Management of Dyslipidaemia in Primary Care

The majority of people who are found to have higher-than-desirable lipid levels and/or low levels of high density lipoprotein (HDL) will have 'polygenic dyslipidaemia', most frequently characterised by raised levels of total and low density lipoprotein (LDL) cholesterol, sometimes associated with raised very-low-density lipoprotein (VLDL) cholesterol resulting in elevated triglyceride, and/or lower-than-usual high density lipoprotein (HDL) cholesterol.

Many will respond to dietary modification and, if they are overweight or obese, weight loss. Intensity of treatment including the need for drug treatment (typically a statin) is based on assessment of overall cardiovascular risk as described in the recently updated Ministry of Health publication. (Cardiovascular Risk Assessment & Management in Primary Care).

However, it is important to consider whether a patient found to be dyslipidaemic might belong to any of the following groups, since each requires individualised management.

1. *Secondary hyperlipidaemia*

Hypothyroidism, inadequately controlled diabetes, nephrotic syndrome, chronic renal failure and a wide range of drugs (e.g. steroids, some antipsychotics, thiazide and loop diuretics, and B blockers) are some of the relatively common causes of secondary hyperlipidaemia which will resolve, or appreciably improve, with treatment of the primary condition.

Overweight or obese individuals and those who have an excessive intake of alcohol may also have raised lipid levels, typically increased triglyceride levels.

2. *Familial hypercholesterolaemia* **(FH)**

Patients with FH, one of the most common conditions associated with *autosomal dominant inheritance,* are typically at considerably greater

cardiovascular risk at any particular level of LDL cholesterol than those with a 'polygenic' dyslipidaemia. Untreated patients often have a first cardiovascular event in their 40s (or sometimes earlier) and die prematurely.

Statins have appreciably improved the outcome for such patients who should be offered intensive diets and drug treatment and follow-up.

Screening of first degree and, if possible, also second degree relatives enables early introduction of preventive measures in affected family members.

Variants of FH [1] can be identified in specialist laboratories but the following clinical features may aid diagnosis:

Raised levels of total and LDL cholesterol

(>7.5 and 4.9mmol/l in adults (>16 years), >6.7 and 4.0mmol/l in children)

PLUS

Tendon xanthomas in patient or relative

(first or second degree)

OR

Family history of early MI, in a first degree relative <60 years, or a second degree relative [2] <50 years

OR

Cholesterol or LDL levels as above in a first or second degree relative

Note: Cholesterol levels measured immediately after a myocardial infarction or stroke may be misleading as they tend to fall and, even if untreated, remain low for several months.

While specialist advice may be helpful in determining a precise diagnosis, intensive dietary advice, follow-up by a dietitian or suitably trained person and statin therapy are the cornerstones of therapy which will dramatically reduce cardiovascular risk.

If patients cannot tolerate any of the currently available statins, ezetimibe and one of the resins (Cholestyramine or Colestipol) should be prescribed.

3. Severe hypertriglyceridaemia

Markedly raised triglyceride levels (arbitrarily defined as a triglyceride level greater than 11mmol/l) may be secondary to uncontrolled diabetes, medications (thiazides, steroids, retinoids) liver conditions such as primary biliary cirrhosis, usually in genetically predisposed individuals and in those who are overweight or obese and/or have excessive intakes of alcohol.

Weight loss in those who are overweight or obese, alcohol restriction or elimination, dietary modification, and where appropriate treatment of diabetes can result in dramatic reductions in triglycerides. Statins should only be prescribed if indicated by guidelines (CVRA and Management, Ministry of Health, New Zealand, 2018) as they reduce isolated, very-high triglyceride levels poorly.

Fibrates (bezafibrate and gemfibrozil are available in New Zealand) reduce triglycerides, and there is limited clinical-trial evidence suggesting that they may reduce coronary heart disease events and ischaemic stroke.

Bezafibrate may be used in conjunction with Atorvastatin. Acipimox and nicotinic acid are additional triglyceride-lowering agents that are used in specialist clinics.

Markedly elevated triglycerides may occasionally be seen in the absence of any obvious predisposing cause, and have a genetic basis.

Such cases often require intensive, individualized dietary advice and a trial of different treatments including insulin, even when blood glucose levels are not appreciably raised.

Appreciably raised levels of triglycerides with chylomicron excess are associated with an increased risk of pancreatitis.

Specialist advice may be helpful in the absence of modifiable predisposing causes if there is no response to lifestyle measures.

4. Metabolic syndrome

There are several different definitions of the metabolic syndrome, which is unsurprising given that it is not an established disease entity, but rather a cluster of clinical and laboratory features typically associated with reduced insulin sensitivity, which identifies people at risk of type 2 diabetes and cardiovascular disease.

The syndrome is characterised by central adiposity, raised blood pressure, glucose intolerance or haemoglobin A_{1c} in the pre-diabetes range (40-50mmol/mol) low HDL cholesterol and raised triglyceride levels. Several other biochemical abnormalities including hyperuricaemia may also be present.

The presence of central adiposity, plus at least two of the other of these characteristics, are usually regarded as sufficient to make the diagnosis.

Recognition of the syndrome is important, as intensive dietary advice may reduce the risk of progression to T2DM as well as cardiovascular risk.

CVRA may suggest the need for drug treatment in addition.

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[1] Mutations in the LDL receptor gene (over 700 identified). Also mutations in the ApoB-100 and PCSK9 gene

[2] First degree (parents, full siblings or children), Second degree (uncles, aunts, nephews, nieces, grandparents, grandchildren)