FORTH VALLEY

LIPID LOWERING GUIDELINE v5 2016

This guideline applies to people over 16 years of age. This guideline is not intended to serve as a standard of medical care or be applicable in every situation. Decisions regarding the treatment of individual patients must be made by the clinician in light of that patient's presenting clinical condition and with reference to current good medical practice.

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General Points

National lipid modification guidelines vary considerably. The majority of recommendations in this guidance are taken from NICE CG181 Lipid Modification 2014 with the following differences –

- For primary prevention of CVD a threshold of 20% 10 year risk, in line with Scottish national recommendation, is recommended for consideration of statin therapy rather than the 10% 10 year risk suggested by NICE. Analysis of our Keep Well database in 2014 with over 12,000 patients age 40-65 showed 11% with ASSIGN score >20 and 44% with ASSIGN score >10.
- The recommended risk assessment tool in Scotland is ASSIGN rather than the QRISK2 tool recommended by NICE. In addition the JBS3 tool may be considered to illustrate lifetime risk and effect of modification of risk factors.
- Recommendations for those with diabetes are simplified but agreed with the local diabetes team.

Cholesterol measurement

- Total Cholesterol and HDL-C are readily measured
- LDL-C is calculated using the Friedewald equation
- LDL-C constitutes 60-70% of total cholesterol
- HDL-C is 5-10% lower in the fasting state
- Triglycerides are 20-30% higher in the fasting state

General Treatment

All guidelines agree on the fundamental importance of lifestyle modification and addressing all modifiable risk factors.

Statin Treatment

- Statin treatment gives a RRR for CV event of 34% in primary prevention, 30% in secondary prevention.
- Every 1mmoll reduction in LDL-C is associated with a 22% reduction in CV mortality and morbidity
- All guidelines recommend reduction to maximum tolerated dose if optimal dose not tolerated.

PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE (CVD)

All adults from 40 years onwards should have their CVD risk reviewed on an ongoing basis.

CVD risk assessment tools provide only an approximate value for CVD risk. The recommended risk assessment tool in Forth Valley is ASSIGN. The JBS3 assessment tool may also be helpful as it includes a lifetime risk assessment and illustration of modification of risk factors.

CVD risk assessment tools should not be used for those with established CVD, diabetes or CKD.

Before starting lipid modification therapy for primary CVD prevention –

- Discuss with the patient the risks and benefis of statin treatment considering potential benefits from lifestyle modification, co-morbidities, polypharmacy, general frailty and life expectancy
- Optimize adherence to diet and lifestyle measures considering smoking status, alcohol consumption, blood pressure control and BMI.
- Take at least one lipid sample to measure a full lipid profile
- Exclude or treat common secondary causes of dyslipidaemia including excess alcohol, hypothyroidism, liver disease and nephrotic syndrome.
- Consider the possiblilty of familial hypercholesterolaemia if total cholesterol is >7.5 mmoll and there is a family history of premature coronary heart disease.
- Check LFTs
- It is not necessary to perform a fasting lipid profile or routinely check Creatine Kinase.

An ASSIGN score of >20 after diet and lifestyle measures should be considered for lipid modification therapy

For primary prevention the recommended statin is **Atorvastatin 20mg**.

A treat and forget strategy is recommended for primary prevention.

LFT should be checked before starting a statin, within 3 months of starting and at 1 year. If LFTs remain normal over that period there is no need to retest.

Standard CVD risk scores underestimate risk in several groups of patients including –

- People with serious mental health problems
- People taking medications that can cause dyslipidaemia such as antipsychotics, steroids and immunosuppresants
- Severe obesity or central obesity
- People with auto-immune disorders
- People of South Asian descent ie from the Indian sub-continent

SECONDARY PREVENTION OF CARDIOVASCULAR DISEASE

In people with established CVD commence **Atorvastatin 80mg**. Use a lower dose of atorvastatin if any of the following apply –

- Potential drug interactions
- High risk of adverse effects
- Patient preference

Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on statin treatment for secondary prevention and aim for a greater than 40% reduction in non-HDL cholesterol. If this target is not achieved –

- Discuss adherence and timing of dose
- Optimize adherence to diet and lifestyle meaures
- Consider increasing the dose if started on less than 80mg atorvastatin

Use of fibrates, nicotinic acid, bile acid sequestrants, omega-3 fatty acid compounds or ezetemibe is not routinely recommended.

Diabetes

Different national guidelines have slightly different and often complex advice regarding lipid modification in people with diabetes.
To keep guidance simple the following approach is recommended.

For type 1 and type 2 diabetes –

- Age 40 and over or
- Under 40 with additional cardiovascular risk factors
- Treat with **Atorvastatin 20mg** using a treat and forget strategy.

Chronic Kidney Disease

NICE CG181 recommends offering **Atorvastatin 20mg** for the primary or secondary prevention of CVD to people with CKD.

- Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is 30 or more.
- Agree the use of higher doses with a renal specialist if eGFR is less than 30.

Cytochrome P450 Interactions

Simvastatin and atorvastatin are metabolized by cytochrome P450 CYP3A4 and co-administration of potent inhibitors of this enzyme increases the risk of side effects including rhabdomyolysis.

MHRA (2012) gives the following advice:

Box 1

Interacting Drug	**Prescribing Advice**
HIV protease inhibitors Itraconazole Ketoconazole Posaconazole Erythromycin Clarithromycin Telithromycin Nefazodone Ciclosporin Gemfibrrozil	**Avoid simvastatin**
Other fibrates (except fenofibrate)	Do not exceed **10mg simvastatin**
Amiodarone Amlodipine Verapamil Diltiazem	Do not exceed **20mg simvastatin**
Fusidic acid	Patients should be closely monitored. Temporary suspension of simvastatin treatment should be considered.
Grapefruit juice	**Avoid grapefruit juice when taking simvastatin**

Warfarin
Care is needed when prescribing some statins to patients taking warfarin - please check the specific product information for further advice on possible interactions.

Follow-up of people started on statin treatment

Annual review is recommended. Use these reviews to discuss medicines adherence and lifestyle modification and address CVD risk factors. In secondary prevention perform an annual non-fasting blood test for non-HDL cholesterol.

Intolerance of statins

NICE classifies statins into 3 groups depending on the percentage reduction in low-density lipoprotein cholesterol they produce –

- Low intensity if the reduction is 20-30%
    - Pravastatin 10mg,20mg and 40mg, simvastatin 10mg
- Medium intensity if the reduction is 31-40%
    - Simvastatin 20mg or 40mg, Atorvastatin 10mg, Rosuvastatin 5mg
- High intensity if the reduction is above 40%
    - Atorvastatin 20mg (43%), 40mg (49%) and 80mg (55%)
    - Rosuvastatin 10mg (43%), 20mg (48%) and 40mg (53%)

If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose.

Consider the following approaches –

- Stopping the statin and trying again when the symptoms have resolved to see if they are related to the statin
- Reducing the dose within the same intensity group
- Changing the statin to a lowerintensity group

Creatine Kinase

Before starting a statin, ask the person if they have had persistent,generalised muscle pain. If they have measure creatine kinase. If creatine kinase levels are more than 5x the upper limit of normal, re-measure creatine kinase after 7 days. If creatine kinase levels are still 5 times the upper limit of normal do not start a statin. If creatine kinase levels are raised but less than 5 times the upper limit of normal start statin treatment at a lower dose. Advise people who are being treated with a statin to report muscle pain, tenderness or weakness and check creatine kinase if they do.

Liver Function Tests (LFTs)

Statins should be used with caution in those with a history of liver disease or with a high alcohol intake. Use should be avoided in active liver disease.

Baseline liver enzymes should be measured before starting a statin. Liver function (transaminases) should be measured within 3 months of starting treatment or dose changes and at 12 months, but not again unless clinically indicated.

If transaminase concentrations reach 3 times the upper limit of normal, levels should be rechecked after a 2 week period. If still elevated, reduce or stop statin. When transaminases return to normal a statin from a different class may be tried i.e. rosuvastatin (hydrophilc) if previously on simvastatin/atorvastatin (lipophilic).

Pregnancy

Statins are contra-indicated in pregnancy.
Advise women of childbearing potential of the possible teratogenic risks of statins and to stop taking them if pregnancy is a possibility.
Advise women planning pregnancy to stop statins 3 months before they attempt to conceive and not to retstart them until breastfeeding is finished.

Ezetimibe

Ezetimibe is a cholesterol absorption inhibitor with moderate cholesterol lowering affect.

Ezetemibe is only recommended by NICE in the treatment of Primary (heterozygous-familial and non-familial) hypercholesterolaemia.

Rosuvastatin

All patients must start on an initial dose of no more than 10mg rosuvastatin once daily (5mg in those aged > 70 years and those of Asian ancestry. Rosuvastatin should only be titrated to 20mg if considered necessary after a 4-week trial of 10mg daily.

The 40mg dose is contraindicated in patients with predisposing risk factors for muscular toxicity and specialist supervision is recommended if the 40mg dose is initiated.