Diabetic Retinopathy and Serum Lipids

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ABSTRACT

The association between serum lipid levels and diabetic retinopathy has been investigated in many studies. Some studies show a positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudation. Other studies show serum triglyceride levels as being important in the progression of retinopathy. Certain other studies show no relationship between serum lipid levels and diabetic retinopathy. We review the literature on this subject and illustrate this report with an example of a diabetic with severe diabetic maculopathy and high serum lipid levels.

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INTRODUCTION

It is known that many diabetics have hypercholesterolemia and hypertriglyceridemia[1,2]. In addition, many studies over the years have suggested a relationship between serum lipid levels and diabetic retinopathy. Dornan et al found an association between total serum cholesterol and diabetic retinopathy[3]. This was further substantiated by Miccoli et al[4]. More recently, the Early Treatment Diabetic Retinopathy Study (ETDRS) group[5,6] and the Wisconsin Epidemiologic Study of Diabetic Retinopathy[7] found a statistically significant association between elevated serum total cholesterol and Low-density Lipoprotein (LDL) cholesterol and the severity of retinal hard exudation in patients with diabetic retinopathy. The progression to proliferative retinopathy was also shown to be related to serum triglycerides and LDL[8]. Findings of the EURODIAB IDDM Complications study group show that cholesterol is related to all levels of retinopathy and that triglycerides are associated with moderately severe non-proliferative and proliferative retinopathy[9].

Several studies have however shown conflicting results. Sinav et al reported that while plasma total cholesterol, LDL cholesterol and High-density Lipoprotein (HDL) cholesterol were related to proliferative retinopathy, serum triglycerides was not[10]. Marshall et al even found that cholesterol was not associated with the onset or progression of diabetic retinopathy in insulin-dependent diabetics[11].

Weber et al reported that serum triglycerides, but not cholesterol, was associated with diabetic retinopathy in children with Type 1 (insulin-dependent) diabetes mellitus[12], while Kordonouri et all showed HDL cholesterol to be the most important variable related to the development of retinal lesions in children with Type 1 diabetes mellitus[13].

The mechanism by which high serum lipids may cause the progression of diabetic retinopathy is not clearly understood. It has been postulated that elevation of blood viscosity and alterations in the fibrinolytic system occurs in hyperlipidemia causing hard exudate formation[14]. There may also be incorporation of triglycerides into the cell membrane leading to changes in membrane fluidity[15] and leakage of plasma constituents into the retina. This results in haemorrhage and oedema in the retina.

An illustrative "typical" case history is that of our patient, Madam LMC. She is a 70-year old housewife who has had non-insulin dependent diabetes mellitus for 10 years and is taking glibenclamide 5mg twice a day. She is also a hypertensive for more than 10 years. Mdm LMC suffered a stroke in January 1997 and was admitted to hospital where her serum total cholesterol was found to be high at 16.76 mmol/1 or 650 mg/dl (desirable <5.2 mmol/l or <200 mg/dl), LDL was 13.2 mmol/1 (desirable <3.4 mmol/l) and triglycerides 7.77 mmol/1 (normal 0.56 - 1.92 mmol/l). HbA_{1C} was 10.6% (normal 4.6 - 6.4%). Her preadmission blood glucose was 12.2 mmol/l (normal 4.0 - 7.8 mmol/l). She was started on pravastatin in January and by August 1997, her serum total cholesterol had fallen to 9.64 mmol/l, LDL 6.64 mmol/l, HDL 1.19 mmol/l and triglycerides 3.98 mmol/l. However, her blood glucose was still 12.8 mmol/l and HbA_{1C} more than 14.0%. The patient had laser photocoagulation for both eyes at 2 other hospitals 2 months prior to being seen at our centre. She was found to have rather severe exudative maculopathy in both eyes which extended beyond the vascular arcades. This

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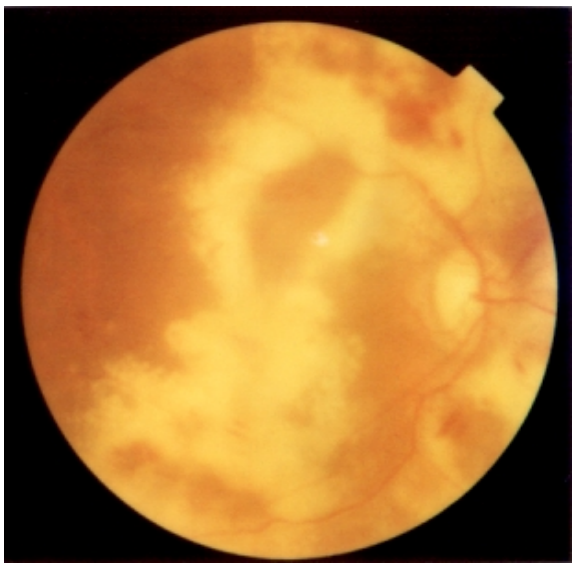

Fig. 1 Severe diabetic maculopathy/diabetic macular oedema (Right eye)

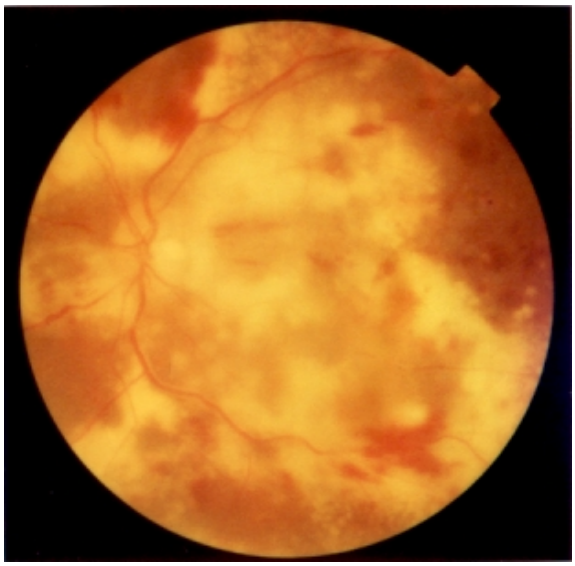

Fig. 2 Severe diabetic maculopathy/diabetic macular oedema (Left eye)

resulted in vision of only 6/120 in her right eye and counting fingers at half a metre in her left eye. (See Figs. 1 and 2)

DISCUSSION

In a small series, Gordon et al found that the use of pravastatin for 1 year in patients with diabetes and moderately high total serum cholesterol levels did result in an improvement in diabetic retinopathy[16]. Pravastatin is a member of the statin family which inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the enzyme that catalyses the rate limiting step in the de novo synthesis of cholesterol. Its use led to an improvement in hard exudation as well as a decrease in microaneurysms. There was even improvement in visual acuity in 1 patient. This was accompanied by a reduction of total serum cholesterol and LDL to desirable levels, with no significant side effects of the drug.

Freyberger et al used etofibrate, a fibric acid derivative, and found that it caused a regression of hard exudates in their series[14]. There was no change in microaneurysms or haemorrhages. A 30% reduction in serum triglyceride levels ($p<0.01$) and 25% increase in HDL cholesterol was also seen. Fibrates reduce the synthesis and increase the breakdown of Very Low Density Lipoprotein (VLDL) particles with secondary effects on LDL and HDL particles. The ETDRS has also suggested that reduction of raised serum lipid levels may help prevent retinal hard exudate formation and loss of vision[6].

In a prospective study to investigate the influence of serum lipids on the visual outcome of patients after central laser photocoagulation, Kremser et al found that patients with normal total cholesterol, LDL, HDL and triglyceride levels tended to have better results than those with abnormal lipid levels. They concluded that serum lipid fractions influence both the course of diabetic macular oedema as well as the success of laser photocoagulation[17]. Reduction of retinal exudates and improvement of visual acuity have also been reported when heparin-induced extracorporal LDL-precipitation (HELP) was used in addition to laser photocoagulation in a patient with exudative diabetic retinopathy and high serum lipids. This is a variant of extracorporal dialysis which reduces LDL and fibrinogen levels in the serum[18].

At present, lipid-lowering medications are recommended only for individuals at increased risk of cardiovascular disease[19]. It is advised that such drugs be prescribed when total serum cholesterol is more than 6.2 mmol/l (240 mg/dl) as this is the value at which the risk of coronary heart disease increases steeply. Bile acid binding resins eg. cholestyramine and HMG CoA reductase inhibitors are preferred for diabetics with hypercholesterolemia, while fibric acid derivatives are a better choice if hypertriglyceridemia is present[18,1].

The patient described above received grid argon laser photocoagulation to reduce the macular oedema. Laser treatment does not totally arrest the progression of maculopathy. Her vision is also unlikely to improve with laser treatment at this late stage with massive exudations but is aimed at preserving useful existing and navigational vision. This would enable her to perform her daily activities and remain as independent as possible. The ETDRS has shown that laser photocoagulation decreases visual loss from diabetic macular oedema by more than 50%[20]. In addition, Akduman et al have shown that 2 years after grid photocoagulation for diabetic macular oedema, up to 75% of patients have stable vision while 15%

actually enjoy an improvement in their visual acuity of > 3 lines[21].

CONCLUSION

Our case history illustrates the importance of looking not only for possible nephropathy but also at the lipid profile of diabetic patients with severe macular hard exudations. The mainstay of treatment for diabetic retinopathy is still laser photocoagulation[20,22]. However, in the light of the results of various studies, there is a possible role for lipid-lowering drugs to be given as adjuvant therapy in the treatment of diabetic retinopathy in patients with hyperlipidemia[6,5,16].

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