Prescribing...

For Statin Intolerance Nov/ Dec 2019

- Statins are first-line therapy for LDL-C reduction.
- Rates of side effects in clinical practice are higher than in trial participants.
- This bulletin summarises advice from Southampton on the care of patients who are intolerant of statins.
- All of the statins and ezetimibe are now off patent.
- Up to date guidelines on the whole management on lipid modification were published in August by NICE.

Background

Rates of side effects reported in statin trial participants are frequently lower than in studies of real life patients. This has puzzled all concerned for many years. It may be due to the study designs or for some other unknown reason(s). Clinical trials frequently have lead-in periods of some weeks, after which only people who respond to and/or can tolerate one or both of the drugs are retained in the study. Because so many paople take statins, over 8,500 islanders, the number of people affected is not insignificant and a consistent approach to required.

The most common adverse effects of statins are as follows

- Myalgia – muscle ache or weakness without creatine kinase (CK)
- Myositis - muscle ache or weakness with CK elevation
- Rhabdomyolysis - muscle ache or weakness with CK elevation > 10 upper limit normal
- Elevation in liver transaminases

How should statin intolerance be managed ?

NICE gives general advice on this topic. Southampton recommends that if the patient is taking the statin for primary prevention the need for the drug should be reassessed. The decision should be based on risk assessment and not on LDL cholesterol levels only. The use of other interventions to lower CVD risk should be optimised. Lifestyle modification – smoking, diet (refer patient to Heart UK website), weight reduction and exercise are **first line interventions** which should be recommended to **all patients**. Blood pressure control should be optimal and treatment started according to the NICE Guidance on Lipid Modification. Hypothyroidism and excessive alcohol ingestion should be excluded as possible causes.

Explaining the absolute risks and benefits of treatment is imperative. The concept of numbers needed to treat is understood by most people and is highly recommended. The absolute benefit of statins in primary prevention is an important piece of information to advise patients on. Over **5 years**, the NNT to prevent **one fatal or non-fatal CV event is 49**, **for combined fatal and non-fatal stroke it is 155** and **for all-cause mortality it is 138.**

A large number of drugs may increase the risk of muscle problems in patients taking statins. This includes but is not limited to; the azole antifungals (itraconazole, ketoconazole and fluconazole), macrolides (erythromycin and clarithromycin), calcium channel blockers (diltiazem and verapamil), many protease inhibitors for HIV, ciclosporin, the fibrates (gemfibrozil, fenofibrate, bezafibrate), as well as warfarin, amiodarone, niacin and grapefruit juice.

What next ?

If a patient presents with symptoms that are suspected to be due to statin intolerance, Southampton recommends the following:

- The statin should be stopped for a 4 week "washout" period.
- For primary prevention switch/remain on atorvastatin and start at **10 mg/wk** increasing frequency of dosing (on a weekly basis) to twice weekly, three times weekly and then daily as tolerated. If tolerated increase to atorvastatin **20 mg weekly** increasing frequency of dosing (on a weekly basis) to twice weekly, three times weekly and then daily as tolerated.
- Stop at maximally tolerated dose. If unable to tolerate any dose of atorvastatin then prescribe ezetimibe 10 mg daily.
- For secondary prevention switch to **rosuvastatin 5 mg weekly** increasing frequency of dosing (on a weekly basis) to twice weekly and then three times weekly as tolerated. If tolerated increase to **rosuvastatin 10 mg weekly** increasing frequency of dosing (on a weekly basis) to twice weekly and then three times weekly as tolerated. If tolerated increase to rosuvastatin 20 mg weekly increasing frequency of dosing (on a weekly basis) to twice weekly and then three times weekly and finally daily as tolerated.
- Stop at maximally tolerated dose. If the final dose is below 20 mg three times weekly add ezetimibe 10 mg daily.

What about the cost ?

The cost of providing lipid-lowering therapy for the islands is now more than three quarters of million pounds less than it was in 2010 (£1.05 million vs £250K). The cost of 28 days treatment of most strengths of rosuvastatin and atorvastatin, and ezetimibe is about £2 or less.

Which drug ? What dose ?

In August of this year NICE updated its guidelines on Lipid Modification. This contains the most up-to-date information on risk assessment, drug choice strength etc etc in different scenarios. The guideline is available at the following link **https://cks.nice.org.uk/lipid-modification-cvd-prevention**.

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