Diabetes journals

Trial confirms benefits of acarbose treatment in people with impaired glucose tolerance

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The STOP-NIDDM trial was a large trial in Europe, Canada and Israel, which examined the possible benefits of acarbose in patients with impaired glucose tolerance (IGT). The primary endpoint was the development of diabetes, and this was significantly reduced in the people who received acarbose.

A relatively large number of patients dropped out of the study, particularly in the acarbose group. Many dropped out because they could not tolerate the drug, as might be expected from clinical use of acarbose in patients with diabetes.

The development of major cardiovascular events (coronary heart disease, cardiovascular death, congestive cardiac failure, cerebrovascular event and peripheral vascular disease) and the development of hypertension were secondary endpoints in the trial. A modified intention-to-treat analysis was performed, which excluded a small number of patients with missing data, but included patients who discontinued the study early.

The results were astonishing! A 49% relative risk reduction was seen in the development of cardiovascular events (2.5% absolute risk reduction), with a 34% relative risk reduction in the development of new hypertension.

Mechanisms were not studied, but acarbose was associated with reductions in weight, BMI, waist circumference and triglycerides, as well as blood pressure and 2 h plasma glucose concentrations. Advocates of the importance of postprandial hyperglycaemia will consider that these data are supportive, although the best predictors of risk on baseline testing were the treatment group, fasting glucose, and systolic blood pressure. Weight loss with concomitant improvement in other cardiovascular risk factors is another possible explanation.

We now have to consider screening at-risk populations for the presence of IGT, and must consider how acarbose use compares with lifestyle measures and metformin, which have not been shown to reduce cardiovascular events in this group. We may also have to reconsider the use of acarbose in people with diabetes.

DIABETIC MEDICINE

Similar degree of atherosclerosis in diabetes and IHD

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

1 The increased susceptibility of patients with diabetes to cardiovascular disease (CVD) is attributed in part to their more advanced and widespread diffusion of atherosclerosis.

2 The prevalence of patients with diabetes and/or ischaemic heart disease (IHD) in four classes of carotid atherosclerosis, compared with subjects without diabetes or IHD (reference group) was studied using high-resolution B-mode ultrasound.

3 There were 598 patients in the reference group, 74 had diabetes but not CVD, 74 had IHD but not diabetes, and 36 had both diabetes and IHD.

4 Compared with the reference group, the frequency of patients with diabetes but not CVD increased significantly from 'normal' (4.1%) to 'stenotic plaque' (14.8%).

5 For patients with IHD but not diabetes the figures were 6% and 23.3%, and for those with both diabetes and IHD they were 0% and 15.9%.

6 Patients with diabetes but not CVD had an advanced degree of carotid atherosclerosis similar to that in patients with IHD but not diabetes, and significantly higher than that in patients with no diabetes or CVD.

Inchiostro S, Dalfollo M, Marzano A et al (2003) Prevalence of diabetes and/or ischaemic heart disease in classes of increasing carotid artery atherosclerosis: an ultrasonograhic study. *Diabetic Medicine* **20**: 670–76

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Acarbose cuts cardiovascular risk in patients with IGT

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

1 The STOP-NIDDM trial was an international, double-blind placebo-controlled, randomised study.

2 Patients with impaired glucose tolerance (IGT) were randomized to receive either placebo (n = 715) or 100mg acarbose three times a day (714), and followed up for 3.3 years.

3 Of the original 1429 patients enrolled in the trial, 61 did not meet the criteria for IGT, leaving 1368 for intention-to-treat analysis. A further 341 dropped out early, but were followed up for outcome measures.

4 Acarbose treatment was associated with a 49% relative risk reduction for cardiovascular events (absolute risk reduction 2.5%) in patients with IGT; 40 patients would need to be treated over 3.3 years to prevent one cardiovascular event.

5 The largest reduction was seen in risk of myocardial infarction.

6 Acarbose treatment also resulted in a 34% relative risk reduction for development of hypertension (absolute risk reduction 5.3%); 19 patients would need to be treated over 3.3 years to prevent one case of hypertension.

7 The STOP-NIDDM trial is the first prospective intervention study showing that acarbose treatment in patients with IGT reduces the incidence of cardiovascular disease (CVD) and hypertension.

8 These results support the hypothesis that postprandial hyperglycaemia is a risk factor for CVD.

The STOP-NIDDM Trial (2003) Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance. *Journal of the American Medical Association* **290**: 486–93

DIABETES CARE

Nurse-led clinics help more patients achieve targets

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

1 This randomised controlled trial evaluated the effectiveness of specialist nurse-led hypertension and hyperlipidaemia clinics for patients with diabetes receiving shared care.

2 Participants comprised 1407 patients with diabetes presenting for annual review with raised BP (≥140/80 mmHg), raised total cholesterol (≥5.0 mmol/l), or both.

3 A total of 629 were randomised to usual care and 778 to specialist nurse-led clinics, with attendance every 4–6 weeks until targets were achieved (intervention group).

4 The primary outcome was the odds ratio (OR) of achieving targets in hypertension and hyperlipidaemia attributable to the nurse-led intervention.

5 Significantly more patients achieved target after 1 year among those attending the nurse-led clinics compared with those receiving usual care (OR 1.37 [95% CI 1.11–1.69]; P = 0.003).

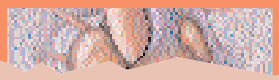
6 Targets were achieved more frequently in patients attending the hyperlipidaemia clinic (OR 1.69 [1.25–2.29], P = 0.007) than in those attending the hypertension clinic (OR 1.14 [0.86–1.51], P = 0.037).

7 There were 25 deaths (3.2%) in those attending either or both clinics compared with 36 deaths (5.7%) in those receiving usual care (OR 0.55 [0.32–0.92], P = 0.02).

8 Specialist nurse-led clinics are an effective adjunct to hospital-based care for people with diabetes.

New JP, Wong LM, Mason JM et al (2003) Specialist nurse-led intervention to treat and control hypertension and hyperlipidaemia in diabetes (SLINT). *Diabetes Care* **26**: 2250–255

DIABETES CARE



Antibiotic use does not protect against MI in diabetes

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

1 The association between infection and coronary heart disease (CHD) in patients with diabetes is of interest because this group has a substantially greater risk of myocardial infarction (MI) than normoglycaemic patients.

2 The relationship between antibiotic use and MI was investigated in a 2-year study of 1041 patients with diabetes and with non-fatal or fatal MI and 5604 matched controls.

3 Researchers found no evidence that usual antibiotic treatment in patients with diabetes was associated with reduced MI for periods of 6, 12 or 24 months after such treatment.

4 Thus, the findings did not support the hypothesis that antibiotic use protects against CHD in patients with diabetes.

Karter AJ, Moffet HH, Thom DH et al (2003) Use of antibiotics is not associated with decreased risk of myocardial infarction among patients with diabetes. *Diabetes Care* **26**: 2100–106

DIABETES/METABOLISM RESEARCH AND REVIEWS

Risk factors in patients with diabetes and AF

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

1 This observational study compared baseline characteristics, additional risk factors for stroke or embolism, rates of mortality, stroke or embolism, and oral anticoagulation in the year 2000, in 419 patients with atrial fibrillation (AF) with and without diabetes over a 10-year period.

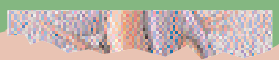
2 All participants had transthoracic and transoesophageal echocardiography and were given oral anticoagulation as recommended at the time.

3 Eighteen per cent had diabetes; of these only 22% had no other risk factor for stroke or embolism.

4 Patients with diabetes were older, and had more frequent heart failure, arterial hypertension and a history of MI, and higher mortality, than participants without diabetes (7%/year vs 4%/year; P=0.0066).

Klem I, Wehinger C, Schneider B et al (2003) Diabetic atrial fibrillation patients: mortality and risk for stroke or embolism during a 10-year follow-up. *Diabetes/Metabolism Research and Reviews* **19**: 320–28

DIABETES



Duration of diabetes may influence onset of MI

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

1 Reports of circadian variation in onset of acute myocardial infarction (MI) in patients with diabetes are conflicting.

2 This multicentre study examined the circadian pattern of acute MI symptom onset in 814 patients with diabetes and 3068 without diabetes to determine whether duration of diabetes might explain the variation in MI onset in patients with diabetes.

3 A significant morning peak in MI onset was seen in patients without diabetes (P < 0.001) but not in patients with type 2 diabetes ≥5 years or type 1 diabetes (P = 0.16).

4 Patients with type 2 diabetes <5 years had a similar pattern of MI onset to patients without diabetes.

5 Findings suggest that previous inconsistency in reports of circadian variation in patients with diabetes may therefore have been due to differences in duration of diabetes and hence the extent of autonomic dysfunction.

Rana JS, Mukamal KJ, Morgan JP, Muller JE, Mittleman MA (2003) Circadian variation in the onset of myocardial infarction:effect of duration of diabetes. *Diabetes* **52**: 1464–468

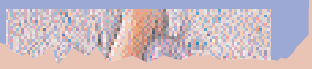
'Significantly more patients achieved target after 1 year among those attending the nurse-led clinics compared with those receiving usual care (OR 1.37 [95% CI 1.11–1.69]; P=0.003).'

'Previous inconsistency in reports of circadian variation in patients with diabetes may have been due to differences in duration of diabetes and hence the extent of autonomic dysfunction.'

'The ADA also recommends low-dose (81–325 mg/day) enteric-coated aspirin as a primary prevention strategy for people with diabetes at high risk of CV events.'

'Statin therapy for the primary prevention of major coronary events in people with type 2 diabetes and LDL cholesterol 100–129mg/dl is affordable and cost-effective relative to statin therapy in those with higher LDL cholesterol levels.'

DIABETES CARE



Serum testosterone and atherosclerosis

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

1 The relationships between serum testosterone and carotid atherosclerosis (determined by ultrasonography), as well as major CVD risk factors, was evaluated in men with type 2 diabetes.

2 Free and total testosterone (F-tes and T-tes) were measured in 253 men with type 2 diabetes and carotid atherosclerosis, determined by intima-media thickness (IMT) and plaque score (PS), and major CVD risk factors, in a subgroup of 154 patients.

3 F-tes and IMT were inversely correlated, as were F-tes and PS; Men with F-tes <10 pg/ml had significantly greater IMT and PS.

4 F-tes and age were inversely correlated; and F-tes and total cholesterol were positively correlated.

5 F-tes was thus inversely associated with carotid atherosclerosis.

Fukui M, Hirata C, Kitagawa Y et al (2003) Association between serum testosterone concentration and carotid atherosclerosis in men with type 2 diabetes. *Diabetes Care* **26**: 1869–73

DIABETES CARE

How cost-effective is statin therapy?

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

1 About 8.2 million Americans have diabetes, LDL cholesterol ≥100 mg/dl and no cardiovascular (CV) disease.

2 Statin therapy in this group could prevent around 71000 major coronary events each year.

3 Statin therapy costs $600–1000 per person per annum in those with LDL cholesterol 100–129 mg/dl, and $700–2100 where LDL cholesterol is ≥130 mg/dl.

4 Annual incremental cost per subject ranges from $480–950 in those with LDL cholesterol 100–129 mg/dl and from $590–1920 in those with LDL cholesterol ≥130 mg/dl.

5 Statin therapy for the primary prevention of major coronary events in people with type 2 diabetes and LDL cholesterol 100–129 mg/dl is thus affordable and cost-effective relative to statin therapy in those with higher LDL cholesterol levels.

Brandle M, Lorber B, Davidson MB et al (2003) Cost-effectiveness of statin therapy for the primary prevention oof major coronary events in individuals with type 2 diabetes. *Diabetes Care* **26**: 1796–801

DIABETES

Subclinical inflammation may predict diabetes

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

1 This study investigated the inflammation–diabetes association, in a case-cohort study.

2 Analyses were performed on the stored plasma of 581 people with diabetes and 572 without diabetes.

3 Statistically significant hazard ratios of developing diabetes for those in the fourth (vs first) quartile of inflammation markers, ranged from 1.9 to 2.8 for sialic acid, orosomucoid, interleukin-6 and C-reactive protein.

4 An inflammation score based on these four markers plus white cell count and fibrinogen predicted diabetes in whites but not African Americans (interaction P=0.005) and in non-smokers but not smokers (interaction P=0.13).

5 The results support the view that low-grade systemic inflammation precedes and predicts the development of type 2 diabetes in adults – at least in white non-smokers.

Duncan BB, Schmidt MI, Pankow JS (2003). Low-grade systemic inflammation and the development of type 2 diabetes. *Diabetes* **52**: 1799–805

DIABETES CARE

Antiplatelet agents recommended for high-risk patients

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

1 Patients with diabetes and atherosclerosis are at especially high risk of additional ischaemic events, including stroke and vascular death.

2 Platelet aggregation plays an integral role in thrombus formation, hence treatment strategies have focused on the use of antiplatelet agents to prevent ischaemic events.

3 A meta-analysis of clinical trials in the Antiplatelet Trialists' Collaboration, which included patients with diabetes, established the efficacy of aspirin as a secondary prevention strategy relative to placebo.

4 Three primary prevention trials used aspirin for primary prevention in patients with diabetes at high risk of cardiovascular (CV) events.

5 Clopidogrel, an adenosine diphosphate receptor blocker, produced additional risk reduction relative to aspirin in two secondary prevention trials (CAPRIE and CURE).

6 The American Diabetes Association (ADA) recommends the use of a secondary prevention strategy that includes antiplatelet agents for patients with diabetes and evidence of macrovascular disease (history of myocardial infarction, vascular bypass procedure, stroke or transient ischaemic attack, peripheral vascular disease, claudication or angina).

7 The ADA also recommends low-dose (81–325 mg/day) enteric-coated aspirin as a primary prevention strategy for people with diabetes at high risk of CV events.

8 Clopidogrel is recommended if aspirin allergy is present.

Colwell JA, Netso RW (2003) The platelet in diabetes. *Diabetes Care* ***26***: 2181–188