Management & prevention of type 2 diabetes

Statins: good for retinal and renal protection as well?

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Type 2 diabetes is a cardiovascular disease and the concurrence of hypertension, dyslipidaemia and hyperglycaemia are among the recognised and modifiable risk factors contributing to adverse cardiovascular outcomes.

In the fight against macrovascular disease in diabetes cholesterol emerges the most significant variable determining adverse outcome in epidemiological studies. Previous large scale randomised control trials which have included small numbers of patients with diabetes have demonstrated powerful effects of lipid lowering in the primary and secondary prevention of cardiovascular disease.

More recently a large scale study of exclusively patients with diabetes has demonstrated the power of therapy with a statin, in this case Atorvastatin, to protect against adverse cardiovascular outcomes in diabetes patients (see the results of the CARDS trial – www.cardstrial.org).

In contrast, the diabetes specific microvascular complications of retinopathy and nephropathy are essentially glucose dependent and complicate relatively poor glycaemic control over moderate duration in genetically susceptible individuals. Blood pressure is an important accelerator of retinal and renal disease with hypertension perhaps the single most important determinant of progressive decline renal function.

Tantalising evidence, not yet rigorous or robust, but nonetheless exciting, suggests that treatment with statins reduces progressive decline in renal function in patients with coronary artery disease (the GREACE study; Athyros et al, 2004) and now the data from Gupta et al, admittedly from a small scale study (summarised on the right), suggests that oral atorvastatin therapy in patients with type 2 diabetes with dyslipidaemia reduces the severity of hard exudates and subfoveal lipid migration in clinically significant macular oedema and could be an important adjunct in the management of clinically significant macular oedema.

Are these the first tentative steps towards integrated vascular protection in diabetes that include optimal lipid, blood pressure and glycaemic control for both large and small-vessel disease? Watch this space!

Athyros G, Mikhailidis DP, Papageorgiou AA, Symeonidis AN, Pehlivanidis AN, Bouloukos VI, Elisaf M (2004) The effect of statins versus untreated dyslipidaemia on renal function in patients with coronary heart disease. A subgroup analysis of the Greek atorvastatin and coronary heart disease evaluation (GREACE) study. *Journal of Clinical Pathology* 2004; **57**: 728–734

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Endothelial dysfunction predicts type 2 in women

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 The objective of this prospective nested case-control study was to determine if the development of type 2 diabetes in women can be predicted by elevated plasma levels of biomarkers reflecting endothelial dysfunction.

2 The number of women initially enrolled was 121 700; 32 826 gave blood samples in 1989–1990; of those free of diabetes, cancer or cardiovascular disease at baseline, 737 developed diabetes by 2000.

3 A total of 785 controls were selected according to age, race and fasting status.

4 The baseline median levels of the biomarkers were significantly higher among the cases than the controls.

5 Endothelial dysfunction predicted incident diabetes in logistic regression models conditioned on matching criteria and adjusted for BMI, family history of diabetes, smoking and other parameters.

6 Type 2 diabetes in women can be predicted by endothelial dysfunction, independent of risk factors such as obesity and subclinical inflammation.

Meigs JB, Hu FB, Rifai N, Manson JE (2004) Biomarkers of endothelial dysfunction and risk of type 2 diabetes mellitus. *Journal of the American Medical Association* **291**(16): 1978–86

AMERICAN JOURNAL OF OPHTHALMOLOGY

Atorvastatin for management of macular oedema

Readability	✓ ✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓ ✓

1 The aim of this randomised case trial was to establish the efficacy of atorvastatin in people with diabetes with elevated serum lipids, in reducing retinal hard exudates and subfoveal lipid migration after focal/grid laser photocoagulation in clinically significant macular oedema.

2 A total of 30 people with type 2 diabetes and clinically significant macular oedema, dyslipidaemia and hard exudates of ≥ grade 4 were assessed.

3 Group A comprised 15 people who received atorvastatin and group B received no lipid-lowering therapy; both groups were subjected to strict metabolic control within 4–6 weeks of enrolling.

4 All participants received laser photocoagulation after a metabolic control period and were followed up for at least 18 weeks.

5 At baseline all participants had elevated serum lipids.

6 In groups A and B, 66.6 % and 13.3 %, respectively, showed reduction in hard exudates.

7 None of group A, and 33.3 % of group B showed subfoveal lipid migration after laser photocoagulation.

8 Regression of macular oedema was seen in nine eyes in group A, and five in group B; none of the eyes in group A and three of the eyes in group B showed worsening of visual acuity.

7 Oral atorvastatin therapy in people with type 2 diabetes and dyslipidaemia could be a vital adjunct in the management of clinically significant macular oedema.

Gupta A, Gupta V, Thapar S, Bhansali A (2004) Lipid-lowering drug atorvastatin as an adjunct in the management of diabetic macular edema. *American Journal of Ophthalmology* **137**: 675–82

Type 2 diabetes

ANNALS OF INTERNAL MEDICINE

Screening targeting hypertension better than universal

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 The study aimed to estimate the incremental cost-effectiveness of two diabetes screening strategies: universal screening and screening targeted to people with hypertension.

2 The UKPDS Hypertension Optimal Treatment trial and recent cost data were the data sources used in the Markov model of diabetes disease progression.

3 At all ages, incremental cost effectiveness ratios were more favourable for screening targeted to hypertensive people than for universal screening.

4 Screening was most cost effective for people aged 55–75 years.

5 In single-way and probabilistic sensitivity analyses, findings were robust to therapy costs, screening lead time and costs, reduced effectiveness of intensive antihypertensive therapy and increased relative risk reduction for stroke attributed to intensive hypertension control.

Hoerger TJ, Harris R, Hicks KA et al (2004) Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. *Annals of Internal Medicine* **140**(9): 689–99

DIABETES

Enhanced basal platelet activation in diabetes

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 This study evaluated basal arachidonic acid metabolism in relation to the redox status of platelets in people with type 1 and type 2 diabetes and no vascular complications, compared with controls.

2 A total of 10 people with type 1 diabetes and 10 people with type 2 diabetes were included in the study, and 20 matched, healthy controls.

3 Through the collection of blood samples it was found that basal thromboxane B_2 significantly increased in resting platelets from people with type 1 and type 2 diabetes; platelet malondialdehyde level was only higher in those with type 2 diabetes.

4 Vitamin E levels and cytosolic glutathione peroxidase activities were lower in platelets from people with diabetes compared with the controls.

5 There is an increase in oxidative stress and impaired antioxidant defence, particularly in people with type 2 diabetes, which contributes to increased risk of vascular diseases.

Vericel E, Januel C, Carreras M, Moulin P, Lagarde M (2004) Diabetic patients without vascular complications display enhanced basal platelet activation and decreased antioxidant status. *Diabetes* **53**:1046–51

CRITICAL CARE MEDICINE

GLP-1 reduces glucose levels

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 The glucose-lowering effect of the incretin hormone glucagon-like peptide 1 (GLP-1) was investigated in people with type 2 diabetes after major surgery.

2 Eight people with type 2 diabetes who had undergone major surgery were given the intravenous administration of GLP-1 and placebo over 8 hours.

3 During the intravenous infusion of GLP-1, plasma glucose concentrations were significantly lowered and reached a normoglycaemic fasting glucose range within 150 minutes, but remained elevated during placebo infusion.

4 The GLP-1 infusion led to a significant increase of secretion of insulin and a suppression of glucagon secretion.

5 GLP-1 can be used to reduce glucose concentrations after major surgery in people with type 2 diabetes.

Meier JJ, Weyhe D, Michaely M et al (2004) Intravenous glucagon-like peptide 1 normalizes blood glucose after major surgery in patients with type 2 diabetes. *Critical Care Medicine* **32**: 848–51