REVIEW ARTICLE

MANAGEMENT OF HYPERLIPIDAEMIA

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ABSTRACT

Recent community-based studies have shown that hypercholesterolaemia is common in Singapore. High low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL) cholesterol as well as hypertriglyceridaemia are associated with higher prevalence of cardiovascular disease. The aim of this article is to discuss the clinical management of adult patients with hyperlipidaemia. For practical purposes, the hyperlipidaemias can be divided into four patterns: 1) hypercholesterolaemia with normal triglyceride, 2) moderate hypertriglyceridaemia with normal cholesterol, 3) combined moderate hypercholesterolaemia and hypertriglyceridaemia, and 4) severe hypertriglyceridaemia with moderate hypercholesterolaemia. Each pattern can be attributed primarily to genetic conditions or secondarily to common diseases. It is important to attempt aetiopathogenetic diagnosis for each hyperlipidaemic patient as treatment of an underlying condition may sometimes reverse the hyperlipidaemia eg hypothyroidism and hypercholesterolaemia. In general, a low cholesterol and low fat (particularly saturated fat) diet is useful in patients with all four patterns of hyperlipidaemia. Patients with severe hypertriglyceridaemia and moderate hypercholesterolaemia may benefit from a further drastic reduction in fat intake. Pharmacological therapy is required for patients who do not achieve target lipid levels after diet modification. The choice of drug therapy is, to a large extent, dependent on the pattern of hyperlipidaemia. In some situations, combination drug therapy may be required. Caution is required in combining hypolipidaemic drugs as the side-effects of individual drugs may be potentiated when used in combination.

Keywords: *hyperlipidaemia, cholesterol, management, therapeutics*

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INTRODUCTION

Coronary artery disease continues to be one of the leading causes of death in Singapore[1]. It has been known for some time that together with hypertension, diabetes mellitus and cigarette smoking, hyperlipidaemia is a major risk factor for the development of atherosclerotic disease[2]. The 1992 Singapore National Health Survey revealed that 19% of the adult population have serum total cholesterol above 6.2 mmol/L[3]. An earlier community-based prevalence study conducted in the mid 1980s suggested that 72% of the adult population have serum total cholesterol above 5.0 mmol/L and 27% have levels above 6.5 mmol/L[4]. The mean lipid levels of adult Singaporeans are comparable to those from Western developed countries.

There is little doubt that hypercholesterolaemia and particularly high levels of low-density lipoprotein (LDL) cholesterol contribute to atherogenesis. Data from prospective observational studies such as the Framingham Study[2], as well as interventional studies such as the Multiple Risk Factor Intervention Trial (MRFIT)[5], together with data accrued from animal, pathologic as well as clinical studies are persuasive[6]. The more recent regression studies have also shown that lowering plasma LDL cholesterol by lifestyle modification as well as the use of lipid lowering pharmacological agents may lead to regression of angiographically demonstrated coronary atherosclerotic lesions[7-10].

Epidemiological evidence suggests that low high-density lipoprotein (HDL) cholesterol is associated with atherosclerosis[11]. The hypothesis that HDL might be important in reverse cholesterol transport from the periphery lends biologic plausibility to this data[12]. Data from the Helsinki Heart Study suggested that besides reduction of LDL cholesterol, raising HDL cholesterol may confer additional benefit in reducing the number of coronary end-points[13]. There is also substantial data linking hypertriglyceridaemia to increased occurrence of coronary artery disease[14]. This association has also been documented in people with type 2 diabetes[15]. Whether hypertriglyceridaemia is causally linked to atherosclerosis remains controversial and readers should refer to a recent review for more information[16]. Besides being often associated with low HDL cholesterol, hypertriglyceridaemia may influence LDL particle composition and lead to a preponderance of more atherogenic small LDL particles[17] or predispose to potentially atherogenic postprandial lipaemia[18]. The presence of a moderately elevated plasma triglyceride, low HDL cholesterol and predominance of small, dense LDL has been associated with a 3 to 7 fold increase in coronary risks[17,19]. There is experimental evidence that treating patients with hypertriglyceridaemia may shift LDL subfraction distribution towards larger, less dense species[20,21]. Hence, it has been suggested that in the evaluation of patients, both HDL cholesterol and triglyceride should be considered in addition to LDL cholesterol[22].

The aim of this article is to discuss the clinical management

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of adult patients with hyperlipidaemia who are at risk of developing cardiovascular disease or pancreatitis.

LIPID MEASUREMENTS

Measurements of total serum cholesterol, HDL cholesterol and triglyceride are easily available from clinical laboratories in Singapore. On the other hand, LDL cholesterol is not measured directly in routine clinical biochemistry but can be estimated by the Friedewald equation: LDL chol (mmol/L) = Total chol (mmol/L) – HDL chol (mmol/L) – TG/2.2 (mmol/L) provided triglyceride is less than 4.5 mmol/L. This calculated LDL cholesterol is often included in prints-out of laboratory results. In people who are able to clear chylomicrons normally, serum triglyceride reflects mainly VLDL triglyceride after a 10-hour overnight fast. Hence, for accurate estimation of VLDL triglyceride or LDL cholesterol (using the Fridewald equation) fasting blood samples are required. It should also be remembered that physiological variation in serum lipids in response to illness can be substantial and an example of such a situation is that occurring between 24 hours and 6-12 weeks after a myocardial infarction[23]. Drugs such as propranolol may also reduce HDL cholesterol and increase triglyceride[24]. Finally, day to day variation as well as laboratory error have to be considered. Hence, documentation of an abnormal lipid profile on at least 2 separate occasions, is recommended, before instituting pharmacotherapy.

Classification of hyperlipidaemia

The Frederickson/WHO classification serves as a useful means in the understanding of the pathophysiology of hyperlipidaemia[25]. However, for practical purposes, the hyperlipidaemias can be divided into four patterns:

1) Hypercholesterolaemia with normal triglyceride (WHO Type IIa)
2) Hypertriglyceridaemia with normal cholesterol (WHO Type IV)
3) Combined moderate hypercholesterolaemia and hypertriglyceridaemia (WHO Types IIb and III)
4) Severe hypertriglyceridaemia (> 10 mmol/L) with moderate hypercholesterolaemia (chylomicronaemia syndrome, WHO Types I and V)

It must be realised that classification of hyperlipidaemia into a pattern is inadequate. Each hyperlipidaemic pattern can be attributed primarily to genetic conditions or secondarily to common diseases. For example, hypercholesterolaemia (Type IIa) can be due to heterozygous familial hypercholesterolaemia or secondary to hypothyroidism. In some secondary hyperlipidaemias, treatment of the underlying disease (eg hypothyroidism) would correct the hyperlipidaemia, whereas in other situations (eg chronic renal failure), it may not be possible to reverse the underlying condition. Hence, a conscious attempt at aetiopathogenetic diagnosis for each hyperlipidaemic patient based on history (not forgetting family history), physical examination and other laboratory tests must be made. Some of the more common primary as well as secondary causes of the different patterns of hyperlipidaemia are listed in Table I.

MANAGEMENT STRATEGY

After classification and diagnosis, the patient's overall coronary risk (including other risk factors such as hypertension, obesity, diabetes mellitus, cigarette smoking and particularly existing atherosclerotic disease) must be evaluated before an individualised management strategy (including consideration of age, gender and the potential to benefit from treatment) is formulated.

Both the American National Cholesterol Education Programme (NCEP) and the European Atherosclerosis (EAS) have recently updated their guidelines on the management of hyperlipidaemia[26,27]. The Adult Treatment Panel (ATP II) of the NCEP have incorporated recommendations from guidelines published earlier on triglyceride and HDL cholesterol[28] as well as on cholesterol lowering in patients with established coronary heart disease[29]. The American Diabetes Association has also recently published guidelines on management of lipid disorders in diabetes[3].

Adult Treatment Panel II of the NCEP has several new features including:

1) Increased emphasis on overall coronary risk as a guide to treatment so that most aggressive therapy is targeted at patients who are at highest risk.
2) More attention to HDL cholesterol
3) Increased emphasis on non-pharmacological components of therapy.

The ATP II has a series of algorithms to guide detection, evaluation and management. The initial algorithm is based on measurement of total serum cholesterol (as a surrogate measurement of LDL cholesterol) with the use of HDL cholesterol as a key branchpoint in classification. All further

Table I – Common primary and secondary causes of hyperlipidaemia

Pattern of Hyperlipidaemia	Primary causes	Secondary causes
Hypercholesterolaemia	Polygenic hypercholesterolaemia Familial hypercholesterolaemia	Nephrotic syndrome Hypothyroidism Anorexia nervosa
Hypertriglyceridaemia	Familial hypertriglyceridaemia Familial combined hyperlipidaemia	Diabetes mellitus Obesity Alcoholism
Hypercholesterolaemia and hypertriglyceridaemia	Familial combined hyperlipidaemia Familial dysbetalipoproteinaemia	Diabetes mellitus Obesity
Severe hypertriglyceridaemia with moderate hypercholesterolaemia (chylomicronaemia)	Familial lipoprotein lipase deficiency Familial apo CII deficiency	*Diabetes mellitus *Alcoholism

* Common precipitating causes in patients with familial hypertriglyceridaemia/familial combined hyperlipidaemia

Table II – NCEP ATP II treatment decisions based on LDL cholesterol level

Patient Category	Initiation Level	LDL Goal
Dietary Therapy		
Without CHD and fewer than two risk factors*	≥ 4.1 mmol/L (160 mg/dL)	< 4.1 mmol/L (160 mg/dL)
Without CHD and two or more risk factors	≥ 3.4 mmol/L (130 mg/dL)	< 3.4 mmol/L (130 mg/dL)
With CHD	> 2.6 mmol/L (100 mg/dL)	≤ 2.6 mmol/L (100 mg/dL)
Drug Therapy		
Without CHD and fewer than two risk factors	≥ 4.9 mmol/L (190 mg/dL)	< 4.1 mmol/L (190 mg/dL)
Without CHD and two or more risk factors	≥ 4.1 mmol/L (160 mg/dL)	< 3.4 mmol/L (160 mg/dL)
With CHD	≥ 3.4 mmol/L (130 mg/dL)	≤ 2.6 mmol/L (130 mg/dL)

***Positive risk factors**
Male ≥ 45years
Female ≥ 55years or premature menopause
Family history of premature CHD
Current cigarette smoking
Hypertension
Low HDL cholesterol (<0.9 mmol/L)
Diabetes mellitus

Negative risk factor
High HDL cholesterol (≥ 1.6 mmol/L)

algorithms are based on LDL cholesterol. In local institutional practice, LDL cholesterol estimates based on measurements of total and HDL cholesterol as well as triglyceride are easily available. Thus it is possible to summarise the guidelines using LDL cholesterol (Table II).

When these guidelines are used, low HDL cholesterol (<0.9 mmol/L) is regarded as a coronary risk factor while high HDL cholesterol (>1.6 mmol/L) is regarded as a negative coronary risk factor (and hence one risk factor can be subtracted during evaluation of the patient's overall coronary risk).

Patients with serum triglyceride more than 10 mmol/L are said to be at increased risk for pancreatitis and should be treated by dietary and/or other means. Patients with hypertriglyceridaemia of a lesser degree should also be treated if they have one or more of the following:

1) clinical evidence of atherosclerotic disease
2) diabetes mellitus
3) high LDL cholesterol: HDL cholesterol ratio (>5)[14]
4) familial combined hyperlipidaemia[31]

It has been suggested that modcrately hypertriglyceridaemic patients who do not fit into one of the above categories should have a measurement of apolipoprotein B (apo B) if a reliable assay is available[32,33]. LDL apo B constitutes up to 90% of measured apo B levels. Since apo B has a stoichiometric relationship with LDL, a high apo B level then implies the presence of a large number of atherogenic small LDL particles for a given LDL cholesterol level. Treatment should be considered for these patients.

It should also be remembered that in the presence of moderate and high triglyceride levels, estimation of LDL cholesterol by the Friedewald equation is possible only after some degree of triglyceride lowering unless direct measurement of LDL cholesterol by ultracentrifugation is available.

Dietary modification/physical activity

Patients with moderate degrees of hypercholesterolaemia, hypertriglyceridaemia and combined hypercholesterolaemia/ hypertriglyceridaemia should first have dietary modification based on the guidelines of the American Heart Association Step 1 and Step 2 diets. These diets (Table III) have a few key features:

1) Caloric intake appropriate for weight and activity

Table III – Guidelines for dietary therapy

	Step 1 Diet	Step 2 Diet
Total fat	< 30% of calories	< 30% of calories
Saturated fat	8-10%	<7%
Cholesterol	<300 mg/day	< 200 mg/day

2) Reduction in dietary cholesterol
3) Reduction in total and saturated fat and substitution with unrefined carbohydrate, monounsaturated and polyunsaturated fat.

Although patients may understand the need for reduction in dietary cholesterol, not many realise that dictary saturated fat may be an even more important contributory factor to high blood cholesterol. The need to reduce intake of saturated fat should be emphasised[34]. As a substitute, monounsaturated fat may have a greater advantage over polyunsaturated fat as the latter is associated with a decrease in HDL cholesterol[35], although not all studies are in agreement[36]. In addition, from a theoretical point of view, monounsaturated fat should also be less liable to oxidation than polyunsaturated fat. Diets incorporating the three key features listed above are suitable for patients with hypercholesterolaemia as well as hypertriglyceridaemia[37] except that in patients with the chylomicronaemia syndrome, an even greater reduction in dietary fat is appropriate[37,38].

As an average, dietary modification may reduce blood lipid levels by 10-15%[39]. However, it is important to realise that when managing the individual patient, much greater reductions are occasionally possible, especially in those patients who are unaware that a particular food item is inappropriate and take it to excess. Hence a careful dietary history with appropriate modification for about three to six months should be attempted in most patients before pharmacological agents are added (and not substituted).

Overweight patients who combine regular physical activity with a prudent diet have a greater improvement in lipid levels[40]. In keeping with this, ATP II of the NCEP recommends that more emphasis be placed on physical activity and diet as means of lowering cholesterol in young adults.

Pharmacotherapy (Tables IV and V)

If dietary modification fails to achieve target lipid levels in 3 to

Table IV – Lipid lowering pharmacological agents

Pattern of Hyperlipidaemia	First-line	Second-line	Combination
Hypercholesterolaemia	Resin Niacin Statin	Fibrate Probucol	Resin + Statin Resin + Niacin
Hypertriglyceridaemia	Fibrate Niacin Acipimox		
Combined hypercholesterolaemia/ hypertriglyceridaemia	Fibrate Niacin	Statin	Fibrate + Resin Niacin + Resin
Severe hypertriglyceridaemia with moderate hypercholesterolaemia (chylomicronaemia)		Fibrate	

Resin = bile acid sequestrant, Statin = HMG CoA reductase inhibitor
Fibrate = fibric acid derivative, Niacin = nicotinic acid

Table V – Lipid lowering pharmacological agents: dose, frequency of administration and cost

Agent	Unit dose	Usual dose & dose frequency per day	Cost for usual dose per day (estimated)
Gemfibrozil	600 mg	600 mg bid	$1.80
Bezafibrate	200 mg	200 mg tid	1.65
Bezafibrate retard	400 mg	400 mg on	1.30
Fenofibrate	100 mg	100 mg tid	1.32
Cholestyramine	4 g (sachet)	4 g bid	3.40
Simvastatin	10 mg	10 mg on	3.15
Pravastatin	20 mg	20 mg on	3.25
Nicotinic acid	100 mg, 200 mg	500 mg tid	1.50
Acipimox	250 mg	250 mg tid	2.40
Probucol	500 mg	500 mg bid	1.65

6 months it is reasonable to add pharmacological agents. The pharmacological agent chosen depends on the pattern of hyperlipidaemia as most agents have different efficacies for reducing different lipid fractions. Since this article must necessarily be brief, the reader should refer to several recent reviews for more information[41-45]. The ATP II of the NCEP makes a distinction in pharmacotherapy initiation levels between patients with established clinical coronary artery disease (secondary prevention) and those without (primary prevention). The threshold for initiating pharmacotherapy in secondary prevention after failure of lifestyle modification is lower, since the benefit of lipid lowering in such instances is more established[7-10]. Although greater reliance is placed on lifestyle modification in patients without clinical coronary artery disease, pharmacotherapy should not be withheld when lifestyle modification fails.

Hypercholesterolaemia

Although dietary modification is the initial step in the management of patients with hypercholesterolaemia, some patients with polygenic hypercholesterolaemia and most patients with heterozygous familial hypercholesterolaemia will require the addition of pharmacological agents. Drugs which have major effects on LDL cholesterol include the bile acid resins, nicotinic acid and hydroxymethylgultaryl coenzyme A (HMG Co A) reductase inhibitors. The fibrates and probucol are generally regarded as having a minor effect in reducing LDL cholesterol levels. Besides being an anti-oxidant, probucol is said to reduce LDL cholesterol via non receptor mediated mechanisms. However, it has the disadvantage of reducing HDL cholesterol. Fibrates are discussed in the section on hypertriglyceridaemia.

Cholestyramine, a bile acid sequestrant, lowers LDL cholesterol by 15% to 30%. It is not well absorbed and its primary action is to bind bile acids in the intestinal lumen, interrupting enterohepatic circulation of bile acids and depleting the bile acid pool. This drives hepatic bile acid synthesis from cholesterol. Hepatic cholesterol is decreased and this results in an upregulation of LDL receptors expressed on the hepatocyte thereby channelling more circulating LDL into the hepatocyte with significant lowering of blood LDL cholesterol. It is important to start with a small dose (eg 1 sachet of 4 g daily). Common side effects include constipation and abdominal discomfort and big doses are not well tolerated. It may also interfere with the absorption of drugs such as thyroxine, warfarin, digoxin and HMG CoA reductase inhibitors. Cholestyramine should be taken about 4 hours before or 1 hour after other medications.

Nicotinic acid is effective and inexpensive. In doses of 3 to 6 g per day, nicotinic acid reduces LDL cholesterol by 20% to 30%. It also raises HDL cholesterol by 10% to 20% and reduces triglyceride by 20% to 40%. Nicotinic acid acts by inhibiting lipolysis and reducing hepatic synthesis and secretion of VLDL. It is extremely important to start with small doses (eg 100 mg t.d.s.) with the initial dose taken after dinner to minimise problems with flushing during activities in the day. Many patients are not able to tolerate the flushing which may sometimes be reduced by taking aspirin 30 minutes before nicotinic acid. Other side effects include nausea, dry skin, abdominal discomfort, dyspepsia and hyperuricaemia. Use of nicotinic acid has been associated with hepatitis[46]; in particular, the sustained release

formulation of nicotinic acid has been associated with fulminant hepatic failure[47]. Nicotinic acid may also worsen blood glucose control in patients with diabetes mellitus. Hence, besides the lipid profile, patients on nicotinic acid should have blood glucose, uric acid and transaminases monitored.

As a class, HMG CoA reductase inhibitors have been in use for about 8 years and have now gained recognition as the most potent of LDL cholesterol lowering agents[48]. The two agents available in Singapore are simvastatin and pravastatin. These agents are capable of up to 40% reduction in LDL cholesterol with minimal adverse effects. They are potent inhibitors of the rate limiting enzyme in cholesterol biosynthesis. This results in a decrease in intracellular cholesterol and an upregulation of LDL receptors expressed on the hepatocyte leading to reduction of blood LDL cholesterol levels. These drugs are more effective when taken at night[49] possibly reflecting increased in vivo cholesterol biosynthesis at night. Side effects include headaches, nausea, skin rash, myopathy, elevation in muscle enzymes and elevation in transaminases. Although clinical myopathy is uncommon, elevation of creatinine kinase while on treatment is more often detected. Hence, both transaminases as well as creatinine kinase should be monitored. Myopathy and rhabdomyolysis has been reported with use of HMG CoA reductase inhibitor together with gemfibrozil, cyclosporin, erythromycin and nicotinic acid[50,51]. The potential clinical advantage of the hydrophilic nature of pravastatin in causing less sleep disturbance when compared to other HMG CoA reductase inhibitors such as lovastatin[52] has so far not been substantiated.

Some patients with hypercholesterolaemia, particularly those with heterozygous familial hypercholesterolaemia, may not achieve target LDL cholesterol levels with fairly large doses of a single agent. Although further reduction of LDL cholesterol of a small magnitude may be obtained by increasing the dose further, combination therapy may be more effective and can be achieved at less risk of toxic side effects. However, appropriate choice of agents is important. Hence combination of HMG CoA reductase inhibitor with low dose cholestyramine (eg 20 mg of simvastatin with 4g b d of cholestyramine) or nicotinic acid and cholestyramine may be useful.

Hypertriglyceridaemia

When it is felt that hypertriglyceridaemia requires treatment, the initial approach should be non-pharmacological. Hypertriglyceridaemia is also often secondarily caused and conditions such as obesity, diabetes mellitus, renal failure, alcohol ingestion should be looked for and corrected where possible. A classical example is in diabetes where improvement in glycaemic levels can bring about reductions in triglyceride. Diets similar to those recommended for hypercholesterolaemia should be tried in patients with moderate hypertriglyceridaemia[37] for a similar period before pharmacological therapy is used. Pharmacological agents which have a major triglyceride lowering effect include fibrates, nicotinic acid and the nicotinic acid analogue, acipimox. There is evidence to suggest that when these pharmacological agents lower serum triglyceride, LDL composition is altered favourably[20,21].

Fibrates include gemfibrozil, bezafibrate and fenofibrate. The mechanisms of action of the fibrates include activation of lipoprotein lipase, suppression of lipolysis, inhibition of hepatic triglyceride synthesis and increased secretion of cholesterol into bile. Hence, besides reduction of triglyceride, fibrates also raise HDL cholesterol. Although fibrates have a modest LDL cholesterol lowering effect when used in patients with hypercholesterolaemia, the LDL cholesterol may paradoxically show a modest rise when used in patients with hypertriglyceridaemia or combined hypercholesterolaemia/hypertriglyceridaemia. Fibrates are generally well tolerated. Side effects include rash, urticaria, headache, increased biliary lithogenicity, and increases in transaminases and creatinine kinase.

Nicotinic acid has been considered in the section on hypercholesterolaemia. Acipimox, a nicotinic acid analogue is an effective triglyceride lowering agent. Although it is thought to be less potent than nicotinic acid, it does not worsen glycaemic status and can be used in the management of hypertriglyceridaemia in diabetic patients[53].

Combined hypercholesterolaemia/hypertriglyceridaemia

Combined hypercholesterolaemia/hypertriglyceridaemia may be due to either WHO Type IIb or III pattern of hyperlipidaemia. In general, patients with mildly raised triglyceride and a higher cholesterol level have Type IIb pattern while patients with almost equimolar elevations of both have Type III pattern[41]. A bile acid resin such as cholestyramine should not be used as the initial agent as it may precipitate further increases in triglyceride[54]. There is limited experience with the use of HMG CoA reductase inhibitors in combined hypercholesterolaemia/hypertriglyceridaemia[55]. Nicotinic acid is an agent which has been successfully used. The fibrates are effective in lowering triglyceride but their effects in lowering LDL cholesterol are less predictable. Fenofibrate and bezafibrate appear to be more effective than gemfibrozil in reducing LDL cholesterol levels[56]. In some patients, however, LDL cholesterol levels may increase with either gemfibrozil or fenofibrate. Fibrates however usually have favourable effects on both LDL cholesterol as well as triglyceride in the Type III pattern.

Combination therapy may be considered in patients who do not achieve target levels of cholesterol whilst on monotherapy[57]. Cholestyramine can be added to either a fibrate or to nicotinic acid. However, until more favourable information is available, HMG CoA reductase inhibitors should not be combined routinely with a fibrate or nicotinic acid.

Severe hypertriglyceridaemia with moderate hypercholesterolaemia (chylomicronaemia syndrome)

Hereditary lipoprotein lipase deficiency is uncommon and patients with severe hypertriglyceridaemia often have underlying primary conditions (such as familial hypertriglyceridaemia or familial combined hyperlipidaemia) which give rise to mild and moderate hypertriglyceridaemia. However, severe hypertriglyceridaemia is often precipitated by a secondary cause such as poorly controlled diabetes and sometimes alcohol ingestion. The risk for developing pancreatitis is said to be increased and lipid lowering treatment is required. Nonpharmacological therapy forms the mainstay of treatment. In the patient with pancreatitis, nutritional support in the form of carbohydrates should be given parenterally (infusion containing 5% dextrose). In the patient without pancreatitis fat content in the diet should initially be reduced to a minimum so that the remaining chylomicron within the body can be cleared. Any underlying diabetes should be treated appropriately with either insulin or oral hypoglycaemic agents. A fibrate such as gemfibrozil is usually added to reduce hypertriglyceridaemia to acceptable levels. Alternative pharmacological agents which are effective in reducing triglyceride levels in this situation are fish oil and nicotinic acid. On the other hand, plasmapheresis is seldom necessary[38].

It is not easy to remain on a minimal fat diet and when severe hypertriglyceridaemia has improved, more moderate diets can

be introduced gradually while monitoring the lipid profile. In any case, it is recommended that the fat content does not exceed 20% of total caloric intake[37].

CONCLUSION

There are still many unanswered questions and unexplored areas in hyperlipidaemia. New pharmacological agents are in the pipeline[58] but whether benefits of lipid lowering can be translated into reduction of total mortality in the primary prevention setting can only be answered by a trial with a large enough sample size. The management of hyperlipidaemia in the young and elderly as well as in the female population has to be better streamlined. Again, the use of hormone replacement therapy as a means of decreasing cardiovascular risk in postmenopausal women has to be addressed. The question of triglyceride has not been satisfactorily resolved[59]. More work on lipoprotein(a) is required. The role of antioxidants in reducing lipid oxidation is being explored[60]. However, although antioxidants found in natural sources such as fruits and vegetables appear to be safe, it is premature to recommend pharmacological antioxidant supplements[61]. LDL apheresis is used for patients with homozygous familial hypercholesterolaemia, but its role in heterozygous patients who are resistant to conventional therapy needs better definition. These are but a few clinical questions. Even before the answers to these and other questions are available, physicians will need to manage patients with hyperlipidaemia. Based on considerations of risk versus potential benefit, physicians will need to formulate individualised management strategies utilising available current knowledge. At the community level the cost-effectiveness of these measures will have to be evaluated.

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