AHC Media

Internal Medicine

Evidence-based summaries of the latest research in internal medicine [ALERT]

Vol. 38, Issue 3, February 15, 2016
AHCMedia.com

ABSTRACT & COMMENTARY

Diabetes, Dementia, and Hormones

By Seema Gupta, MD, MSPH

Clinical Assistant Professor, Department of Family and Community Health, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

Dr. Gupta reports no financial relationships relevant to this field of study.

SYNOPSIS: Research using data from the long-term follow-up of the Women's Health Initiative Memory Study found that higher levels of estrogen can increase the risk of cognitive decline and dementia in older women with type 2 diabetes.

SOURCE: Espeland MA, et al. Impact of type 2 diabetes and postmenopausal hormone therapy on incidence of cognitive impairment in older women. *Diabetes Care* 2015;38:2316-2324.

Type 2 diabetes is associated with an increased risk of cognitive impairment and dementia. This increased risk of dementia may include both Alzheimer's disease and vascular dementia. Based on epidemiologic studies, physicians believed estrogen to be a protective factor for dementia. However, recent evidence has revealed that estrogens provide no benefit, and instead may be associated with an increased risk of dementia and cognitive decline in certain groups. The Women's Health Initiative Memory Study (WHIMS) found that for women ≥ 65 years of age who are at increased risk for brain atrophy due to type 2 diabetes, prescription of postmenopausal hormone therapy was associated with lower gray matter volumes compared to placebo.[1] Similarly, a French study found that in postmenopausal women ≥ 65 years of age, higher endogenous estradiol level is an independent predictor of incident dementia, and the risk is dramatically higher in women with diabetes compared with nondiabetic women.[2] In a multicenter, randomized, double-blind, placebo-controlled clinical trial of a subgroup of women who participated in the WHIMS, conjugated equine estrogens with or without medroxyprogesterone acetate, administered to women ≥ 65 years of age, not only failed to protect against dementia or cognitive

Financial Disclosure: *Internal Medicine Alert's* Editor Stephen Brunton, MD, is a retained consultant for Abbott, Actavis, AstraZeneca, Becton Dickinson, Boehringer Ingelheim, Cempra, Exact Sciences, Janssen, Lilly, Mylan, Novo Nordisk, and Teva; he serves on the speakers bureau of AstraZeneca, Boehringer Ingelheim, Janssen, Lilly, Novo Nordisk, and Teva. Contributing Editor Louis Kuritzky, MD, is a retained consultant for AbbVie, Allergan, AstraZeneca, Janssen, Lilly, Lundbeck, Medscape, Novo Nordisk, and Sanofi Aventis; he serves on the speakers bureau of Lilly and Lundbeck. Peer Reviewer Gerald Roberts, MD; Executive Editor Leslie Coplin; and Associate Managing Editor Jonathan Springston report no financial relationships relevant to this field of study.

Internal Medicine
Evidence-based summaries of the latest research in internal medicine [ALERT]

Internal Medicine Alert,
ISSN 0195-315X, is published monthly by
AHC Media, LLC
One Atlanta Plaza,
950 East Paces Ferry Road NE, Suite 2850
Atlanta, GA 30326.
AHCMedia.com

GST Registration Number: R128870672.
Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to
***Internal Medicine Alert*,**
P.O. Box 550669,
Atlanta, GA 30355.

SUBSCRIBER INFORMATION
(800) 688-2421
customerservice@ahcmedia.com
AHCMedia.com

Questions & Comments
Please call Jonathan Springston, Associate Managing Editor, at (404) 262-5416 or email at jonathan.springston@ahcmedia.com.

Subscription Prices
United States:
Print: 1 year with free *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.
Online only: 1 year (Single user) with ***free*** *AMA PRA Category 1 Credits™*: $299
Back issues: $21. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of 48 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This Enduring Material activity, *Internal Medicine Alert*, has been reviewed and is acceptable for up to 24.00 Prescribed credit(s) by the American Academy of Family Physicians. Term of approval begins Jan. 1, 2016. Term of approval is for one year from this date. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic Association has approved this continuing education activity for up to 48 AOA Category 2-B credits.

This CME activity is intended for the internist/family physician. It is in effect for 36 months from the date of the publication.

AHC Media

decline but substantially increased the risk of dementia of any cause as well as cognitive decline.[3]

In their study, Espeland et al examined data from the long-term follow-up of the WHIMS to determine whether the effect of postmenopausal hormone therapy on cognitive impairment incidence varies depending on type 2 diabetes status of women. A total of 7233 women between 65 and 80 years of age were assigned to hormone therapy or matching placebo for an average of 4.7 to 5.9 years. Women were classified according to type 2 diabetes status and followed for probable dementia and cognitive impairment. Through a maximum 18 years of follow-up, researchers found that women with type 2 diabetes had an increased risk of probable dementia (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.16-2.06) and cognitive impairment (HR, 1.83; 95% CI, 1.50-2.23). They also found that the combination of diabetes and random assignment to hormone therapy increased the risk of dementia (HR, 2.12; 95% CI, 1.47-3.06) and cognitive impairment (HR, 2.20; 95% CI, 1.70-2.87) compared to women without these conditions. The interactions seemed to be limited to women assigned to unopposed conjugated equine estrogens. The authors concluded that higher levels of estrogen may exacerbate risks that type 2 diabetes pose for cognitive function decline in older women.

■ COMMENTARY

The study by Espeland et al finds that women with type 2 diabetes who were assigned to receive hormone therapy were more likely to develop dementia and cognitive impairment than those receiving placebo, while women without type 2 diabetes who were assigned to receive placebo were the least likely to develop dementia and cognitive impairment. This study suggests that women with type 2 diabetes may be more likely to develop dementia and cognitive impairment than women without diabetes. The effect of hormone therapy seemed to last through 18 years of follow-up. The study included only postmenopausal women, and it is still unknown if the results apply to younger women. However, it seems clear that the adverse effects of diabetes on the cognitive function of older women appear to be augmented by higher levels of estrogen, such as in older women on hormone replacement therapy. Therefore, based on this evidence, estrogens cannot be recommended in non-demented older women with type 2 diabetes as preventive therapy for maintaining cognitive function. ■

REFERENCES

1. Espeland MA, et al. Postmenopausal hormone therapy, type 2 diabetes mellitus, and brain volumes. *Neurology* 2015;85:1131-1138.
2. Carcaillon L, et al. High plasma estradiol interacts with diabetes on risk of dementia in older postmenopausal women. *Neurology* 2014;82:504-511.
3. Craig MC, et al. The Women's Health Initiative Memory Study: Findings and implications for treatment. *Lancet Neurol* 2005;4:190-194.

ABSTRACT & COMMENTARY

Why Dentists Are Suddenly Smiling

By Barbara Phillips, MD, MSPH

Professor of Medicine, University of Kentucky; Director, Sleep Disorders Center, Samaritan Hospital, Lexington

Dr. Phillips reports no financial relationships relevant to this field of study.

SYNOPSIS: In this meta-analysis of 51 randomized, controlled studies that included nearly 5000 patients, continuous positive airway pressure and oral appliances resulted in comparable and statistically significant reductions in blood pressure.

SOURCE: Bratton DJ, et al. CPAP vs mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: A systematic review and meta-analysis. *JAMA* 2015;314:2280-2293.

This report is the result of a meta-analysis of 51 studies evaluating the effect of two treatments — continuous positive airway pressure (CPAP) and oral appliances (also known as mandibular advancement devices or MADs) — on blood pressure in patients with obstructive sleep apnea (OSA). To be included in the analysis, studies had to contain adult patients with OSA (defined as an apnea-hypopnea index of ≥ 5/h) randomized to at least two of the following treatments: 1) CPAP, 2) oral appliance, or 3) control. The authors reported the treatment on both systolic blood pressure (SBP) and diastolic blood pressure (DBP). The authors also examined duration of hours/night of CPAP use and blood pressure. Including only patients with a diagnosis of hypertension apparently was not a prerequisite for inclusion in this analysis. The authors had to perform fancy statistical footwork in cases where studies reported the difference in blood pressure between treatments but not the absolute change in SBP and DBP.

Forty-four of the 51 studies compared CPAP with a control. Only three evaluated oral appliances compared with control. One compared CPAP with oral appliances, and three compared CPAP, oral appliances, and controls. Mean blood pressure was fairly consistent between studies.

Compared with controls, CPAP was associated with a reduction in SBP of 2.5 mmHg ($P < 0.001$) and oral appliances were associated with a reduction of 2.1 mmHg ($P = 0.002$). CPAP was associated with a reduction in DBP of 2.0 mmHg (< 0.001) and oral appliances were associated with a reduction in DBP of 1.9 mmHg ($P = 0.008$). There was no significant difference between CPAP and oral appliances in the reduction of blood pressure in intention-to-treat comparisons.

CPAP compliance (or adherence) made a difference. Mean CPAP use (hours/night) could be obtained from 44 of the 47 studies of CPAP. A 1-hour-per-night increase in mean CPAP use was associated with an additional reduction in SBP of 1.5 mmHg ($P < 0.001$) and an additional reduction in DBP of 0.9 mmHg ($P = 0.001$).

Whether the patient was hypertensive also made a difference. The association of CPAP with reductions of both SBP and DBP was greater in patients with higher baseline blood pressure levels, although there was no difference between the reported treatment effects in this subgroup of trials that included only patients who had a diagnosis of hypertension. The authors also reported no difference in effect by severity of sleep-disordered breathing.

There were some weak signals that CPAP might be more effective than oral appliances in some situations. The authors reported " … there was some suggestion that the effect of CPAP reported in the studies was larger in those in which morning blood pressure data were extracted." In addition, the primary analysis was a network analysis. The authors also performed a pairwise analysis and found similar results, except for a smaller reduction in DBP of -1.1 mmHg ($P = 0.11$).

■ COMMENTARY

OSA is a prevalent and deadly condition. Recent estimates of prevalence are about 10%, depending on the population studied.[1] Treatment of OSA with CPAP is associated with improved outcomes from many important consequences, including motor vehicle collisions , atrial fibrillation, hypertension, and overall mortality in men, women, and the elderly.[2-7]

But CPAP is a burdensome treatment. Overall, adherence to CPAP is probably slowly improving because of increased efforts at education and follow-up, but CPAP use is still much less than optimum. Further, patients with mild sleep apnea are less likely to suffer medical consequences and also are less likely to be able to adhere to CPAP. Mandibular advancement devices (better known as "oral appliances") are a reasonable alternative to CPAP for those who are CPAP-intolerant or who have mild disease.

Hypertension is the best-proven consequence of untreated sleep apnea and likely contributes to OSA's link to cardiovascular disease and stroke. Treatment for sleep apnea that does not result in improvement in hypertension cannot be considered truly effective treatment. This paper supports the use of oral appliances in lieu of CPAP in OSA patients who suffer from hypertension. It does not demonstrate that oral appliances reduce the risk of many of the other well-documented complications of OSA. Such data are still sparse and take a long time to generate. But the fact that these devices have been demonstrated to improve sleep-disordered breathing and blood pressure to a similar extent as CPAP strongly suggests that they reduce other risks as well.

There are some practical issues to consider. Some knowledge of local dentists and their approach to this issue is helpful. Not all dentists craft oral appliances. Some confuse them with bite guards for bruxism (not the same thing at all). Some will offer the patient a "boil and bite" or "off the shelf" device; these have been shown to be less effective than custom-made, adjustable devices. In our practice, we use a handout that lists dentists in our area who

craft oral appliances well and who follow-up with their patients (because the "bite" can change, which is apparently a big deal to dentists). Our handout also lists some questions to ask their personal dentist, if they are going that route ("How many have you made? Is it custom made and adjustable?"). In general, it takes a few months to deliver and titrate a device, so this might not be the best option for a patient who has severe sleep apnea and is falling asleep at the wheel today. Some dentists cannot craft these devices for edentulous patients, though some will. We ask patients to come back after the device has been delivered and adjusted, and sometimes (not always, depending on insurance and symptoms) undertake a portable sleep study (cheap, quick) to assess efficacy.

I still recommend CPAP as first-line therapy for OSA, and some signals in this paper suggest that CPAP is still the better choice for people who have difficult-to-control blood pressure and who are likely to be adherent. But for people who are CPAP-intolerant or who have mild disease, oral appliances are much better than nothing, which is essentially what they are going to receive unless they are offered an alternative. Additionally, oral appliances are vastly superior to upper airway surgery,[8] which I do not consider to be a viable alternative.

Oral appliances are not just less burdensome for the patient, they are far less burdensome to the prescribing physician. In the United States, a physician who prescribes CPAP is currently expected to more or less police such CPAP use and to attest that the patient is using it (by objective measurement) and benefitting from it within 3 months of its initiation, all on an annual basis. "CPAP compliance visits" are a huge and often unpleasant part of my practice. With an oral appliance, one simply writes the prescription, recommends a dentist, and asks the patient to come back for follow-up after the device is delivered and titrated. Looking ahead, I predict there will be many more oral appliance prescriptions and fewer CPAP prescriptions. Looking even farther ahead, I predict that patients will be buying CPAP off the shelves at big box stores. ■

REFERENCES

1. Peppard PE, et al. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013;177:1006-1014.
2. Tregear S, et al. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: Systematic review and meta-analysis. *Sleep* 2010;33:1373-1380.
3. Holmqvist F, et al. Impact of obstructive sleep apnea and continuous positive airway pressure therapy on outcomes in patients with atrial fibrillation — Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Am Heart J* 2015;169:647-654.
4. Fava C, et al. Effect of CPAP on blood pressure in patients with OSA/hypopnea a systematic review and meta-analysis. *Chest* 2014;145:762-771.
5. Marin JM, et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: An observational study. *Lancet* 2005;365:1046-1053.
6. Campos-Rodriguez F, et al. Cardiovascular mortality in women with obstructive sleep apnea with or without continuous positive airway pressure treatment: A cohort study. *Ann Intern Med* 2012;156:115-122.
7. Martínez-García MA, et al. Cardiovascular mortality in obstructive sleep apnea in the elderly: Role of long-term continuous positive airway pressure treatment: A prospective observational study. *Am J Respir Crit Care Med* 2012;186:909-916.
8. Walker-Engstrom ML, et al. 4-year follow up of treatment with dental appliance or uvulopalatopharyngoplasty in patients with obstructive sleep apnea: A randomized study. *Chest* 2002;121:739-746.

PHARMACOLOGY UPDATE

Lesinurad Tablets (Zurampic)

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

Dr. Elliott is Medical Director, Pharmacy, 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. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved the first selective uric acid reabsorption inhibitor for the treatment of hyperuricemia associated with gout, in combination with a xanthine oxidase inhibitor (XOI). This is the first uricosuric agent to be approved since probenecid. Lesinurad is marketed by AstraZeneca as Zurampic.

INDICATION

Lesinurad is indicated in combination with a XOI (allopurinol or febuxostat) for the treatment of hyperuricemia associated with gout in patients who have not achieved target uric acid levels. The drug should not be initiated in patients with estimated CrCl < 45 mL/min.

DOSAGE

The recommended and maximum dose is 200 mg taken once daily in the morning with food and water at the same time as the XOI.[1] Gout flare prophylaxis is recommended. Lesinurad is available as 200 mg tablets.

POTENTIAL ADVANTAGES

Lesinurad is a drug with a different mechanism of action to augment the action of a XOI, resulting in additional reduction of serum uric acid levels.

POTENTIAL DISADVANTAGES

Lesinurad has been associated with serum creatinine elevation. The drug carries a boxed warning regarding the risk of acute renal failure if used in higher than recommended doses or without a XOI. Renal function should be assessed prior to treatment initiation.[1] Major cardiovascular events (death, nonfatal myocardial infarction, or stroke) were numerically higher with lesinurad compared to placebo. Co-administration with a CYP2C9 inhibitor increases the exposure of lesinurad.[1] Levels are reduced if co-administered with a CYP2C9 inducer. Co-administration with an epoxide hydrolase inhibitor (e.g., valproic acid) is not recommended. Doses of aspirin > 325 mg/day may reduce the effectiveness of lesinurad.

COMMENTS

Lesinurad reduces serum uric acid levels by inhibiting two transporters, uric acid transporter and organic anion transporter.[1] Its efficacy was evaluated in three randomized, 12-month, double-blind, placebo-controlled studies in 1537 adults with gout and hyperuricemia. In two studies, lesinurad was added to allopurinol (300 mg/day or 200 mg with renal impairment) in subjects with inadequate lowering of uric acid, and the third to febuxostat in subjects with tophaceous gout. The primary endpoint was the proportion of subjects achieving serum uric acid levels < 6 mg/dL or < 5 mg/dL. In the first two studies, the combination of lesinurad (200 mg/day) and allopurinol, 54% and 55% achieved target (< 6 mg/dL) compared to 28% and 23%, respectively in patients on placebo and allopurinol, at 6 months. The response was maintained at 12 months. In the third study, the combination of lesinurad (200 mg) and febuxostat (80 mg/day) achieved uric acid target of < 5 mg/dL in 57% compared to 47% with febuxostat plus placebo. This did not achieve statistical significance. In all three studies, the rate of gout flares and tophus outcome were not statistically different; however, all subjects received prophylaxis for gout flares with colchicine or nonsteroidal anti-inflammatory drugs for the first 5 months of treatment. The efficacy of lesinurad appears to be reduced in subjects with decreased renal function.[1] Most frequently reported adverse events (compared to placebo) were headache (5.3% vs 4.1%), influenza (5.1% vs 2.7%), and gastroesophageal reflux disease (2.7% vs 0.8%). There are no published comparisons between lesinurad and probenecid.

[Because its mechanism of action is different from xanthine oxidase inhibitor, lesinurad may be used to effect an additional level of reduction in serum uric acid levels.]

CLINICAL IMPLICATIONS

Gout is a common rheumatic disease in adults, with symptoms generally manifested due to hyperuricemia. The goal for pharmacotherapy is to reduce urine acid levels. The first line of therapy is an XOI (allopurinol or febuxostat) with a serum urate target of < 6 mg/dL and, in some cases, < 5 mg/dL. If this is inadequate, the American College or Rheumatology recommends adding an uricosuric agent such as probenecid, fenofibratre, or losartan.[2] Lesinurad provides another option for the management of hyperuricemia inadequately controlled on a XOI, particularly allopurinol. The future role remains to be determined. The FDA is requiring postmarketing studies to evaluate renal and cardiovascular safety. The cost and availability are not known at the time of this review. ■

REFERENCES

1. Zurampic Prescribing Information. AstraZeneca. December 2015.
2. Khanna D, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: Systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res* 2012;64:1431-1446.

Internal Medicine [ALERT]

Clinical Briefs

By Louis Kuritzky, MD

Markers of Hidradenitis Suppurativa

SOURCE: Hessam S, et al. *J Am Acad Dermatol* 2015;73:998-1005.

Hidradenitis suppurativa sometimes has been called a "heart sink" diagnosis. Patients often suffer chronic bacterial infections in multiple body sites (axillae, chest wall, perineum, glutei) that are unsightly, often painful, and require multiple, often not fully satisfactory treatments. Recently, insights into some of the underlying immunologic pathologies in hidradenitis have prompted utilization of systemic pharmacotherapies usually reserved for patients with rheumatoid arthritis or advanced psoriasis. Though such rheumatologic immunomodulatory agents are expensive, and not without risk, the serious disease burden of hidradenitis, coupled with the generally poor results seen with "traditional" therapies, justifies their consideration.

Probably the two most commonly used scales in the dermatological literature to stratify disease severity in hidradenitis are the Hurley stage scale (stages I, II, and III, with III being most severe) and the modified Hidradenitis Suppurativa Score. Both scores use characteristics noted on physical exam, such as number of lesions, presence of fistulas, presence of sinus tracts, etc. to assess severity.

Hessam et al studied whether systemic markers of inflammation, such as C-reactive protein (CRP) and white blood cell (WBC) count, might correlate with disease severity as assessed through the two severity scales. By evaluating 275 cases of hidradenitis in which CRP and/or WBC had been reported, the investigators determined that there was significant correlation between CRP levels and both clinical scoring systems; WBC correlated only with Hurley stage scores. The authors suggested that measurement of CRP, an inexpensive and readily available test, in hidradenitis patients may enhance assessment of disease severity. ■

Antibiotic Exposure and Mood Disorders?

SOURCE: Lurie I, et al. *J Clin Psychiatry* 2015;7:1522-1528.

There might be a more important gut-brain connection than we have previously recognized. Animal data indicate that germ-free mice, whose intestinal tract is absent bacteriae, have magnified hypothalamic-pituitary-adrenal responses to stress, which may be normalized by restoration of the intestinal microbiome with probiotics (*Bifidobacterium infantis*). Similarly, germ-free mice differ in turnover of neurotransmitters associated with mood disorders (e.g., norepinephrine, dopamine, serotonin) from mice with established intestinal bacterial flora. Since gut flora alteration through antibiotic administration is a commonplace experience for most adults, might such exposures, by altering the intestinal microbiome, also be associated with mood disorders in humans?

Lurie et al performed a case-control study using medical records from a very large database in the United Kingdom inclusive of the interval from 1995-2013. Patients with depression (n = 202,974 with 803,961 age- and sex-matched controls), anxiety (n = 14,570 with 57,862 matched controls), and psychosis (n = 2690 with 10,644 matched controls) were compared for likelihood of having received an antibiotic prescription at least 1 year prior to the recorded mental health diagnosis.

Patients who had received a prescription for penicillin, cephalosporin, or quinolone were more than 20% more likely to incur depression, which increased to 40% more likely if multiple penicillin prescriptions had been issued. Similar odds ratios for anxiety occurred in relation to penicillin and sulfa drugs. Psychosis was not associated with antibiotic administration. Indeed, all antibiotic classes studied demonstrated increased risk for subsequent incident depression. Of course, it could be that persons with anxiety and depression, even in the pre-morbid state, might be more likely to become ill and receive an antibiotic prescription, nullifying a cause-and-effect relationship. Until the causal relationship between antibiotic administration and mental health is better understood, clinicians could consider adding still another rationale for why we might need to be ever more judicious about the appropriate use of antibiotics. ■

On-demand Pre-exposure HIV Prophylaxis

SOURCE: Molina JM, et al. *N Engl J Med* 2015;373:2237-2246.

There is no doubt that continuous pre-exposure prophylaxis (PrEP) with antiretroviral therapy in HIV-discordant men who have sex with men (MSM) substantially reduces the risk of seroconversion (> 40%). Curiously, similar trials among heterosexual women have not demonstrated the same risk reduction. Experts opine that failed efficacy in this population might be attributed to poor compliance. Might PrEP administration timed immediately before and after sexual activity, rather than daily, be effective?

Molina et al randomized MSM (n = 400) to antiretroviral treatment (tenofovir + emtricitabine) or placebo administered before and after sexual activity. The method of administration was two pills 2-24 hours before sex, a third pill 24 hours after the first dose, and a fourth pill 24 hours later. At a median of 9.3 months follow-up, there was a relative risk reduction in incident HIV infection of 86% (two cases in the antiretroviral group vs 16 in the placebo group).

These results stack up very favorably with continuous prophylaxis trials, and may be less cumbersome for some patients to administer. The authors cautioned that early enthusiasm for treatment might support better adherence, which could wane over time and potentially reduce efficacy. ■

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:
1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right, or log on to **AHCMedia.com** and click on My Account. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice, or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After completing the test, a credit letter will be emailed to you instantly.
5. Twice yearly after the test, your browser will be directed to an activity evaluation form, which must be completed to receive your credit letter.

CME QUESTIONS

1. **Based on the study by Espeland et al, researchers found an association between:**
   a. diabetes and dementia.
   b. diabetes, estrogens, and dementia.
   c. diabetes, estrogens, dementia, and older age.
   d. diabetes, estrogens, dementia, older age, and malignancy.

2. **Regarding the effects of oral appliances and continuous positive airway pressure (CPAP) on blood pressure in patients with obstructive sleep apnea (OSA):**
   a. neither oral appliances nor CPAP results in significant reductions in blood pressure in patients with OSA.
   b. oral appliances result in significant reductions in blood pressure in patients with OSA but CPAP does not.
   c. CPAP results in significant reductions in blood pressure in patients with OSA but oral appliances do not.
   d. both CPAP and oral appliances result in significant reductions in blood pressure in patients with OSA.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages, and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

[IN FUTURE ISSUES]

SPRINT and a New Meta-analysis

Should Postmenopausal Women Be Encouraged to Take Calcium?

Internal Medicine [ALERT]

ECG Review

By Ken Grauer, MD

Professor Emeritus in Family Medicine, College of Medicine, University of Florida

Dr. Grauer is the sole proprietor of KG-EKG Press, and publisher of an ECG pocket brain book.

What Has Happened in 8 Minutes?

The 12-lead ECG in the figure below belongs to a 50-year-old man who presented to the ED with new-onset chest discomfort. His initial ECG (that was taken when he arrived in the ED) was the tracing shown in the ECG Review that appeared in the January 15 issue of *Internal Medicine Alert*. No more than minimal ST-T wave changes were seen on the initial ECG. The tracing in the figure below was obtained just 8 minutes later.

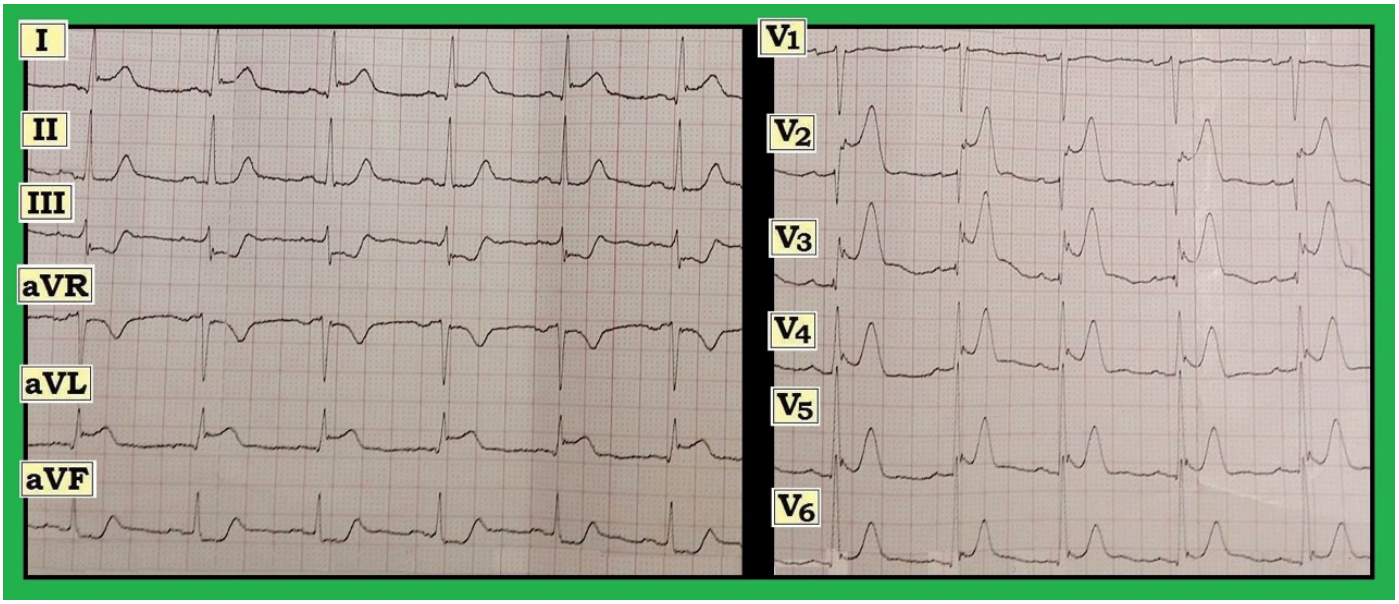

Figure 1: 12-lead ECG obtained from a 50-year-old man with new-onset chest discomfort.

The ECG in the figure illustrates how rapidly ST-T wave changes may develop during active stages of acute ST elevation myocardial infarction. In this case, no more than 8 minutes was necessary for the ECG to evolve from a minimally abnormal tracing to the dramatic picture of diffuse ST-T wave changes seen here.

The rhythm is sinus. Obvious ST segment elevation occurs in leads I, aVL, and V2-V6. ST segment changes are most marked in leads V2 and V3, where the amount of J point ST elevation exceeds 5 millimeters. Inferior leads III and aVF show prominent reciprocal ST segment depression. Small Q waves have developed in leads I, aVL and V6, which probably are significant given the distribution of ST-T wave changes. Overall, the hyperacute picture of tall and peaked T waves in all chest leads with ST elevation is striking.

The history of new-onset chest discomfort in association with ECG findings in the figure strongly suggests acute occlusion of the left anterior descending coronary artery.

The clinical significance of ECG findings in the initial tracing (taken when the patient first presents for medical care) is not always apparent. This may be due to a lag time between the onset of symptoms and the resultant physiologic effect this may have on the electrocardiogram. Awareness of how short the time interval can last for evolution from a minimally abnormal tracing to one with the marked changes seen in the figure emphasizes the utility of obtaining frequent serial tracings in a patient with new-onset symptoms and a non-diagnostic ECG, until such time that the diagnosis can be clarified.

NOTE: A picture is worth a thousand words. To facilitate comparison of the ECG shown here with the minimally abnormal tracing performed just 8 minutes earlier, please visit ***http://tinyurl.com/KG-Blog-115*** for additional details on this case.