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HMG-CoA-reductase inhibitors and decreased libido

Introduction

Pravastatin (Selectine®) is a hydroxymethylglutaryl-coenzyme-A-reductase (HMG-CoA-reductase) inhibitor and has been approved for the Dutch market in 1990 for the indication hypercholesterolaemia. The most severe adverse drug reactions of pravastatin and other HMG-CoA-reductase inhibitors are myopathy and disturbances in hepatic function. Other adverse drug events mentioned in the SPC are gastrointestinal complaints, chest pain, fatigue, headache, dizziness, respiratory tract infections and rash. The SPC of atorvastatin also mentions impotence as an infrequently occurring adverse drug reaction [1-5].

Reports

Lareb received a report of a decrease in testosterone levels and loss of libido in suspected association with the use of pravastatin. This 54-years-old male developed loss of libido shortly after starting pravastatin indicated for hypercholesterolaemia. During therapy his testosterone level was 5.8 mmol/l (morning value). Pravastatin was discontinued after seven months, where after the man's libido quickly returned to normal. Four months later, his testosterone level was determined again and had risen to 22.8 mmol/l (morning value).

Lareb received four additional reports of decreased libido or impotence in suspected association with the use of pravastatin and a total number of 33 reports of decreased libido, impotence or decreased erection in suspected association with the other HMG-CoA-reductase inhibitors simvastatin (Zocor®), atorvastatin (Lipitor®), fluvastatin (Canef®, Lescol®)(table 1). All but one patient, who reported sexual dysfunction, were men. The mean age was 53 years.

Table 1. Reports of sexual dysfunction associated with the use of HMG-CoA-reductase inhibitors

Adverse drug event	pravastatin	simvastatin	Atorvastatin	fluvastatin
Impotence	3	14	4	1
Libido decreased	2	2	3	-
Erection decreased	-	2	5	-

Other sources of information

Literature

In literature erectile dysfunction is associated with the use of HMG-CoA-reductase inhibitors [6]. Furthermore, Azzarito et al. investigated the effect of prolonged simvastatin treatment on free testosterone and total testosterone level. They found a mild, but significant decrease of both basal and hCG-stimulated free testosterone levels [7].

Databases

The WHO database contains significant associations of impotence and decreased libido for all in the Netherlands approved HMG-CoA-reductase inhibitors (table 2).

Table 2. Reports of sexual dysfunction associated with the use of HMG-CoA-reductase inhibitors in the database of the Uppsala Monitoring Centre (WHO).

Libido decreased	Impotence

	ROR (95%-CI)	Number of reports	ROR (95%-CI)	Number of reports
pravastatin	2.06 (1.36-3.14)	22	2.74 (2.14-3.51)	64
simvastatin	2.46 (1.97-3.06)	80	3.99 (3.54-4.50)	277
atorvastatin	1.61 (1.14-2.28)	32	2.64 (2.21-3.16)	123
fluvastatin	2.22 (1.19-4.13)	10	3.44 (2.45-7.83)	34

Mechanism

Cholesterol is necessary for biosynthesis of steroid hormones. Testes derive cholesterol from two sources: de novo synthesis and uptake of plasma lipoproteins, especially LDL. Since HMG-CoA-reductase inhibitors reduce total cholesterol and LDL levels, they could interfere with steroid production [7]. Low testosterone levels decrease sex drive and erectile function [8].

Conclusion

The reports in the Lareb database indicate that sexual dysfunction may be an adverse drug reaction of the HMG-CoA-reductase inhibitors. Moreover, this might be the result of a decrease in testosterone levels. Literature data and the UMC database support this association.

References

1. Dutch Summary of Product Characteristics of Selektine®. www.cbg-meb.nl (access date 12-12-2002).
2. Dutch Summary of Product Characteristics of Zocor®. www.cbg-meb.nl (access date 12-12-2002).
3. Dutch Summary of Product Characteristics of Lipitor®. www.cbg-meb.nl (access date 12-12-2002).
4. Dutch Summary of Product Characteristics of Canef®. www.cbg-meb.nl (access date 12-12-2002).
5. Dutch Summary of Product Characteristics of Lescol®. www.cbg-meb.nl (access date 12-12-2002).
6. Rizvi K, Hampson J and Harvey JN. Do lipid-lowering drugs cause erectile dysfunction? A systemic review. Fam Pract 2002;19(1):95-8.
7. Azzarito C, Boiardi L, Vergoni W, Zini M and Portioli I. Testicular function in hypercholesterolemic male patients during prolonged simvastatin treatment. Horm Metab Res 1996;28(4):193-8
8. Van Dyck R and Gunning WB. Psychiatrie. In: Eyskens E et al. Codex Medicus. 10th Ed.1996. Elsevier Arnhem.