SCIENTIFIC LETTER

Long term persistence with statin treatment in daily medical practice

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Statin treatment is a safe and effective method of reducing cardiovascular events in both primary and secondary prevention.[1 2] Persistence with statin use in trials is generally high. Analysis of the WOSCOPS (west of Scotland coronary prevention study) showed that the efficacy of pravastatin depends on compliance. Although long term persistence with statin treatment in elderly patients has been studied,[3 4] little is known about long term persistence in the general population including all age categories and both primary and secondary prevention. The aim of this study was to assess long term persistence with statin use in the general Dutch population and to identify the determinants of failure to persist with these drugs.

METHODS

We used data from the PHARMO medical record linkage system including drug dispensing records from community pharmacies and hospital discharge records of 865 000 subjects in the Netherlands. Clustering pharmacies within PHARMO areas results in drug dispensing histories containing $>$ 95% of all prescriptions dispensed to a particular patient.

Persistence was assessed for all new users of statins (not receiving any statin for at least two years before being prescribed the first statin) during 1998–2002. Cerivastatin was withdrawn from the market and so patients receiving cerivastatin were excluded. Episodes of statin use were constructed for each patient. In cases of interruptions of $<$ 45 days between two prescriptions, the episode was considered uninterrupted. Patients may have more than one treatment episode in their life. Switching between different statins was allowed in the analysis of statins as one group, but not in the analysis of individual statins (this would mean discontinuation of that treatment episode and the start of a new episode). Follow up lasted two years after the start of treatment.

Determinants of persistence in the first episode were assessed using the Cox proportional hazard analysis. Characteristics noted at the index date included age, sex, and type of statin. Previous use of antihypertensive drugs, antidiabetic drugs, and psychotropic drugs was established in the year before the index date. A chronic disease score was calculated based on pharmacy records. Linked hospital discharge records were used to assess previous hospitalisation for ischaemic heart disease (ICD-9-CM codes 410–414) two years before the index date. Statin potency at the index date was based on achievable reductions in total cholesterol, and ranged from 1 (−12%) to 7 (−42%).[5] Differences between statin potency was assessed using the Student's *t* test.

RESULTS

We selected 8335 new users of statins who had started 9962 episodes of statin use; switching between statins was allowed. Persistence was 61.5% at one year, decreasing to 46.5% by two years. There was a notable difference in persistence between first episodes (one year 63.7%, two years 48.5%) and following episodes (one year 50.1%, two years 35.9%). In primary prevention, only 47.7% of patients were still undergoing statin treatment after two years of follow up (first episodes only). In patients hospitalised for ischaemic heart disease in the two years before the start of statin treatment, persistence was 57.7%.

Persistence with statin use was lower in the younger age group and also in patients with a history of psychotropic drug use (table 1), whereas persistence was higher in patients who had previously used antihypertensive drugs or were previously hospitalised for ischaemic heart disease. Compared to new users of simvastatin, new users of atorvastatin had a lower risk of discontinuing drug use (relative risk (RR) 0.90, 95% confidence interval (CI) 0.83 to 0.96), whereas new users of fluvastatin had a higher risk of discontinuing drug use (RR 1.27, 95% CI 1.12 to 1.39). We observed no difference between new users of pravastatin and new users of simvastatin (RR 0.99, 95% CI 0.91 to 1.08). The mean potency of simvastatin and pravastatin is comparable (3.6 and 3.3, respectively), but is lower for fluvastatin (2.4, $p < 0.05$) and higher for atorvastatin (4.4, $p < 0.05$). Higher potency was associated with a lower risk of discontinuation (crude RR 0.90 per unit, 95% CI 0.87 to 0.93). Adjustment for potency slightly changed the relative risk for atorvastatin (RR 0.93, 95% CI 0.86 to 1.01) and for fluvastatin (RR 1.20, 95% CI 1.07 to 1.33). All other estimates remained unchanged (data not shown).

DISCUSSION

This large population based study demonstrates that persistence with statin treatment decreases after two years in daily medical practice and also identifies predictors of failure to persist. These results are in line with previous studies showing discontinuation rates ranging from 15–60% and identifying several similar determinants. Two recent studies in elderly patients showed relatively low persistence rates.[3 4] In our study, elderly patients ($\geq$ 65 years of age) had a lower risk of failure to persist than patients $<$ 45 years of age.

We observed a notable difference in persistence between statins, which could in part be explained by the difference in potency of the statins. Patients treated with atorvastatin received the highest potency statin and are therefore most likely to attain treatment goals, whereas the opposite is true for fluvastatin. Adverse drug effects may also partially explain the discontinuation rates observed in this study, but statins are usually well tolerated and in clinical trials withdrawal because of adverse effects was rare. The occurrence of other previously suggested reasons for discontinuation including conversion to non-statin treatment,

Table 1 Crude and adjusted relative risks (RR) obtained from Cox regression analyses predicting failure of new users to persist with statin treatment after two years.

	Crude RR	95% CI	Adjusted* RR	95% CI
Characteristics at index date				
Sex				
Male	1		1	
Female	0.98	0.93 to 1.04	1.01	0.95 to 1.07
Age group (year)				
0–44	1		1	
45–64	0.83	0.76 to 0.92	0.84†	0.76 to 0.93
⩾65	0.81	0.73 to 0.89	0.82†	0.74 to 0.91
Type of statin				
Simvastatin	1		1	
Atorvastatin	0.90	0.84 to 0.97	0.90†	0.83 to 0.96
Fluvastatin	1.23	1.13 to 1.34	1.27†	1.12 to 1.39
Pravastatin	0.98	0.91 to 1.06	0.99	0.91 to 1.08
Characteristics 1 year before index date				
Antihypertensive treatment				
No	1		1	
Yes	0.87	0.82 to 0.93	0.91†	0.85 to 0.98
Psychotropic agents				
No	1		1	
Yes	1.11	1.04 to 1.18	1.13†	1.06 to 1.20
Antidiabetic drugs				
No	1		1	
Yes	1.02	0.95 to 1.10	1.05	0.97 to 1.14
‡Chronic disease score				
0–1	1		1	
2–4	0.92	0.86 to 0.99	0.99	0.91 to 1.07
>4	0.89	0.83 to 0.96	0.96	0.88 to 1.05
Hospitalisation for ischaemic heart disease in 2 years before index date				
No	1		1	
Yes	0.76	0.68 to 0.85	0.78†	0.70 to 0.88

*Adjusted for all variables listed.
†Significantly different from reference category; RR >1 indicates that the variable increases failure to persist on statin treatment; RR <1 indicates that the variable decreases failure to persist on statin treatment.
‡Chronic disease score: 0–1, no or minimal co-morbidity; 2–4, low and average co-morbidity; >4, high co-morbidity.

or filling prescriptions elsewhere is unusual, and there are no indications for differential occurrence between statins.[4] Discontinuation because of financial reasons is also unlikely as the cost of statin treatment is reimbursed to every patient without co-payment in the Netherlands.

The clinical implications of our findings are significant. In primary prevention, the number of patients needed to be treated (NNT) for five years with a statin to prevent one case of fatal or non-fatal myocardial infarction would increase from 57[2] to 85, if persistence in daily medical practice is taken into account. Similarly, in secondary prevention the NNT would increase from 20[1] to 30. As we used two year persistence rates in daily medical practice instead of five year persistence rates for these estimates, the actual increase in the NNT might be even larger, resulting in lower cost effectiveness in daily medical practice.

In conclusion, persistence with statin treatment is low in daily medical practice compared with clinical trial settings. The medical and economical consequences may be considerable. Optimisation of statin use in those most benefiting from lipid lowering treatment is needed. This includes increasing treatment for hypercholesterolaemia, encouraging persistence with current statin treatment, and optimising statin dosage.

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