statins in patients receiving oral antidiabetic treatment. This trend was observed in both long-term and new users.

Figure 1 shows the proportion of co-medication of statins and oral blood glucose-lowering drugs by age and gender in long-term and new users in 2006. Table 2 gives an overview of the numbers of users in each group. In women, the proportion of statin users increased with age up to 80+ in both long-term and new users of oral antidiabetics. In men, the proportion of statin users increased up to 70 years of age in both groups. The proportion receiving statins was higher in men than in women for all age groups in both long-term and new users of oral blood glucose-lowering drugs. One exception was the age group 70-79 years, where the proportions of statin users were similar for men and women. In the long-term user group, 60% men and 53% women received a statin in the age group 50-59 years.

DISCUSSION

In 2006, over 76 000 persons were registered as long-term users of oral antidiabetics. Approximately half of them also received statins. Previous studies in Norway have found that in all age groups >40 years the prevalence of oral blood glucose-lowering therapy is higher in men than in women.⁸ Our study confirms that men are more likely to be exposed to oral antidiabetics than women. It is well known that in the general population the risk of coronary heart disease is higher in men than in women. Thus, in the age groups >40 probably more diabetic men than women have established CVD (e.g.; previous myocardial infarction). However, women with diabetes seem to lose their relative CVD protection as compared with men.⁹ A study concludes that the overall relative risk of fatal CVD among people

with and without diabetes was significantly greater among women with diabetes than among men with diabetes.¹⁰ Thus, when considering statin therapy in adult patients with type 2 diabetes, gender may be a less important factor. The proportion of co-medication of statins and oral blood glucose-lowering drugs was lower in new users than in long-term users in both men and women. This can indicate that the physicians prescribe statins to those considered to be at high risk of CVD.

A limitation of the study is that clinical characteristics of the patients were unknown. We had no information confirming whether or not there was an established CVD. Patients receiving oral blood glucose-lowering drugs most likely have type 2 diabetes. However, in the age groups 20-29 and 30-39 women with polycystic ovary syndrome could be treated with insulin-sensitizers (metformin or thiazolidindiones).¹¹ The total number of users of blood glucose-lowering drugs for those <40 years of age was low. Thus, the low proportions of statin users in the age groups <40 did not influence the overall results.

We only looked at the use of oral blood glucose-lowering drugs in combination with statins. Thus, the identified users of oral antidiabetics and statins could have received other cardiovascular drugs. This is a possible way forward to separate primary prevention therapy with statins from secondary prevention therapy which will be further investigated.

The strength of this study is its high quality data achieved by using a population-based registry allowing complete medication history of each patient not affected by recall bias.

Even though both international and national guidelines recommend using statins in type 2 diabetes patients, our study indicates that this is not always applied in clinical practice. Physicians make an overall cardiovascular risk assessment also in type 2 diabetes patients before statin therapy is initiated. Thus, type 2 diabetes does not seem to be a valid indicator alone for the use of statins. Established CVD or other risk factors are certainly taken into consideration. In Norway, different recommendations concerning the use of

Table 2. Total number of new and long-term users of oral blood glucose-lowering drugs and numbers using statins in 2006. Data from the Norwegian Prescription Database according to gender and age.

Age	Number of long-term users				Number of new users			
	Men		Women		Men		Women	
	Total	Statin users	Total	Statin users	Total	Statin users	Total	Statin users
0-9	2	0	2	0	0	0	0	0
10-19	11	1	55	0	10	0	73	0
20-29	79	16	479	22	88	12	588	9
30-39	993	331	1422	208	461	105	945	57
40-49	3751	1738	2725	978	1191	415	880	208
50-59	9088	5426	5749	3040	2011	925	1354	590
60-69	12049	7711	8176	5005	2153	1184	1483	749
70-79	9348	5797	9009	5562	1309	696	1384	750
80+	5298	2125	8052	2928	697	266	1019	335

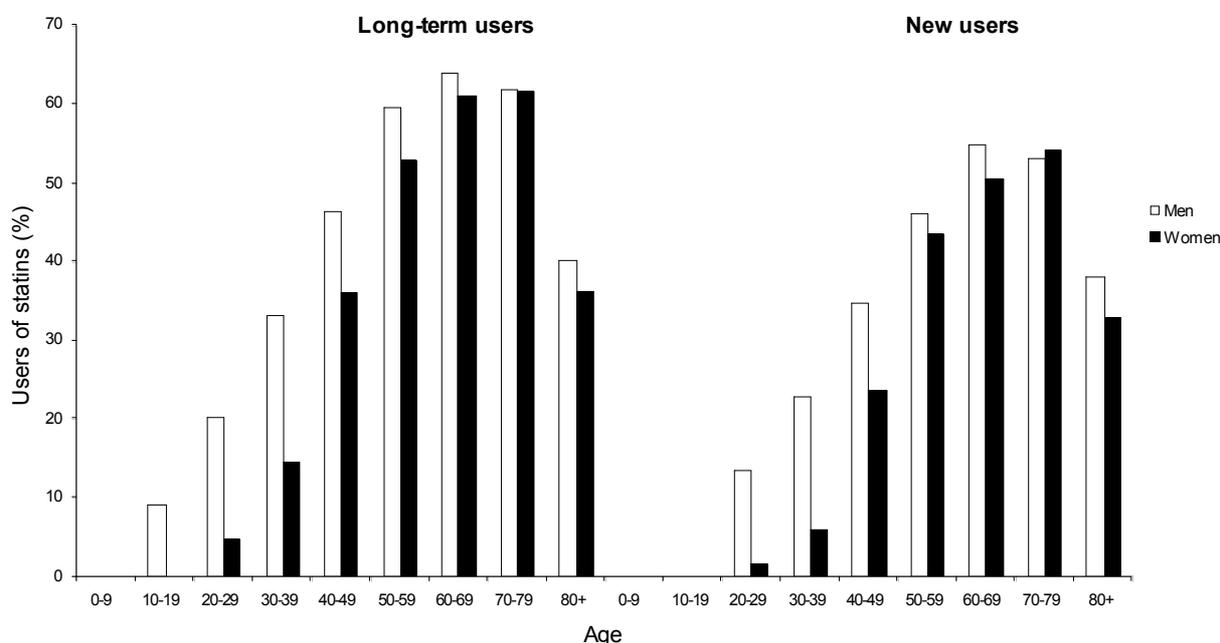


Figure 1. Proportion of patients receiving statins in 2006 among long-term and new users of oral antidiabetics. Data from the Norwegian Prescription Database analysed by gender and age.

statins in type 2 diabetes patients exist and may be a reason for our findings.¹² Adverse drug reactions could also explain why statin therapy has to be avoided in some patients. In Norway, new clinical practice guidelines concerning the use of lipid lowering drugs for primary prevention of CVD are under development and are expected to be published in 2008. A recent Danish study concludes that all patients ≥ 30 years of age with diabetes who require glucose-lowering therapy should also receive primary prevention for CVD, regardless of other risk factors, sex, or type of diabetes mellitus.¹³ Thus, further investigations will be initiated

to study the prevalence of co-medication of statins in both insulin users and users of other blood glucose-lowering drugs.

In conclusion, only 54% of long-term users and 40% of new users of oral glucose-lowering drugs received statins in 2006. These proportions represented an increase from 2005. The findings may indicate that the prescribing practice in this patient group differs and could be improved. Men were more likely to receive co-medication with statins than women, which can reflect that, in the general population, the overall cardiovascular risk in men is higher than in women.

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