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INSIDE

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Acute Coronary Syndromes: Women are Stronger

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Professor, University of California, San Diego

Dr. Scherger reports no financial relationship to this field of study.

Synopsis: *Among men and women with an acute coronary syndrome without ST segment elevation, men are much more likely than women to develop an acute myocardial infarction.*

Source: Svensson L, et al. Are predictors for myocardial infarction the same for women and men when evaluated prior to hospital admission? *Int J Cardiol.* 2006;109:241-247.

This prospective study from Sweden looked at 433 men and women presenting acutely with an acute coronary syndrome without ST elevation. Forty-five per cent of the patients were women. The average age of the men was 67 and of the women 73. Two thirds of the patients in both groups had a previous history of angina pectoris. The study looked at symptoms, clinical findings, ECG pattern and biochemical markers.

The clinical picture of acute coronary syndrome among men and women in this study was similar. Almost all the patients had chest pain and about half had dyspnea. Men were more likely than women to develop a cold sweat (35 to 26%). More women than men had nausea (33 to 26%). The most dramatic finding was that fewer women (17%) than men (26%) developed an acute myocardial infarction (AMI). Among the patients with ST segment depression (23% of men and 30% of women), the difference was more striking with 54% of men and only 22% of women developing an AMI.

COMMENTARY

Coronary heart disease is the most common cause of death in women and men. Studies through the years have suggested that women may present differently with acute coronary syndromes than men, with whom the classic findings of angina and acute myocardial infarction have been described. Women have been suggested as more often having coronary spasm and chest pain which rules out as a myocardial infarc-

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tion. Prior to hospital admission women appear to have a lower mortality than men.[1,2] The opposite is found after hospital admission where women have a higher mortality especially in younger age groups.[1,2] It has been reported that women are treated less aggressively than men which may be related to a different clinical picture.[3,4]

This large prospective study from Sweden looked at differences between men and women with acute coronary syndromes without initial evidence of an acute myocardial infarction by ST segment elevation. Men are more likely to develop a cold sweat, a more certain sign of acute coronary disease than nausea, which was more common in women. For whatever reasons, men are more likely than women to develop an AMI in this situation, especially if there is initial ST segment depression.

Compared to men, women with acute coronary syndromes appear to be more resilient. Their clinical picture is often more subtle. Traditional classic signs of angina appear more often in men than women. Hence women need a higher index of suspicion for acute coronary disease when they present acutely with chest pain in the emergency setting. ■

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TIA Management: Emphasis on Urgent Evaluation and Treatment

ABSTRACT & COMMENTARY

By Dana Leifer, MD

Associate Professor, Neurology, Weill Medical College, Cornell University.

Dr. Leifer reports no financial relationship relevant to this field of study.

Synopsis: *Patients with transient ischemic attacks should usually be admitted to the hospital and receive rapid evaluation and treatment.*

Source: Johnston, SC, et al. National Stroke Association Guidelines for the Management of Transient Ischemic Attacks. *Ann Neurol.* 2006:60:301-313.

A GROWING BODY OF EVIDENCE INDICATES THAT there is a significant risk of stroke in the days immediately after a transient ischemic attack. Johnston et al found that 5% of TIA patients had a stroke within 48 hours and another 5% had a stroke within 90 days. Several other groups have obtained similar results. In addition, Rothwell et al showed that approximately 20% of stroke patients have a TIA before their stroke and that of these, 26% occurred on the day of the stroke or the day before the stroke, and an additional 19% occurred between 2 and 7 days before the stroke.[1] Taken together, these data indicate a need to take TIAs seriously, to initiate appropriate preventive treatment quickly, and to

facilitate rapid intervention if a stroke develops.

In this background, the National Stroke Association (NSA) established an expert panel to develop guidelines for TIA management. The panel was chosen objectively on the basis of publications related to TIA and stroke. After a literature search, the quality of evidence was rated, and recommendations were derived from the rated evidence. Multiple rounds of comments from the panel were used to derive a consensus, and panel members were excluded from contributing to topics for which they had a possible conflict of interest. This approach was designed to avoid bias in selection of experts, to prevent overweighting of dominant personalities in the consensus process, and to permit efficient updating of the recommendations.

The guidelines emphasize the need for timely treatment of TIAs. The chief points are: 1) Hospitalization should be considered for all patients presenting within 48 hours of their first TIA to facilitate thrombolytic therapy if a stroke develops and to begin secondary prevention rapidly. An important corollary that the guidelines do not address, however, is that if patients are admitted, they need to be monitored closely to minimize the delay in recognizing in-hospital strokes. 2) Timely referral to a hospital is also advisable for all patients within one week of a TIA and hospital admission is generally recommended for patients with crescendo TIAs, TIAs lasting more than one hour, > 50% carotid stenosis if symptomatic, known cardioembolic sources, known hypercoagulability, and combinations of other factors placing patients at high risk based on recently developed scales for rating stroke risk after TIA (*Stroke.* 2006;37:320-322).

The guidelines also make recommendations about the infrastructure that should be available for evaluation of TIA patients: 1) Local protocols should be established to identify patients who will be admitted and those who will be referred for outpatient evaluation. Specialty clinics for outpatient evaluation within 24 to 48 hours should be available for patients who are not admitted. Patients who are not admitted should be instructed to return at once if they have recurrent symptoms. 2) Patients not admitted should have access within 12 hours to CT or MRI, EKG, and carotid Doppler. These should be done within 24 to 48 hours if they are not done in an emergency room. If they are done and are normal, a longer period of up to 7 days may be appropriate for further work-up. 3) Patients with TIA within 2 weeks who are not admitted should be worked up within 24 to 48 hours (ie, carotid Doppler, blood work, cardiac evaluation such as EKG, rhythm strips, and echocardiography). 4) Medical assessment should at least include EKG, CBC, electrolytes, creatinine, glucose, and lipid studies. 5) Imaging should include CT or MRI for all patients to rule out structural lesions such as acute stroke, subdural hemorrhage, and brain tumor (25% or more of patients with a clinical TIA may actually have had a small stroke). Some form of vascular imaging (ie, ultrasound, CTA, or MRA) should also be performed. Catheter angiography remains the gold standard, but should be used for diagnostic purposes primarily when the other tests are discordant or cannot be performed. 6) Cardiac evaluation with transthoracic or transesophageal echocardiography and testing for right to left shunting is advised in patients younger than 45 years of age if other studies do not identify a cause for the TIA.

The guidelines go on to make specific recommendation for antithrombotic therapy and for treatment of other specific risk factors that are identified during the work-up. These are important and emphasize the need for antiplatelet therapy for most patients, anticoagulation when indicated, and aggressive management of risk factors including carotid stenosis, hypertension, hyperlipidemia, and diabetes. The recommendations are largely similar to those of the American Heart Association's 2006 statement on stroke prevention (*Stroke.* 2006;37:577-617). Those guidelines, however, did not address the importance of rapid evaluation of TIA patients. The main importance of the new NSA guidelines is that they stress the need for rapid evaluation and treatment of TIA patients. ■

Simple Measures to Prevent Vasovagal Syncope

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco

Dr. Crawford reports no financial relationship to this field of study.

Synopsis: *Physical counterpressure maneuvers are a risk-free, effective, and low-cost treatment method in patients with vasovagal syncope and recognizable prodromal symptoms, and should be advised as first-line treatment in patients presenting with vasovagal syncope with prodromal symptoms.*

Source: van Dijk N, et al. Effectiveness of physical counterpressure maneuvers in preventing vasovagal syncope. *J Am Coll Cardiol*. 2006;48:1652-1657.

VASOVAGAL SYNCOPE IS A COMMON AND OFTEN DISabling disorder that lacks solid evidence-based treat-

ment options. Thus, the Physical Counterpressure Maneuvers trial was conducted in 15 centers worldwide that treat syncope patients. Patients with recurrent typical vasovagal syncope with prodromal symptoms were recruited. Patients with overt heart disease, orthostatic hypotension and other causes of syncope were excluded. Patients with negative head-up tilt-table tests were included if their symptoms were classic. Patients were randomized to standardized optimal conventional therapy with or without training in physical counterpressure maneuvers. Conventional therapy included the admonition to increase salt and water intake, but not drug therapy. The physical maneuvers included leg crossing, handgrip and arm tensing without doing the Valsalva maneuver. The primary end point was the risk of recurrent syncope. Conventional therapy was applied to 117 patients and counterpressure to 106. Mean follow-up of the 208 patients (mean age 38 years) not lost to follow-up was 14 months. Syncope recurred 142 times in the conventional group and 76 in the counterpressure group for a recurrence rate of 51% and 32%, respectively (RR .36, CI = .11–.53, P = .005). Presyncopal events were similar in both groups, 74% vs 83% (P = NS). Women had more recurrences then men, but the effectiveness of counterpressure was not different. Patients preferred arm tensing to handgrip and leg tensing. There were no injuries during follow-up. The authors concluded that physical counterpressure maneuvers are an effective risk-free, low-cost method to prevent vasovagal syncope in patients with prodromal symptoms and should be the therapy tried first.

COMMENTARY

Recurrent vasovagal syncope is often treated by drugs such as fludrocortisone to increase salt and water retention, but this therapy has not been subjected to a randomized controlled trial. Vasoactive drugs have not been superior to placebo in trials and pacemaker studies have had mixed results. Thus, this is the first randomized controlled trial that has shown benefit from any treatment for vasovagal syncope. Unfortunately, although simple, it cannot be applied to everyone with vasovagal syncope. Some patients may have no prodromal symptoms or symptoms that are too brief to act quickly to prevent syncope. The authors believe this may explain some of the treatment failures, since not every syncopal event is the same in a patient. They may have prodromal symptoms, but not always.

There are some limitations to the study. Not everyone got carotid sinus massage, so some with this condition could have been in the trial and explained some of the treatment failures. Also, some may have inadvertently performed a Valsalva maneuver which would thwart the benefit of muscle tensing. Only the patients were blinded, so physician interpretation of recurrences could have been biased in some cases. In addition, head-up tilt-table testing was not positive in everyone, so some could have had other causes of syncope that would not respond to muscle tensing. There may have been some patients in the trial that could have responded to drug therapy.

Despite these limitations, this was an impressive study with a number needed to treat of 5 to prevent one recurrent syncopal event. It makes sense to try this simple approach first in appropriate patients before embarking on drug therapy or devices. ■

Prolonged Hormone Replacement Therapy Linked to Increased Ovarian Cancer Risk

ABSTRACT & COMMENTARY

By William B. Ershler, MD

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Dr. Ershler reports no financial relationship to this field of study.

Synopsis: *There have been conflicting reports on the risks of ovarian cancer in users of hormone replacement therapy. In the NIH-AARP Diet and Health Study Cohort, analysis of various aspects of HRT and the development of ovarian cancer in approximately 100,000 women aged 50-71 years was undertaken. Long durations of use of unopposed estrogen and of estrogen plus progestin, especially sequential regimens, were found to be associated with increased ovarian cancer risk.*

Source: Lacey JV, et al. Menopausal hormone therapy and ovarian cancer risk in the National Institutes of Health-AARP Diet and Health Study cohort. *J Natl Cancer Inst*. 2006;98:1397-1405.

THERE HAVE BEEN MANY STUDIES EXAMINING THE relationship between hormone replacement therapy and ovarian cancer risk, but none have been conclusive in demonstrating increased risk.

The National Institutes of Health-AARP Diet and Health Study was originally conducted in 1995when a questionnaire addressing health related issues was mailed to 3.5 million AARP members. This baseline

instrument addressed details of demographics, reproductive history, family history and hormone replacement therapy use including duration and type of treatment. The survey was followed by a second questionnaire (1996 to 1997) that requested more detailed information about the actual hormone replacement therapy.

The study was conducted on 136,409 women aged 50-71 years who completed the second questionnaire. Of these, 97,638 met the criteria for inclusion in the current analysis. Women who used unopposed estrogen for longer than 10 years were found to have a statistically significant increased risk for developing ovarian cancer (RR, 1.89; 95% confidence interval [CI], 1.22-2.95; P = 0.004). This association was slightly attenuated in women with hysterectomy (RR, 1.70; 95% CI, 0.87-3.31; P = 0.06). A similar pattern was found for women with intact uteri who used combination estrogen/progesterone therapy (RR, 1.50; 95% CI, 1.03-2.19; P = 0.04).

Interestingly, risk of ovarian cancer for women with intact uteri was found to be higher for women taking sequential regimens (RR, 1.94; 95% CI, 1.17-3.22; P = 0.01) in contrast those who received continuous regimens (RR, 1.41; 95% CI, 0.90-2.22; P = 0.14). Furthermore, this increase in risk with sequential regimens was apparent even after a shorter duration of treatment (eg, 5 years).

COMMENTARY

Due to its large sample size and detailed questionnaire addressing multiple different patterns of hormone use, this study allows for better determination of hormone replacement risk in post-menopausal women. Based on this analysis, it would appear that short duration with low-dose regimens of hormones may be an option for women with severe symptoms of menopause without significantly increasing risk of developing ovarian cancer.

The finding of increased risk with sequential versus continuous therapy is in line with a large Swedish case-control study published in 2002.[1] Sequential regimens typically result in monthly withdrawal bleeding and these are most commonly used by perimenopausal, or early post-menopausal women. The convenience of continuous regimens (including continuous combined regimens) and absence of breakthrough bleeding in most women after the first few months of use are thought to contribute to preferential use among women who are years past menopause.[2,3] Because younger women have a lower incidence of ovarian cancer, the more frequent use of the sequential regimen in this age group might have over-emphasized the magnitude of the risk.

Hormonal replacement therapy has declined dramatically since the publication of the Women's Health Initiative in 2003[4] and it is likely that the increased ovarian cancer risk observed among long-duration users of unopposed estrogens will diminish in scope over the next several years. However, the current study also provides evidence that links use of estrogen plus progestin, especially in sequential regimens to increased ovarian cancer risk. If confirmed, this is a modifiable risk factor that may be explored in strategies to reduce incidence of this often lethal cancer. ■

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Diabetes in Modern Air Travel

ABSTRACT & COMMENTARY

By Carol A. Kemper, MD, FACP

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Dr. Kemper reports no financial relationship relevant to this field of study.

Synopsis: *Patient education may help to reduce the incidence of problems related to travel in those with diabetes mellitus.*

Source: Burnett JC, et al. Long- and short-haul travel by air: issues for people with diabetes on insulin. *J Travel Med*. 2006;13:255–260.

These authors in Aberdeen queried 493 insulin-using diabetics presenting for routine care at the diabetes center regarding their experiences traveling abroad within the previous 12 months. Surprisingly, nearly two-thirds had some kind of air travel abroad in the previous year. Nearly half (44%) had traveled once or twice in the

previous 12 months, and 24% had traveled > 10 times. The patients were grouped into those with short air flights (< 4 hrs) or long-haul flights (> 4 hrs).

One-tenth of each group experienced hypoglycemia either during the flight or within 24 hrs of arrival. Delays in air travel departure and landing times occurred in nearly one-third of subjects. While 91% carried some food with them during their flight, 10% reported problems with meals, including delays in obtaining meals and difficulty obtaining a pre-ordered diabetic tray. Of those with hypoglycemia, 31% were severe and required assistance. Unfortunately, in order to compensate for the possibility of hypoglycemia, many travelers reported deliberately experiencing hyperglycemia. This was 10-times more likely to be reported by individuals with long-haul flights.

While most insulin-using diabetics traveled with a companion or informed the airline staff they were using insulin, fully 15% told no one they were using insulin. Less than half had sought medical advice about managing their diabetes during travel.

COMMENTARY

Air travel has just gotten harder, and with the latest restriction on food/fluids on board, except when declared medically necessary, I suspect many travelers with medical illness may experience more frequent problems. During a recent flight from San Francisco to Toronto, no meals were served, although a snack of Oreo cookies, granola bars, and cheddar fish crackers was available for $5, hardly a healthy snack, especially for someone with diabetes. The authors suggest that diabetes clinics consider incorporating travel advice into their routine diabetes education. Pre-printed educational pamphlets for diabetics, even for short flights, may be useful. ■

Pharmacology Update

Rasagiline Tablets (Azilect®)

By William T. Elliott, MD, FACP, and James Chan, PhD, PharmD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; Assistant Clinical Professor of Medicine, University of California, San Francisco; Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Chan and Elliott report no financial relationships to this field of study.

A SECOND GENERATION, SELECTIVE, IRREVERSIBLE, monoamine oxidase type B inhibitor has been approved for the treatment of Parkinson's disease (PD). Rasagiline is manufactured by Teva Pharmaceutical Industries Ltd in Israel and marketed by Teva Neurosciences, Inc. and Eisai Inc. in the United States as "Azilect®."

Indications

Rasagiline is indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease both as initial therapy and as adjunct therapy with levodopa.[1]

Dosage

The recommended dose for monotherapy is 1 mg daily. For adjunctive therapy, the recommended initial dose is 0.5 mg daily. The dose may be increased to 1 mg daily. The dose of levodopa may be reduced based on individual response such as dopaminergic side effects. In clinical trials, 9-17% of patients had levodopa dosage reduction with an average dose reduction of 9%-13%.[1]

Potential Advantages

Rasagiline is dosed once daily and titration is generally not necessary. Rasagiline is 5 to 10 times more potent than selegiline. In contrast to selegiline, rasagiline is not metabolized to L-amphetamine and L-methamphetamine.[2]

Potential Disadvantages

Rasagiline does not appear to be as effective as other anti-Parkinson drugs as monotherapy.[2] Dyskinesia was reported in 18% of patients who had rasagiline added to levodopa and dopamine agonist compared to 10% for placebo ($P = 0.03$).[3] Dietary restriction and avoidance of exogenous amines are recommended.[1] A higher incidence of depression, hallucination, and postural hypotension has been reported in patients older than 65 or 70 years when combined with levodopa.[4] Coadministration of tricyclic, SSRI, and SNRI antidepressants should be avoided and dosage reduction of rasagiline is recommended if coadministered with a CYP1A2 inhibitor (eg, ciprofloxacin).[1]

Comments

The efficacy of rasagiline has been demonstrated in one study in early PD not requiring dopaminergic therapy and 2 studies in patients with PD and motor fluctuations.[3,5,6] As initial therapy, the TEMPO Study showed that patients randomized to rasagiline had a adjusted reduction in the United Parkinson's Disease Rating Scale (UPDRS) of -4.20 compared to placebo at 26 weeks, (n = 404).[5] As adjunct therapy, rasagiline was added as adjunct to levodopa in patients with mean

disease duration of 9-10 years.[3,6] These patients were on a mean levodopa dose of 700-800 mg, and 60-70% were also on dopamine agonist. The mean "off" (poor or absent motor function) time was about 6 hours. The follow-up time was 18 weeks in one study (LARGO; n = 687) and 26 weeks in another (PRESTO; n = 472). The addition of 1 mg of rasagiline decreased "off" time by 0.94-1.18 hours. This improvement was similar to entacapone, which was an active arm in one study.[3] As a continuation of the TEMPO Study, patients in the placebo group were given rasagiline for an additional 26 weeks and those on rasagiline continued for another 26 weeks.[7] Patients treated with rasagiline for 12 months showed less functional decline than those with treatment delayed for 6 months. This along with animal models showing antioxidant and antiapoptotic properties suggest that rasagiline and/or its metabolite, aminoindane, may have neuroprotective effects. Further study is required to substantiate whether rasagiline affects disease progression. A multicenter study (ADIAGO) was initiated in 2005 to investigate this possible effect. Rasagiline is generally well tolerated. The frequencies of worsening cognitive and behavioral symptoms appear to be low.[8] Dyskinesia has been reported when rasagiline is added to levodopa and the elderly may be more likely to experience postural hypotension, depression, or hallucinations. The wholesale cost of rasagiline is $6.82 per day.

Clinical Implications

Parkinson's disease is a progressive neurodegenerative disease. Rasagiline is the newest anti-Parkinson drug and has demonstrated efficacy in early PD as well as an adjunct to levodopa in moderate-to-advanced disease. While rasagiline is conveniently dosed and well tolerated it may not be as effective as levodopa for early PD. As adjunct to levodopa, its effects may be similar to entacapone. Since comparative studies are not available and the potential neuroprotective effects need to be proven, the role of rasagiline remains to be established. ■

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CME Questions

31. Which of the following is NOT consistent with women presenting with an acute coronary syndrome compared with men?

a. Women more present with nausea than men
b. Women less often have a cold sweat
c. Women with ST segment depression are more likely than men to develop an acute myocardial infarction
d. Women have a lower mortality than men prior to hospital admission

32. Which of the following may prevent vasovagal syncope?

a. Increased salt and water intake
b. Diuretics
c. Isometric limb muscle contraction
d. A and C

Answers: 31 (c); 32 (b)

CME Objectives

The objectives of *Internal Medicine Alert* are:

- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances;
- to describe cost-effective treatment regimens;
- to describe the pros and cons of new screening procedures.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Is There a Link between Coffee and Diabetes?

The relationship between coffee and diabetes is complex. For instance, even though cohort studies suggest less risk of diabetes in coffee drinkers, similar results have been seen in data evaluating decaffeinated coffee consumption, suggesting that some other component than caffeine might be responsible. Another limiting factor of previous studies is the inclusion of subjects based upon definition of diabetes by self report, rather than as confirmed by oral glucose tolerance testing (OGTT).

Smith, et al followed middle-aged adults (n = 910) for 8 years, comparing coffee drinkers with non-coffee drinkers. The population was also compartmentalized into persons with and without prediabetes as baseline. New development of diabetes was confirmed with OGTT.

The odds ratio for development of new-onset diabetes was 0.36 for coffee drinkers compared to non-drinkers. Similar risk reduction was seen in the population who were prediabetic at baseline. There was no relationship between the amount of coffee imbibed daily with outcomes. Coffee drinkers have about a 60% reduced risk of developing diabetes than non-drinkers. Persons with prediabetes enjoy similar reductions in risk as persons with normal glucose metabolism. ■

Smith B, et al. Diabetes Care. 2006;29: 2385-2390.

Is it Time to Start Screening for Lung Cancer?

Trials of screening for lung cancer have not provided robust support, and major consensus groups do not endorse lung cancer screening. Because the burden of lung cancer is epidemiologically compelling, and the volume of at risk-individuals is equally prominent, investigators have sought to determine whether progressively more sensitive tools (ie, capable of detecting lung CA at smaller size) might provide advantage.

The Early Lung Cancer Action Program enrolled at-risk asymptomatic men and women over the age of 40 (n = 31,567). Participants were considered at increased risk for lung cancer due to cigarette smoking, occupational exposure (eg, asbestos), or second-hand smoke exposure. After a baseline low-dose spiral CT (and appropriate followup if suspicious lesions were discerned) 21,456 participants underwent annual low-dose spiral CT for up to 12 years.

Most of the cancers were detected at the initial baseline screen (over 80%). Utilizing combined strategies of a baseline screen and annual followup, most of the cancers were identified at Stage 1, where the 10 year survival rate was 88%. The authors suggest that the detection rate of lung cancer in this trial compares favorably with rates of breast cancer detected by mammography. ■

The International Early Lung Cancer Action Program Investigators. N Engl J Med. 2006;355:1763-1771.

Can Ramipril Prevent Progression from Pre-Diabetes to Diabetes?

Some cardiovascular trials, like the HOPE trial, have shown that ACE inhibitors such as ramipril (RAM) can reduce the incidence of new onset diabetes (DM). Whether similar effects might be seen in specifically in a population known to be at high risk for development of diabetes—persons with known prediabetes—has received little study. Prediabetes is defined as either a fasting glucose 110-125 mg/dL or glucose 2 hours post glucose-load of 140-199.

The DREAM (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication) trial enrolled prediabetic adults (n = 5,269) and randomized them to ramipril (15 mg/d target dose) or placebo for 3 years. In contrast to the HOPE trial, subjects had to be free of CV disease and diabetes at entry. This same trial also examined the impact of rosiglitazone, reported in a separate publication.

After 3 years, there was no difference between ramipril and placebo in the incidence of diabetes among persons with prediabetes. ■

The DREAM Trial Investigators. N Engl J Med. 2006;355:1551-1562.

In Future Issues: Statins for Heart Failure