MANAGEMENT OF HYPERLIPOPROTEINAEMIAS

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In discussion on managernent of hyperlipoproteinaemias, the approach will be based on three aspects ;

a) Preventive steps.

b) Selection of drugs available based on effectiveness for particular type of hyperlipoproteinaemia. Surgical measures advocated in some specific types will not be included in this presentation.

c) Future possibilities of recognition of gene polymorphism by DNA probe for hyperlipoproteinaemia. Restriction fragment length polymorphism (RFLP) studies in apolipoprotein B have indicated specific allele on chromosome-2, a code for myocardial infarction[1]. Such identification will elucidate the molecular basis for susceptibility to atherosclerosis:

In prevention of hyperlipoproteinaemia, the steps may be categorized into :

a) Primary, wherein population is screened in childhood, especially children of parents with vascular disease or hyperlipidaemia. There is thus a modification introduced in diet, life style with regular monitoring to ensure that lipids are maintained in the normal range.

b) Secondary prevention refers to such instances who on routine screening becauss of cardiovascular risk factor reveal hyperlipoproteinaemia though they are asymptomatic so far for a vascular event. Such instances include following categories:

i. Those with family history of premature cardio-vascular disease, or hyperlipidaemia.

ii. Those with increased risk for cardiovascular disease, e.g. hypertension, glucose intolerance or hyperuricaemia.

iii. Those with history of recurrent pancreatitis or abdominal pain.

iv. Those with presence of xanthelesema, lipemia retinalis or arcus juvenilis.

v. Those whose serum is noticed to be turbid.

c) Tertiary prevention includes instances with established large vessel disease who have hyperlipoproteinaemia. In common practise, this is the group which is mostly offered the drug treatment.

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Prior to criterion selection for treatment, some pertinent facts in regard to lipoprotein abnormalities and their interpretation may be worthy of mention. These include the following :

1. Unreliability of single value determination.

2. Iatrogenic lipid alterations that relate to use of diuretics, beta blockers, oral contraceptives, steroids or alcohol.

3. Irreversible nature of complicated atherosclerotic process - plaque formation or thrombosis, sub-intimal haemorrhage, that do not as such seem to be affected by antilipidaemie agents.

4. Failure to recognize the fact that percentage reduction in serum lipid is not synonymous with normalized serum lipid levels.

5. Again, epidemiological inferences are not same as clinical events and holistic assessment of a patient including other risk factors may have more relevance in deciding outcome for management of hyperlipoproteinaemias.

A stepwise approach warrants initial determination of serum cholesterol and serum triglyceride. If abnormal value is found, the biochemical determination should be repeated and on this repeat evaluation, determination of HDL cholesterol be included. If the lipid values are still abnormal, dietary measures for control of hyperlipidaemias are initiated and again investigations to exclude a likely secoadary cause, e.g. hypothyroidism, diabetes mellitus, renal or hepatic disease should be pursued.

The summary from a article in Postgraduate Medicine[2] is reproduced here to emphasise the role of dietary measures for control of hyperlipidaemia. "Lipid abnormalities can be treated effectively with various lipid lowering agents. However, it bears repeating that no patient with hyperlipoproteinaemia should be treated with drugs until an adequate trial of dietary intervention, which may take as long as six months has been attempted. While knowledge of a patient's precise metabolic and generic abnormality is often desirable, it generally is not necessary for the initiation of lipid lowering drug therapy. Judicious use of total cholesterol, high density lipoprotein cholesterol and total triglyceride measurements is sufficient for selection of proper drug or drugs. A patient who does not respond should be referred to a specialised lipid centre for more sophisticated evaluation and therapy"[2].

In this *dietary management*, the following aspects need to be taken into consideration:

a) Total fat content.

b) Proportion of various unsaturated fats.

c) Allowance of cholesterol in diet.

d) Effective fibre content.

Firstly total calories should be so adjusted that individual achieves standard weight for the age and sex. Patient should have body mass index between 19 and 22.

Total amount of calories from fats should be less than 30%. Reducing fats further usually implies high carbohydrate content and this may in turn lead to rise in triglycerides or lowering of HDLc.

In regard to reduction in saturated fats, this improves the LDL receptor activity. The proportion of different unsaturated fats should be 10% each, i.e. monounsaturated (olive oil or rape seed) 10%, polyunsaturated n-6 (linolenic acid-plant oils) 10%, polyunsaturated n-3 (fish oils) 10%.

The commonly available cooking oils are listed herewith with the content of polyunsaturated fatty acids. (Table 1)

Table 1

Polyunsaturated fatty acid content in some edible fats and oils.

No.	Fat or oil	PUFA contents (gms./100 gms:)
l.	Coconut oil	2
2.	Cottonseed oil	50
3.	Ghee (butter fat)	4
4.	Groundnut oil	28
5.	Maize oil (corn oil)	45
6.	Mustard oil	25
7.	Olive oil	10
8.	Rice bran oil	35
9.	Sufflower oil (Kusuma oil)	75
10.	Soyabean oil	55
11.	Vanaspati	6

The cholesterol content in diet should be kept below 300 mg per day. Cholesterol content of various foods is indicated as below in table II.

Table II

Cholesterol content of common food items

Foods	Qty. (gms)	Cholesterol (mg)
Milk Group		
Milk 3.5% fat	245	34
Curd 3.5% fat	245	30
Cheese (prosessed)	40	37
Cottage cheese	50	20
Meat Group		
Egg whole (I)	50	252
Egg yolk (I)	17	252
Egg white (I)	33	--
Chicken	60	45
Lamb	60	57
Brain/liver	50	2000
Fish (sea fresh)	60	43
Fats and Oils		
Butter	14	35.0
Ghee (Pure)	15	47.0
Cream	15	6.0
Vanaspati	15	0.0
Sweets and Desserts		
Ice cream (1 cup)	I30	53
Plain cake (1 pc.)	40	21
Kheer (rice/suji)	170	34

Low saturated fat content of diet has antithrombogenic effects, lowers blood pressure and overall, contributes to reduced coronary death rates.

Abstinence from smoking, regular exercise and a balanced life style also contribute to normalising the serum lipid levels.

The *Selection of Drugs* for lipid lowering depends on the type of hyperlipoproteinaemia. It is a long term investment for both the patient and the physician. The following table summarises drugs available, their mode of action, dosage, efficacy and side effects (table III).

Table III

Hypolipidaemic drugs in use

Drug	Mode of action	Daily dose	Indication	Efficacy Per cent reduction	Side effects
Cholestyramine	Bile acid sequestration : more cholesterol converted bile acids	12-24 g.	Type II LDL	LDL 20	GI upset. Fat soluble vitamin deficiency.
Nicotinic acid	Blocks formation of lipoproteins by the liver. Increased cholesterol oxidation	1.5- 3 g.	Type III, IV VLDL, IDL.	LDL 10-15 Tg 20.	Flushing, itching, GI upset, hepatic dysfunction.
Clofibrate	Increases activity of lipoprotein lipase, increases catabolism of VLDL	1.5-2.0 g.	VLDL Type II	Cholesterol 5—10 Tg 50	Gastrointestinal upset. Weight gain, skin rash, alopecia, myositis, cholelithiogenecity.
Neomycin	Blocks cholesterol absorption. Increases synthesis of LDL receptors	0.5 - 2 g.	Type II LDL	Variable	Diarrhoea, malabsorption
Probucol	Increases clearance of LDL additive to sequestrant	0.5-1.5 g.	Type II LDL	LDL 10-15	GI upset
Gemfibrozil	Inhibits production of VLDL	1-2 g.	Type III, IV VLDL	Tg 40	GI upset Lithogenicity
Compactin and Mevinolin	Competitive inhibition of 3 hydroxy 3 methyl glutaryl coenzyme A (HMG CoA) reductase.	20-40 mg	II, Type II, III, IV.	LDL 30	—

One may repeat that if serum cholesterol is >240 mg%, triglyceride <250 mg%, HDL cholesterol <40 mg%, choice will be cholestyramine or nicotinic acid. However, if serum cholesterol is >240 mg%, triglyceride >500 mg%, HDLc <40 mg%, one should employ clofibrate or gemifibrozil (cholestyramine is not useful; however, nicotinic acid may be of value). In instances with hypertriglyceridaemia of moderate or severe degree, treatment is called for only if total cholesterol and HDL cholesterol are also affected. Cholestyramine and nicotinic acid may be combined or gemfibrozil is prescribed.

The objective should be to normalize the lipid profile, as to safeguard against the cardiovascular events. Pursual of such a goal requires regular monitoring and following of diet and drug regimes continuously. Long term follow up in large number of patients with calculation of results based on life tables can provide information on the precise beneficial effects.

References

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