ACE inhibitors and ARBs lower diabetes risk

Treatment with ACE inhibitors or angiotensin receptor blockers (ARBs) can lower the risk of developing type 2 diabetes, according to the results of a meta-analysis of randomised controlled trials.

This study by Coleman et al clearly demonstrates that ACE inhibitors or ARBs can also prevent the onset of type 2 diabetes. These two drug classes have been known to slow the progression of kidney disease in patients with diabetes. However, the finding of a diabetes preventive effect is new, and will likely have an impact on the drugs we choose for patients with high blood pressure.

Coleman and colleagues studied pooled data from six trials of ACE inhibitors and five of ARBs involving more than 66,000 patients.

Both agents led to a similar reduction in new-onset diabetes, the researchers report in Diabetes Care. The odds ratio was 0.79 for ACE inhibitors and 0.76 for ARBs. Reductions were maintained regardless of the treatment indication. However, neither drug reduced the odds of mortality or cardiovascular or cerebrovascular events.

For patients who might benefit similarly from any blood pressure-lowering drug, and particularly for patients who are at high risk for developing diabetes, the study demonstrates the use of either an ACE inhibitor or ARB makes sense.

In these patients you are get two benefits in one. You receive a highly effective medication for your primary health problem and prevent the onset of a second deadly disease.


Statins safely reduce risk of major vascular events: meta-analysis

Lowering LDL cholesterol levels with statin therapy significantly reduces the incidence of major coronary events, coronary revascularization, and ischaemic stroke, without increasing cancer risk or deaths due to other causes, suggests this meta-analysis.

Although individual studies have demonstrated the beneficial effects of statins, questions remained about particular outcomes and effects in different subgroups. The Cholesterol Treatment Trialists’ Collaborators therefore performed a meta-analysis of 14 trials of statin therapy that included approximately 90,000 subjects. They report their findings in The Lancet, of 27 September 2005.

The results show a 19% reduction in deaths from coronary heart disease per mmol/L LDL cholesterol reduction (p < 0.0001).

There was also a 23% reduction in the incidence of first major coronary events, a 24% reduction in the incidence of first coronary revascularization, and a 22% reduction in ischaemic strokes per mmol/L LDL cholesterol reduction (p < 0.0001 for each).

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Metformin may reduce morbidity, mortality in heart failure

A new study suggests metformin may improve survival and clinical outcome in diabetic patients with heart failure, even though FDA labelling recommends against using the drug in these patients.

Stable heart failure and diabetes can be safely treated with metformin,“ Jeffrey A. Johnson of the University of Alberta in Edmonton concluded.

Warnings against using metformin are based on past experience with the similar drug phenformin, which was withdrawn from the market in the 1970s after being linked to hundreds of cases of lactic acidosis, Johnson notes in the October issue of Diabetes Care.

However, there is a scarcity of information linking the newer drug to this side effect, and recent studies suggest metformin may actually be more effective than sulphonylureas in reducing mortality from cardiovascular causes. As many as 10% to 15% diabetic patients with heart failure are prescribed the drug despite the labelling, Johnson adds, largely due to the scarcity of other treatment options.

To investigate whether contraindications are warranted, the researchers identified 12,272 new users of oral anti-diabetic drugs, 1833 of whom developed heart failure, and classified them based on the type of drug they were taking.

Compared to sulphonylurea monotherapy, the researchers found, metformin reduced mortality and hospitalisation among patients with heart failure. One third of patients on metformin died, compared with 52% of patients on sulphonylureas only. Seventy-seven percent of patients on metformin died or were hospitalised, compared with 85% of patients on sulphonylurea alone.

Given that this is a comparative study, Johnson notes, it's not possible to say whether metformin improved outcomes or sulphonylureas worsened them. He points out that some older sulphonylureas have been shown to have some cardio toxicity, while newer members of the drug family likely are safer.

Nevertheless, he adds, "we think there's probably strong enough evidence to say that it should not be contraindicated. There's no real evidence of the lactic acidosis happening in most patients with heart failure and diabetes. We are speculating from our study that there may even be a benefit."

Better studies are needed to answer the question of metformin's effectiveness, Johnson concludes.

Source: Diabetes Care 2005;28:2345-2351
Impaired insulin sensitivity independently predicts mortality in patients with otherwise stable chronic heart failure (CHF), according to the September 20th Journal of the American College of Cardiology.

Impaired insulin sensitivity commonly complicates CHF, but its clinical significance remains unclear. Wolfram Doehner and colleagues from Berlin, investigated whether insulin resistance independently impaired prognosis in 105 men with ischaemic (63%) or non-ischaemic (37%) CHF. Patients who died during follow-up had 42% lower baseline insulin sensitivity than patients who survived. Insulin sensitivity also showed stepwise decreases as the NYHA functional class worsened and as left ventricular ejection fraction decreased, the report indicates.

In multivariate analysis that adjusted for age, body mass index (BMI), triglyceride levels, physical activity, family history, and smoking status, subjects in the top three quintiles of FPG levels had significantly higher risk of diabetes compared with the lowest quintile.

Among men who were obese (BMI > 30) and in the highest quintile of FPG, the hazard ratio for diabetes was 8.29 compared with normal weight men in the lowest quintile of FPG. Similarly, among men with elevated serum triglyceride levels (beyond 150 mg/dL) and in the highest quintile of FPG, the hazard ratio was 8.23.

"The identification of a high-normal FPG level as a risk factor for type 2 diabetes may help to identify young, healthy men for whom preventive interventions might be considered," Tiros's team observes. They suggest that lifestyle modifications, glucose-lowering medications, and the anti-obesity drug orlistat could be used to delay the onset of diabetes in these patients.

Writing in a related editorial, Ronald A. Arky from Harvard Medical School agrees and adds that there is no reason to believe that the lessons from the study are sex specific, and are thus likely to extend to women.


Having a higher fasting plasma glucose (FPG) level within the normoglycaemic range is an independent risk factor for type 2 diabetes among young men, Israeli researchers report in the October issue of the New England Journal of Medicine.

Amir Tirosh et al, from Sheba Medical Center evaluated data on 13,163 men, ages 26 to 45, with FPG levels of less than 5.6 mmol/l at baseline. During mean follow-up of 5.7 years, there were 208 documented incident cases of type 2 diabetes.

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High normal fasting plasma glucose points to diabetes

Insulin resistance predicts mortality in chronic heart failure

Impaired insulin sensitivity independently predicts mortality in patients with otherwise stable chronic heart failure (CHF), according to the September 20th Journal of the American College of Cardiology.

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In multivariate analyses, insulin sensitivity predicted mortality independently of all other clinical parameters, with decreasing insulin sensitivity consistently predicting impaired survival. Two-year survival was 83% in patients with insulin sensitivity above the median, whereas survival was only 61% in patients with insulin sensitivity below the median. The difference was even more marked at 4 years (73% versus 37%, respectively).

Insulin resistance provides additional prognostic information independent of well-established prognosticators, such as clinical status, age, left ventricular ejection fraction, and exercise capacity, as well as body composition measures. “From the present data, it seems promising to test in future studies whether early detection and therapeutic targeting of insulin resistance in CHF may improve the outcome in these patients,” the authors conclude.

“These studies suggest a possibility of improving heart failure outcomes by treating insulin resistance,” agrees Javed Butler from Vanderbilt University, Nashville, in a related editorial.

"Indeed, a recent study showed significant benefit with insulin sensitizers in heart failure patients with diabetes," Butler continues. "If these results are replicated, it would not be surprising that such drugs like thiazolidinediones may become part of the therapeutic armamentarium for heart failure."

Patients with type 2 diabetes commonly experience regression or remission of microalbuminuria, especially when blood glucose is carefully controlled, according to a report in the October issue of Diabetes.

"We think that we should shift the goal on diabetic patients' care from the treatment for preventing progression of diabetic complications to the treatment aiming at remission," says Shin-ichi Araki from Japan. "Our study suggests that we can do it." Araki et al estimated the frequency of remission and regression of microalbuminuria in 216 patients with type 2 diabetes. Overall, about half the patients experienced remission of microalbuminuria at some point during the 6-year study.

Fifty-four percent of the patients had at least a 50% reduction in microalbuminuria during the study, and only 28% experienced progression of their microalbuminuria to overt proteinuria.

The use of ACE inhibitors or ARBs, lower tertiles of HbA1c, and lower tertiles of systolic blood pressure were independently associated with regression of microalbuminuria.

Similar factors were associated with remission. The coexistence of more than one independent factor enhanced the chances of remission or regression.

"This observation should not be construed as indicating that microalbuminuria is an unreliable indicator," the investigators write. "Rather, it should be taken to emphasise the importance of aggressive multifactorial control including glycaemic exposure, blood pressure, and the use of drugs blocking the renin-angiotensin system as early as possible to prevent progression of diabetic nephropathy and cardiovascular events."

"Our study does not provide any evidence regarding the beneficial effect of remission / regression of microalbuminuria on future outcomes in diabetic patients," Araki added. "We just suppose that remission / regression of microalbuminuria will result in reduction of the incidence of advanced nephropathy or cardiovascular mortality." The researchers are continuing to follow the study participants to clarify these points.

Source: Diabetes 2005;54:2983-2987

Good glycaemic control is associated with an enhanced response in patients with diabetic retinopathy undergoing pan retinal photocoagulation.

"Strict metabolic control of diabetes mellitus is essential for a better treatment response of high-risk proliferative diabetic retinopathy to laser pan retinal photocoagulation," Marua Kotoula, of University Hospital of Larissa, et al note that there is a direct relationship between glycaemic control and diabetic retinopathy. However, the effect on the response to photocoagulation has not been studied. This is also the case for the influence of microalbuminuria. To investigate, a prospective study of photocoagulation procedures in 115 eyes in diabetic patients with high-risk proliferative diabetic retinopathy was conducted.

The patients were treated in 3 divided sessions at 2-week intervals. The patients were followed-up at 12 weeks after the last pan retinal photocoagulation session. Overall, response was successful in 65 eyes (56.5%). The likelihood of a successful response was significantly related to HbA1c but not with microalbuminuria.

The researchers conclude that HbA1c levels below 8% during the pre-treatment, treatment and post-treatment periods are associated with a regression of proliferative diabetic retinopathy.

Based on the results, the authors suggest further studies for the discovery of the local mechanisms under which the better glycaemic control inhibits neovascularization.