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INSIDE

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Safety of Testosterone Replacement Questioned

ABSTRACT & COMMENTARY

By Rahul Gupta, MD, MPH, FACP

Clinical Assistant Professor, West Virginia University School of Medicine, Charleston, WV

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

Synopsis: *In a study of men in the Veterans Affairs health care system with low serum testosterone levels, the use of testosterone therapy was associated with an increased risk of mortality, myocardial infarction, or ischemic stroke.*

Source: Vigen R, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. *JAMA* 2013;310:1829-1836.

Testosterone replacement therapy is widely prescribed to help reverse the effects of hypogonadism. However, the research is uncertain whether testosterone therapy would have any benefit for older men who are otherwise healthy. Widespread marketing for a condition named as "Low T" has led to a recent rapid expansion in the market for demand of testosterone replacement therapy and has often led men to believe that taking testosterone replacement may help them feel younger and more vigorous as they age. As a result, the prescribing rates of testosterone therapy have increased approximately five times over the past decade or so in the United States. Along with this booming business has been a trend to take advantage of the various pharmacokinetic properties of the drug to increase the range of testosterone preparations in the market and provide for a consumer choice as well as competition. Various marketed preparations include transdermal delivery (patches and gels), as well as oral (including buccal tablets) and parenteral (subcutaneous pellets, intramuscular) formulations. While it is recommended that patients who are treated with testosterone should be monitored regularly to determine that normal serum testosterone concentrations are being achieved, it is not always done in the clinical

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setting due to a variety of reasons. Similarly, it is recommended that certain other tests (such as hematocrit, and prostate cancer screening) also be conducted in most or selected patients. When administered to a hypogonadal male patient, the principal goal of testosterone therapy is to restore the serum testosterone concentration to the normal range. As a result, the patient's symptoms improve, including increases in libido, muscle strength, fat-free mass, and bone density.[1] In addition to beneficial effects, testosterone replacement therapy can also have potential adverse effects, including increases in hemoglobin and hematocrit, increases in serum prostate specific antigen, and worsening of sleep apnea among others. Whether the use of testosterone replacement therapy is associated with an increased risk of cardiovascular adverse events has not been conclusively proven since little research has been done in this area and the most recent data demonstrate a varied picture.

In their study, Vigen et al conducted a retrospective cohort study of 8709 men with low testosterone levels (< 300 ng/dL) who underwent coronary angiography in the Veterans Affairs (VA) system between 2005 and 2011. These veterans had a high existing burden of disease, with approximately 20% having a prior history of myocardial infarction (MI), 50% diabetes, and more than 80% having coronary artery disease (CAD). These 8709 patients were divided into two groups, one was placed on testosterone therapy and the other was not on such therapy. Approximately 14% (1223 veterans) were initiated on testosterone therapy. Patients who were initiated on testosterone therapy tended to be younger and have lower rates of comorbidities compared with those in the control population. These patients were prescribed varying forms of testosterone treatments, including gel, injections, and patches. The primary outcome of the study was a composite of all-cause mortality, MI, and ischemic stroke. After an average follow-up of 840 days (27.5 months), a total of 1710 events in the entire cohort was noted, including 748 deaths, 443 MIs, and 519 strokes. Of these total events at 3 years after coronary angiography, 19.9% of events occurred in the group not on testosterone therapy vs 25.7% in the testosterone therapy group, with an absolute risk difference of 5.8% (95% confidence interval [CI], -1.4% to 13.1%). In further analysis adjusting for the presence of CAD, testosterone therapy use as a time-varying covariate was associated with an increased risk of adverse outcomes (hazard ratio, 1.29; 95% CI, 1.04-1.58). The authors conclude their observations by stating that the use of testosterone therapy in their study cohort — which included veterans with significant medical comorbidities — was associated with an increased risk of mortality, MI, or ischemic stroke, and the findings were not modified by the presence of CAD.

■ COMMENTARY

The discussion surrounding the population subgroup in which testosterone replacement therapy can be used safely and appropriately is far from being concluded. While several prior studies have shown that testosterone therapy may protect against heart disease and improve mortality, they have typically been of short duration or included a smaller sample size.[2] The current finding is relatively new, since only a handful of research data may have shown that the use of testosterone treatment could be associated with an increased risk of cardiovascular adverse events while a number of studies have shown either no impact or being beneficial.[3] In the current study by Vigen et al, several possible mechanisms by which testosterone therapy may raise cardiovascular risk are suggested, including increasing platelet thromboxane A2 receptor density and platelet aggregation, stimulating smooth muscle proliferation and expression of vascular cell adhesion molecule 1, and worsening obstructive sleep apnea, a risk factor for atherosclerosis. However, several design weaknesses also are associated with this research, including being a retrospective study. For this reason, it is difficult to generalize the study findings or even recommend a particular patient population to whom the study results would apply. However, it is clear that prospective data from large, well-designed, long-term trials of testosterone treatment are lacking and will be required to verify the cardiovascular efficacy and safety of chronic treatment practices. However, in the interim, it is essential that prescribers take every precau-

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Questions & Comments
Please call **Neill Kimball**, Managing Editor, at (404) 262-5404.

tion possible to be punctilious in the manner in which we prescribe these long-term medications. ■

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Is Dabigatran Better Than Warfarin in Patients with Mechanical Heart Valves?

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, UCLA School of Medicine

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

Synopsis: *The use of dabigatran in patients with mechanical heart valves compared with patients receiving warfarin was associated with increased rates of thromboembolic and bleeding complications, thus demonstrating no benefit and an excess risk.*

Source: Eikelboom JW, et al. Dabigatran versus warfarin in patients with mechanical heart valves. *N Engl J Med* 2013; 369:1206-1214.

Prosthetic heart valve replacement is performed worldwide on several hundred thousand patients with severe valvular heart disease each year.[1] Mechanical valves are more durable than bioprosthetic valves,[2] but the latter are frequently selected by the patient and the attending physician because mechanical valve implantation requires lifelong anticoagulant therapy, which requires lifelong coagulation monitoring and restrictions on the intake of certain foods, alcohol, and drugs. Dabigatran is a new oral direct thrombin inhibitor that has been shown to be as effective as warfarin in the treatment of patients with atrial fibrillation.[3] In addition, it is a simple oral anticoagulant that requires no coagulation monitoring, which makes it an appealing alternative to warfarin.

Because promising studies in animals demonstrated the efficacy of dabigatran in preventing mechanical valve thrombosis,[3-5] Eikelboom and colleagues did a study to validate a new regimen for the administration of dabigatran to prevent thromboembolic complication in patients after mechanical heart valve implantation. The warfarin dose in the study was adjusted to obtain an international normalized ratio (INR) of 2.0-3.5 based on the thromboembolic risk. The initial dabigatran dose (150, 220, or 300 mg twice daily) was based on kidney function. After enrollment of 252 patients, the trial was terminated prematurely because of excess thromboembolic and bleeding events among patients in the dabigatran group. The study concluded that the use of dabigatran in patients with mechanical heart valves was associated with increased rates of thromboembolic and bleeding complications when compared with patients on warfarin, thus showing no benefits and an excess risk.

■ COMMENTARY

It must be recognized that the Eikelboom study was limited to two populations of patients: those who had undergone aortic or mitral valve replacement within the previous 7 days and those who had undergone a valve replacement at least 3 months earlier.[6] Most of the thromboembolic events in the study occurred in patients in the dabigatran group who started the study drug within 7 days after the valve surgery, with fewer episodes occurring in the patients who had undergone valve implantation more than 3 months previously. Bleeding episodes conceivably may have been diminished if lower doses of dabigatran had been used for the first 3 months after valve implantation and then increased to higher doses (of course only if renal function was adequate). Other oral anticoagulants (rivaroxaban) have been successfully tested for the prevention of thromboembolic complications associated with mechanical heart valves in preclinical studies,[7] but the Eikelboom study did not provide evidence of the safety and efficacy of the selected dabigatran dosing algorithm despite the favorable results observed in the preclinical studies.[6,8,9] Since all episodes of major bleeding in the dabigatran group were in the pericardium, Eikelboom et al suggested that these occurrences might be explained by the relative inability of dabigatran to suppress activation of coagulation that occurs when blood is exposed to the artificial surfaces of the valve prosthesis. Dabigatran and other direct factor Xa inhibitors are effective for stroke prevention in patients with atrial fibrillation,[10,11] but these data cannot be extrapolated to patients with mechanical heart valves probably because the mechanisms of thrombosis are different.

In summary, the results of the current study indicated that, at the present time, dabigatran is not appropriate as an alternative to warfarin for the prevention of thromboembolic complications in patients who require anticoagulation after the implantation of a prosthetic mechanical heart valve. However, it must be clearly recognized that additional clinical trials, possibly including those that change the time of the initiation of the drug and/or which use other dosing regimens, are necessary before drawing

final conclusions. Also, it must be recognized that one or several of the other newer anticoagulant drugs may not exhibit the untoward effects demonstrated by dabigatran in the present study. ■

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Modern Radiation Therapy and ADT for High-risk Prostate Cancer Result in Improved Survival

ABSTRACT & COMMENTARY

By Samir Kanani, MD

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Dr. Kanani reports no financial relationships relevant to this field of study. This article originally appeared in the October 2013 issue of Clinical Oncology Alert.

Synopsis: *Historically, men with high-risk prostate cancer were believed to have low survival rates after definitive treatment with either surgery or radiation. However, long-term results of dose-escalated radiotherapy of doses ≥ 75.6 Gy, along with long-term androgen deprivation therapy (ADT), demonstrate 5-year survival rate of 92%, 5-year biochemical control rate of 82%, and symptomatic local failure rate of 0%. Death from prostate cancer was only 5.5% at 10 years in men treated with high-dose radiation therapy and ADT.*

Source: Nguyen Q, et al. Long-term outcomes for men with high-risk prostate cancer treated definitively with external beam radiotherapy with or without androgen deprivation. *Cancer* 2013;119:3265-3271.

Historically, disease-free survival rates have been disappointing with external beam radiotherapy alone. Over the last 30 years, significant technological improvements in the delivery of radiotherapy have resulted in the successful and safe delivery of escalating doses. In addition, studies in the 1990s demonstrated improvement in outcomes with long-term androgen deprivation therapy (ADT) in high-risk prostate cancer patients. This led to the hypothesis that the combination of long-term ADT and dose-escalated radiotherapy would likely produce at least an additive effect.

To address the question of whether high doses of radiotherapy combined with long-term ADT results in improved outcomes, Nguyen and colleagues performed a retrospective analysis of 741 men with high-risk prostate cancer treated at M.D. Anderson Cancer Center between 1987 and 2004. High-risk disease was defined as T3 disease, Gleason score 8-10, or PSA > 20 ng/mL. Patients were typically staged with CT scans and bone scans. The median PSA for the cohort was 15.6 ng/mL and the median age was 68 years old. Three hundred seventy-five men were treated with low-dose radiation defined as < 75.6 Gy, 122 men were treated with ADT and low-dose radiation therapy, 71 men were treated with high-dose radiation therapy without ADT, and 173 men were treated with ADT and high-dose radiotherapy (> 75.6 Gy). ADT was started 2 months prior to radiotherapy and continued for a median of 2.9 years. The target for radiotherapy was the prostate and the seminal vesicles and did not include the pelvic lymph nodes.

Compared with low-dose radiotherapy alone, ADT combined with high-dose radiation therapy resulted in improved 5-year overall survival (82% vs 92%), 5-year prostate cancer survival (93% vs 96%), and 5-year clinical failure-free survival (67% vs 92%). There were no local failures in men treated with ADT and high-dose radiotherapy. The 10-year symptomatic local failure rate was only 2% for all patients. High-dose radiotherapy resulted in a 5% absolute benefit in 5-year survival either with or without ADT. Prostate cancer specific deaths were rare among all cohorts at 5.5% at 10 years. The use of ADT improved local failure rates, overall survival rates, and biochemical control.

■ COMMENTARY

High-risk prostate cancer represents between 13% and 21% of newly diagnosed patients.[1] A number of randomized trials done in the United States including RTOG 92-02 have demonstrated improved overall survival in patients with high-risk prostate cancer treated with long-term hormones and radiation compared to short-term hormones and radiation.[2] These trials have essentially outlined the standard of care for the last decade in the

management of high-risk prostate cancer. Many of these trials including RTOG 92-02 used lower doses of radiation therapy (65-70 Gy). Several trials have demonstrated a benefit to a higher dose of radiation therapy in high-risk patients, which results in improved outcomes when compared to lower doses.[3]

So what have I learned from this trial as a radiation oncologist who treats prostate cancer patients? Every radiation oncologist is likely already giving a dose of at least 75.6 Gy using Intensity Modulated Radiation Therapy (IMRT), so my radiation dose will likely remain unchanged. However, the debate as to what areas need to be irradiated continues to rage on. It is very interesting in this study that there were no local failures in men treated to only the prostate and seminal vesicles. Many radiation oncologists continue to treat the pelvic nodes as well as the prostate and seminal vesicles based on other RTOG trials demonstrating a small benefit early on in progression-free survival.[4] There are still questions remaining to be answered. Should men with high-risk prostate cancer be offered surgery when the risk of prostate cancer mortality is < 5% even in high-risk populations or should the standard of care be radiation and hormones? What about the use of combination external beam radiation and brachytherapy? In my opinion, it's hard to argue against the combination of hormones and high-dose modern radiation therapy in this high-risk population with such excellent results. The alternative is a prostatectomy with a high likelihood of requiring postoperative radiation therapy because of positive margins or extracapsular penetration. Why treat with two treatment modalities when you can treat with one? ■

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Pharmacology Update

Riociguat Tablets (Adempas®)

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

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant 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 FIRST IN THE CLASS OF SOLUBLE GUANYLATE CYCLASE (sGC) stimulators has been approved by the FDA for the treatment of pulmonary hypertension. Riociguat was given a priority review, which provides for expedited review of drugs that may offer major advances in treatment. It is marketed by Bayer HealthCare Pharmaceuticals as Adempas.

Indications

Riociguat is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment or inoperable CTEPH, and pulmonary arterial hypertension (PAH) secondary to connective tissue disease or of unknown cause.[1] The desired clinical response is improved exercise capacity and WHO functional class, and delay in clinical worsening (especially for PAH).

Dosage

The recommended starting dose is 1 mg three times a day.[1] For patients who are intolerant of the hypotensive effect, the starting dose should be reduced to 0.5 mg three times daily. The dose may be increased at 0.5 mg increments at no less than 2 week intervals to a maximum dose of 2.5 mg three times daily. The starting dose should be 0.5 mg three times a day if coadministered with a strong CYP or P-gp/BCRP inhibitor. Strong CYP inducers may reduce the systemic exposure of riociguat. Coadministration with an antacid should be separated by at least 1 hour.

Riociguat is available as 0.5 mg, 1 mg, 2 mg, and 2.5 mg tablets.

Potential Advantages

Riociguat is the first drug to be effective in CTEPH. It also provides an agent with a different mechanism of action to treat PAH.

Potential Disadvantages

Common adverse events associated with riociguat are headache (27% vs 18% placebo), dyspepsia/gastritis (21% vs 8%), dizziness (20% vs 13%), diarrhea (12% vs 8%), hypotension (10% vs 4%), and anemia (7% vs 2%).

Comments

Riociguat has a dual action on the nitric acid-sGC-cCMP pathway. It stabilizes nitric acid-sGC binding as well as directly stimulating sGC.[1] This leads to increased production of cCMP and vasodilation. In contrast, phosphodiesterase inhibitors such as sildenafil slow the degradation of cCMP. The efficacy and safety of riociguat

were evaluated in two, double-blind, placebo-controlled, parallel studies, one for PAH and one for CTEPH. In the first study (PATIENT-1), 405 subjects with mainly idiopathic PAH (60%) and connective tissue disease (25%) and Functional Class II-III at baseline were randomized 4:1:2 to riociguat titrated between 1 and 2.5 mg, titrated between 1 and 1.5 mg, and placebo. The primary endpoint was the change from baseline in distance walked in 6 minutes (6MWD) at week 12. The overall mean baseline 6MWD was 363 meters. Approximately 75% were titrated to the maximum dose of 2.5 mg three times daily. The mean drug effect was about 30 meters compared to -6 meters for placebo (least square difference of 36 m (95% CI, 20-52; $P < 0.001$). Seventy-six percent of patients on riociguat showed an improvement in 6MWD of 20 meters compared to 59% on placebo. Twenty-one percent had improvement in WHO Functional Class compared to 14% for placebo. Four percent had deterioration on riociguat compared to 14% for placebo. Benefit was seen by week 2 and there was no difference in drug effect between those with WHO III/IV treatment-naïve or those previously treated with an endothelin receptor antagonist or prostacyclin. In the second study (CHEST-1), 262 subjects with CTEPH were randomized 2:1 to riociguat titrated 1 to 2.5 mg or placebo. The primary endpoint was 6MWD. Secondary endpoints included change in pulmonary vascular resistance and WHO functional class. At week 16, the riociguat group showed a mean increase of 39 meters compared to -6 meters for placebo. The least square mean difference was 46 meters (95% CI, 25-67; $P < 0.001$). Riociguat also showed significant improvement in pulmonary vascular resistance and WHO functional class. In the open-label extensions of both PATIENT-1 (n = 363) and CHEST-1 (n = 237), with mean treatment durations of 663 (± 319) and 582 (± 317) days, the probability of survival at year 2 was 93% and 94%, respectively.[1]

Clinical Implications

Limited treatment options exist for patients with pulmonary hypertension, especially for those with CTEPH for whom pulmonary thromboendarterectomy has been the only option. Riociguat is approved for both CTEPH and for idiopathic PAH, or PAH caused by connective tissue disease. CTEPH and PAH are both serious, life-threatening conditions with a survival of several months to several years, depending on severity. For CTEPH, riociguat is an option in patients with symptoms after surgery or for those who are are inoperable. For PAH, there are currently several pharmacotherapeutic options, including prostanoids, endothelin-receptor antagonists, and phosphodiesterase inhibitors. Riociguat offers an orally effective drug with a different mechanism of action. The benefit of riociguat is, however, modest. The magnitude of the improvement in 6MWD is similar to that reported for bosentan and sildenafil.[4,5] The monthly wholesale acquisition cost for riociguat (2.5 mg three times daily) is $7500 compared to $6840 for bosentan (125 mg twice daily), $1920 (branded sildenafil 20 mg three times daily), and $364 (generic sildenafil). ■

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CME Questions

1. **In the study by Vigen et al, testosterone replacement therapy in male veterans was associated with:**
   a. a decrease in mortality.
   b. an increase in mortality.
   c. no impact on mortality.
   d. an increase in cardiovascular, but a decrease in cancer mortality.

2. **The use of dabigatran in patients with mechanical heart valves compared to patients receiving warfarin therapy was associated with:**
   a. an increased rate of thromboembolic and bleeding complications.
   b. a decreased rate of thromboembolic and bleeding complications.
   c. essentially the same rate of thromboembolic and bleeding complications.

3. **High-dose radiation therapy and androgen deprivation therapy result in a local failure rate of:**
   a. 10%.
   b. 5%.
   c. 2%.
   d. 0%.

Clinical Briefs

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

Dr. Kuritzky is a retained consultant for Boehringer Ingelheim, Daiichi Sankyo, Forest Pharmaceuticals, Janssen, Lilly, Novo Nordisk, Pfizer, and Sanofi.

Downstream Benefits of Influenza Vaccine: Cardiovascular Outcomes

Source: Udell JA, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: A meta-analysis. *JAMA* 2013;310:1711-1720.

Few clinicians would disagree that influenza (flu) vaccine has generally recognized benefits in all age groups, with senior citizens deriving the greatest risk reduction in flu-related mortality. Nonetheless, it is easy to overlook the fact that flu vaccination has important impact on other downstream clinical consequences besides upper respiratory symptoms, including otitis media and — as this report details — cardiovascular (CV) health.

The death toll from flu disproportionately affects seniors, and is recorded during the annual flu epidemic as "pneumonia and influenza" deaths. Although flu is credited as the culprit, many of the pneumonia deaths are actually due to bacterial superinfection, often with staphylococci.

In a review of data beginning as early as 1946, the authors scrutinized more than 2000 reports on flu outcomes, ultimately defining 12 randomized, clinical trials (n = 6735) within their selection criteria of flu vaccine vs placebo in midlife adults (mean age = 67) considered to be at high CV risk.

The primary outcome of interest was a composite of fatal and nonfatal myocardial infarction and stroke as well as unstable angina, heart failure, and coronary revascularization. The data indicated that flu vaccine was associated with a 36% lower risk for this primary outcome. Clinician endorsement of vaccines has a powerful impact on patient concordance. Such data as these should stimulate intensified vigor for ensuring that our highest risk citizens enjoy the opportunity for CV risk reduction afforded through the flu vaccine. ■

Colchicine for Acute Pericarditis

Source: Imazio M, et al. A randomized trial of colchicine for acute pericarditis. *N Engl J Med* 2013;369:1522-1528.

Patients who suffer recurrent pericarditis differ from the larger population who incur an initial acute pericarditis, since the former often are burdened with an immune-modulated dysfunction (e.g., familial Mediterranean fever) and the latter includes a large number of diverse infectious etiologies (bacterial and viral). Guidelines have provided some support for the role of colchicine in recurrent pericarditis based primarily on small clinical trials and expert opinion. An open-label trial in acute pericarditis also supported a role for colchicine, but no large, randomized, double-blind trial has confirmed this experience.

Imazio et al report on data from a multicenter, placebo-controlled trial of colchicine in acute pericarditis (n = 240). The primary outcome was "incessant" pericarditis (failure to remit) or recurrent pericarditis. Colchicine or placebo was administered *in addition* to traditional treatment of pericarditis, and was dosed according to body weight (0.5 mg/d if < 70 kg, 1.0 mg/d if > 70 kg).

The primary outcome occurred 44% less often in the colchicine treatment group, and colchicine was successful for both components (improving remission rates and reducing recurrences). ■

Necrobiosis Lipoidica: A Review

Source: Reid SD, et al. Update on necrobiosis lipoidica: A review of etiology, diagnosis, and treatment options. *J Am Acad Dermatol* 2013;69:783-791.

The dermatologic words necrobiosis lipoidica are almost always followed by the word diabeticorum, since the disorder is seen predominantly in diabetics. Readers are encouraged to view photos of necrobiosis lipoidica diabeticorum (NLD) online. Although NLD is regarded as rare, in my experience it is one of the most commonly misdiagnosed cutaneous disorders in diabetics. NLD most commonly presents as symmetrical red-to-brown discolored irregular plaque-like deposits on the lower legs. Because the etiology — aside from its association with diabetes — is unclear, it should not be surprising that treatment regimens for NLD remain under study.

There are several evidence-based treatments for NLD. Immune modulation may be a key factor, since corticosteroids (topical, intralesional, or systemic) as well as other immunomodulators (e.g., infliximab, etanercept) have each had some success. The treatment with the highest rate of NLD resolution is psoralen plus ultraviolet A; unfortunately, the treatment regimen intensity (average 47 sessions) is well beyond that of many patients, and the method is not within the typical boundaries of primary care practice. Variable results have been seen among diverse categories of intervention (e.g., cyclosporine, tacrolimus, pioglitazone, hyperbaric oxygen). Refractory cases of NLD may merit consideration of dermatologic referral. Because outcomes are often less than optimal, patients should be informed that NLD is frequently a refractory dermatologic problem. ■

Clarification

In the November 29, 2013, issue of *Internal Medicine Alert*, we published the same three clinical briefs that were published in the November 15, 2013, issue.

We apologize for this mistake. If you would like an updated file sent to you, please send your request to customerservice@ahcmedia.com with IMA November 29 in the subject line. ■

Does the AV Block Get Worse?

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.

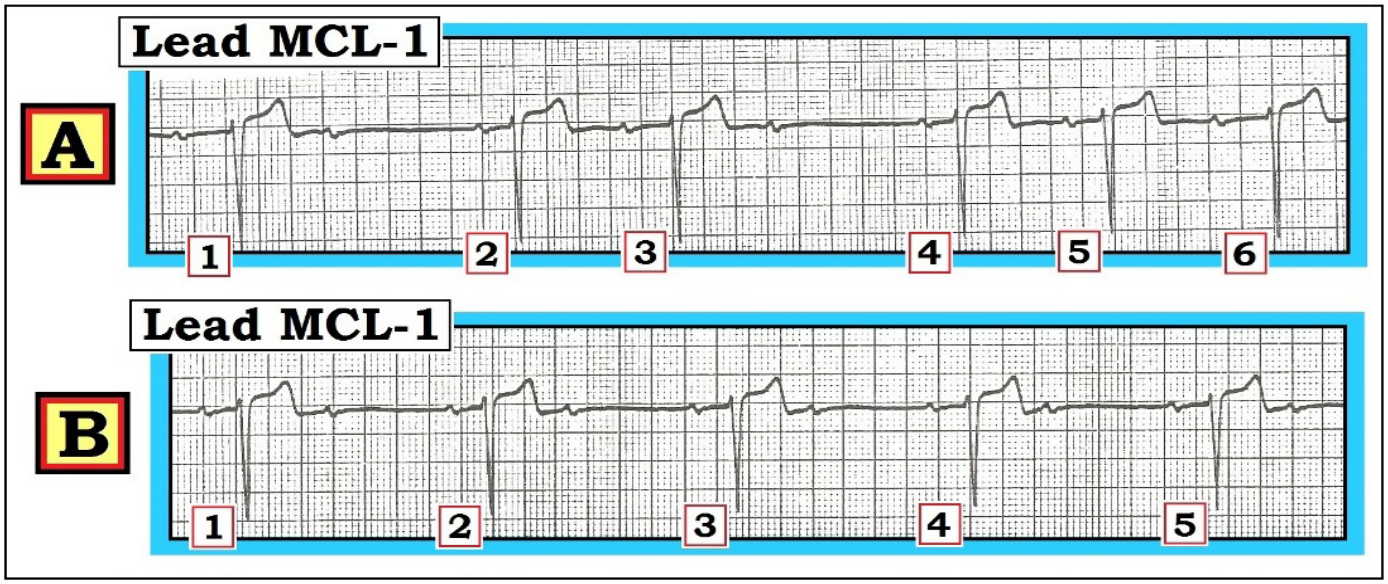

Figure — Sequential tracings from a patient with syncope.

Scenario: Imagine the ECG tracings shown above were sequentially obtained from a patient with syncope. What kind of atrioventricular (AV) block is present in each tracing? Does the degree of AV block worsen from tracing A to tracing B?

Interpretation: Beginning with tracing A, there is group beating. The QRS complex is narrow. Underlying sinus arrhythmia is present. The PR interval progressively increases within each group until a beat is dropped. This is second-degree AV block, Mobitz Type I (*AV Wenckebach*).

In tracing B obtained a little while later on this same patient, the overall ventricular rate has slowed. The QRS complex is again narrow. Now, only one out of every two P waves is conducted to the ventricles. Every other P wave *does* conduct — as evidenced by the constant (albeit slightly prolonged) PR interval preceding each QRS complex. This is second-degree AV block with 2:1 AV conduction.

Although at first glance one might think that the degree of AV block in tracing B has become "worse," this is not the case. Note that the underlying atrial rate is *faster* in tracing B than it was in tracing A. Thus, only one out of every two P waves is able to penetrate the AV node when the atrial rate is 80-85/minute — whereas a greater percentage of P waves penetrate in Tracing A when the atrial rate is slower (in the 60-70/minute range).

Distinction between Mobitz I vs Mobitz II second-degree AV block is not possible from inspection of tracing B alone. Because there is never conduction of two *consecutive* P waves in a row, we simply cannot tell if the PR interval would prolong if given a chance to do so. This distinction is important because Mobitz II usually requires treatment with pacing, whereas Mobitz I does not. That said, it is probable that tracings A and B *both* represent Mobitz I because: 1) Mobitz I AV block is far more common than Mobitz II; 2) the QRS complex is narrow (whereas Mobitz II usually manifests QRS widening; 3) the PR interval for beats that conduct in Tracing B appears to be long (more common with Mobitz I); and 4) it is rare for a patient to switch back-and-forth between Mobitz I and Mobitz II conduction defects, and we know that Tracing A clearly manifests Mobitz I AV block. ■

In Future Issues:

Linagliptin in Seniors with Type 2 Diabetes