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INSIDE

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Do Compression Stockings Prevent Post-Thrombotic Syndrome?

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 multicenter study of patients with an episode of first proximal deep venous thrombosis, elastic compression stocking use did not prevent the development of post-thrombotic syndrome.*

Source: Kahn SR, et al; for the SOX Trial Investigators. Compression stockings to prevent post-thrombotic syndrome: A randomised placebo-controlled trial. *Lancet* 2013; Dec 5. Doi: 10.1016/S0140-6736(13)61902-9. [Epub ahead of print].

POST-THROMBOTIC SYNDROME (PTS) IS A LONG-TERM COMPLICATION OF deep venous thrombosis (DVT) resulting from injury to the venous valvular system. It is often characterized by the development of symptoms such as pain, swelling, and skin changes in the affected limb following an episode of DVT. Venous dilation, pigmentation, and venous ulcers can often be seen upon examination. PTS has been estimated to affect up to 60% of individuals with DVT, frequently occurring within 2 years of the DVT episode.[1] In a large study, researchers found that one in three patients with DVT will develop PTS within 5 years.[2] Higher body mass index, persistent leg symptoms 1 month after acute DVT, anatomically extensive DVT, recurrent ipsilateral DVT, and older age appear to be the main risk factors for development of PTS following DVT. PTS can severely impact an individual's quality of life. Prevention of PTS is critical since treatments are not very effective. The current standard of care for the prevention of PTS following DVT is the use of elastic compression stockings (ECS). Of course, preventing initial DVT and DVT recurrence will prevent most cases of PTS in the first place.

A limited number of small research studies suggests that the dai-

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ly use of elastic compression stockings for 2 years after proximal DVT appears to reduce the risk of PTS.[3,4] However, a great deal of uncertainty exists surrounding the optimal duration of use as well as the compression strength. Additionally, it is not yet known whether the same principles would apply to distal DVTs.

Kahn et al conducted a large multicenter, randomized, placebo-controlled trial to establish evidence regarding the efficacy of the use of ECS to prevent PTS. Between 2004 and 2010 in institutions across the United States and Canada, patients who suffered from first proximal symptomatic DVT were randomly assigned to active vs placebo ECS study groups by a web-based randomization system. Patients were asked to wear the stocking on the affected leg from waking until retiring for 2 years, and were encouraged to stay active. The primary outcome was PTS diagnosed at 6 months or later. A total of 410 patients were randomly assigned to receive active ECS and 396 received placebo ECS.

Overall, 483 (60%) of 803 patients were men, mean age was 55.1 years (SD 15.5), and 699 (87%) of 803 study participants were outpatients. Mean time from DVT diagnosis to randomization was 4.7 days (SD 3.9). The most common proximal extent of DVT was in femoral vein (31.3%), followed by popliteal vein (30.3%), common femoral vein (26.9%), and iliac vein (11.6%).

The researchers found that the cumulative incidence of PTS was 14.2% in the active ECS group vs 12.7% in the placebo ECS group; the difference was not statistically significant (hazard ratio, 1.13; 95% confidence interval, 0.73-1.76; $P = 0.58$). Furthermore, the secondary analyses failed to reveal any between-group differences in the cumulative incidence of PTS, distribution of PTS severity category, or rate of ipsilateral leg ulcers. The study authors concluded that their findings demonstrate that compared with wearing placebo stockings, wearing a graduated ECS did not reduce the incidence of PTS at 2 years in patients with a first proximal DVT. They also stated that wearing ECS did not affect the occurrence of venous ulcers, rate of recurrent venous thromboembolism, prevalence of venous valvular reflux at 12 months, or generic or venous disease-specific quality of life.

■ COMMENTARY

These findings are unexpected. While the cumulative incidence of PTS was lower in both groups of the study than would be anticipated, it was primarily due to the type of criteria applied (Ginsberg's definition). However, the researchers had a consistent finding when the other criterion (Villalta definition) was applied in the secondary outcome of the study. Although 14% of the study patients either withdrew or were lost to follow-up, the study methodology was strong with the large number of study participants. These results are in striking contrast with the beneficial findings of ECS shown in previous, smaller, open-label trials. There may be several explanations for such conflicting findings including that in previous studies, patients using ECS may have performed other beneficial activities or the ECS may have provided benefits beyond the measurable compressions. However, with the largest study to date on the subject, along with utilizing a placebo arm, it is clear the research suggests that ECS do not reduce the subsequent development of PTS in patients with newly diagnosed DVT. This compels us to reconsider the existing paradigm. The utility of compression stockings in treating established PTS is yet to be addressed with further studies. Nevertheless, the best strategy for preventing PTS perhaps remains preventing the DVTs in the first place! ■

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Not All Patients with Acute, Uncomplicated Diverticulitis Require Hospitalization

ABSTRACT & COMMENTARY

By Jennifer A. Best, MD

Assistant Professor, University of Washington School of Medicine, Seattle, WA

Dr. Best reports no financial relationships relevant to this field of study. This article originally appeared in the March 2014 issue of Hospital Medicine Alert.

Synopsis: *The authors conclude that outpatient treatment with oral antibiotics is as safe and effective as initial hospitalization for intravenous therapy, at a lower cost and without decline in quality of life.*

Source: Biondo S, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis. *Ann Surg* 2014; 259:38-44.

DIVERTICULITIS OF THE COLON IS A COMMON CONDITION frequently implicated as an admitting diagnosis among hospitalized adults in the United States and elsewhere. Most often, hospitalists initially manage this condition with intravenous antibiotics and transition to oral therapy upon improvement in clinical status, as evidenced by normalization of vital signs, diminished gastrointestinal symptoms and ability to tolerate an oral diet. Current guidelines lack clear recommendations on the ambulatory management of uncomplicated diverticulitis, which can be defined as lacking a complication such as perforation, obstruction, gastrointestinal bleeding, or fistula. The majority of diagnosed episodes of diverticulitis can be classified in this fashion. Given a lack of prospective and randomized studies, it is uncertain whether acute, uncomplicated diverticulitis can safely be managed in the outpatient setting with oral agents alone. It is worth noting that only approximately 15% of patients admitted with acute diverticulitis require urgent surgical intervention during that admission.

In this trial, Biondo and colleagues evaluated the result of two different management strategies for acute, uncomplicated left-sided diverticulitis. Their randomized study was performed at five university hospitals in Spain. Potential subjects were recruited from a population of patients > 18 years of age who presented to the emergency department (ED) with suspicion of diverticulitis with fever and acute abdominal pain and tenderness. These patients were evaluated initially with radiographs of the chest and abdomen to exclude other etiologies for symptoms and an abdominal CT scan with contrast. Patients were excluded from participation if they exhibited signs of complicated diverticular disease (including even small abscesses), failed to respond to initial therapy or tolerate oral intake in the ED, or carried additional comorbidities which rendered them high risk for decompensation (pregnancy, recent antibiotic use, suspicion of malignancy, immunosuppression). On-call surgeons at each site, not investigators, assumed responsibility for recruitment and randomization.

Patients were randomized to two groups. Group 1 was admitted to the hospital. Group 2 was discharged from the ED and contacted daily by investigators for 5 days subsequent to that discharge. All patients received an initial dose of intravenous antibiotics in the ED (amoxicillin and clavulanic acid; ciprofloxacin and metronidazole substituted for patients with penicillin allergy). Group 1 was then admitted to the hospital and managed with intravenous antibiotics and fluids for 36-48 hours to tolerance of oral intake and adequate pain control, followed by discharge. Group 2 was discharged directly from the ED with instructions to continue oral amoxicillin-clavulanic acid (or ciprofloxacin-metronidazole, if allergic). Both groups completed 10 days of total antibiotic therapy and received dietary recommendations. For the outpatient cohort (group 2), this consisted of liquid diet with electrolyte drinks for 2 days, then escalation to low fiber. Pain was managed with paracetamol (acetaminophen). Phone calls to the outpatient subjects included assessment of temperature, diet, bowel function and pain. All patients were seen in clinic at 14 days and referred for colonoscopy to exclude neoplasm between days 45 and 60. The study's primary outcome was treatment failure of the outpatient strategy, as compared with initial hospitalization. Treatment failure was documented to have occurred in the setting of persistent pain and fever, progression to bowel obstruction or drainable abscess, surgical indication or mortality in the 60 days post-randomization. Other endpoints included quality of life (as assessed by the SF-12 tool) and a cost analysis completed at the coordinating institution, based on services for diagnosis, treatment, follow-up, and mean length of stay.

A total of 132 patients were ultimately randomized, and no significant differences were noted between the groups at baseline. Of this number, only 7 (5.3%) were readmitted, with no difference in readmission between the groups. No patients died and none required emergency surgery. There were no differences observed between initial inpatient and outpatient therapy related to quality of life at days 14 and 60, although within each group, quality of life improved between these two clinic visits. The cost was three times lower with outpatient therapy than with initial hospitalization (1124.70 euros less per patient — equivalent to $1532.74 US at the time of this article). The authors conclude that outpatient treatment with oral antibiotics is as safe and effective as initial hospitalization for

intravenous therapy, at a lower cost and without decline in quality of life.

■ **COMMENTARY**

Although this is the first randomized, controlled trial to address the risks and benefits of outpatient management of acute uncomplicated diverticulitis directly, there are a number of weaknesses with this study. Subject numbers were small. Many patients were not randomized due to the presence of complicated disease — only those with confined phlegmon were included. Patients with confined small abscess were excluded for simplicity here, but this modestly more complicated population likely warrants additional study. Furthermore, a substantial number of patients otherwise eligible refused to be randomized, given the possibility of outpatient management. This reader notes that patients randomized to group 2 received a single dose of intravenous antibiotics prior to discharge, so it remains unclear whether these patients would have recovered with a strictly oral antibiotic regimen — this too should be investigated. In summary, however, these data suggest that many patients with acute, complicated diverticulitis, as manifested by inflammation/phlegmon without abscess, may be safely treated with early discharge and oral antibiotics. On a related note, interesting data are arising about the utility and necessity of follow-up colonoscopy in these patients, but we'll save that for another review. ■

Calcium-Channel Blocker Clarithromycin Drug Interactions and Kidney Injury

ABSTRACT & COMMENTARY

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports no financial relationships relevant to this field of study.
This article originally appeared in the February 2014 issue of Infectious Disease Alert.

Synopsis: *In a retrospective cohort study, elderly patients who were prescribed calcium-channel blockers (CCBs) with clarithromycin were at increased risk for developing acute kidney injury. Moreover, all-cause mortality was greater with clarithromycin and CCB co-prescription (1.02%) vs azithromycin and CCBs (0.59%). Co-prescription of CCBs and clarithromycin should be avoided.*

Source: Gandhi S, et al. Calcium-channel blocker-clarithromycin drug interactions and acute kidney injury. *JAMA* 2013;310: 2544-2553.

Calcium channel blockers are a commonly prescribed class of medications for managing hypertension and are metabolized by the CYP3A4 enzyme. Pharmacokinetic studies have shown that coadministration of CYP3A4 inhibitors (e.g., erythromycin and fluconazole) with CCBs can raise serum CCB concentrations up to 500%, leading to associated toxicities such as excessive blood pressure lowering. The kidney is particularly susceptible to acute ischemic injury from hypotension and acute kidney injury (AKI) often leads to increased morbidity, mortality, and resource utilization. Gandhi and colleagues investigated the association between co-prescription of CCBs and clarithromycin with the development of AKI.

The study was a population-based, retrospective cohort of patients aged 65 years or older from June 2003 until March 2012 that used a health care database from Ontario, Canada. The investigators identified 96,226 patients who took a CCB along with clarithromycin and 94,083 who took a CCB with azithromycin as a comparison group. Baseline characteristics between the two groups were almost identical. The primary outcome measured was hospitalization with AKI and the secondary outcomes included hospitalization due to hypotension and all-cause mortality. All three outcomes were assessed within 30 days of the index date. Of note, the investigators were careful to have the dates covered by the CCB prescription overlap the dates covered by the antibiotic.

Co-prescribing clarithromycin with a CCB was associated with a higher risk for developing AKI (0.44% of patients) compared to azithromycin and a CCB (0.22%; odds ratio [OR], 1.98; 95% confidence interval [CI], 1.68-2.34). Median doses of clarithromycin were similar among patients with and without chronic kidney disease. The risk for hospitalization from hypotension was greater among patients taking clarithromycin and a CCB (0.12% of patients) than with azithromycin and a CCB (0.07%); absolute risk increase, 0.04%; OR, 1.60 [95% CI, 1.18-2.16]. Among the CCBs, nifedipine (the most potent vasodilator) was associated with the highest risk. All-cause mortality was also higher in the clarithromycin/CCB group (1.02% of patients) vs the azithromycin/CCB group (0.59%); absolute risk increase, 0.43%; OR 1.74 [95% CI, 1.57-1.93]. Gandhi and colleagues also found that a higher dose of clarithromycin (1000 mg/d) co-prescribed with a CCB resulted in a higher risk for hospitalization with AKI (307 patients out of 28,591 taking a high dose [1.07%] vs 95 out of 65,801 taking a low dose [0.14%]; absolute risk increase 0.93%; OR, 1.42 [95% CI, 1.13-1.79]. Finally, no significant difference was found in outcomes between patients who took clarithromycin vs

azithromycin with a CCB at 90 days following the co-prescription.

■ **COMMENTARY**

This was an interesting study that showed a small but significant risk for developing AKI in older adults within 30 days of taking clarithromycin and a CCB. Although less commonly prescribed in clinical practice than other macrolides, clarithromycin still has many uses, for example, in combination therapy for nontuberculosis Mycobacterium and *H. pylori* infections. It is, therefore, important that prescribers be aware of the potential risks with clarithromycin and carefully consider the potential for drug-drug interactions. Indeed, azithromycin has similar clinical indications to clarithromycin, yet is a much less potent inhibitor of CYP3A4.

There were a few important limitations to the study. Because of the retrospective and observational design, the results may have been influenced by unmeasured confounding variables. Drug-drug interactions are complex, and factors besides CYP34A enzyme inhibition may have also affected the results. Furthermore, older adults are more susceptible to both drug-drug interactions and AKI so the findings of the study may not be generalizable to other patient populations (i.e., younger patients). Finally, the circumstances for which clarithromycin was chosen over azithromycin were not ascertained, thus making it challenging to know how much the illness being treated contributed to AKI and/or mortality.

Based on this study as well as prior data showing similar adverse events, I suggest that co-prescribing clarithromycin and CCBs be avoided whenever possible. Clinicians should either choose an alternative antibiotic that does not inhibit the CYP3A4 enzyme for a patient taking a CCB or else switch the CCB to an alternative antihypertensive agent for the duration of clarithromycin therapy. ■

Pharmacology Update

Tasimelteon Capsules (Hetlioz™)

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 FDA HAS APPROVED THE FIRST DRUG FOR THE TREATMENT of chronic circadian rhythm disorder known as non-24 sleep-wake disorder (non-24). This condition occurs in individuals who are completely blind and have abnormal synchronization with 24-hour light/dark cycles. Tasimelteon is a melatonin (MT1 and MT2) receptor agonist. It is marketed by Vanda Pharmaceuticals as Hetlioz.

Indications

Tasimelteon is indicated for the treatment of non-24 sleep-wake disorder.[1]

Dosage

Tasimelteon is taken at the same time every night.[1] It should be taken without food. It is available as a 20 mg capsule.

Potential Advantages

Tasimelteon is the first drug approved for non-24 disorder. It improved nighttime sleep and reduced daytime naps in patients with non-24.[1]

Potential Disadvantages

Tasimelteon may cause somnolence and reduce mental alertness.[1] Headache, increased alanine aminotransferase, nightmares, or unusual dreams may occur. The frequency varies from 10-17% compared to 0-7% for placebo.[1] Concomitant use of strong CYP1A2 inhibitors or CYUP3A4 inducers should be avoided.

Comments

The endogenous circadian pacemaker, or biological clock, is mainly synchronized by light. Since light perception is lacking in completely blind individuals, their biological clock is not synchronized to the 24-hour day.[2,3] As a result, their sleep-wake patterns may drift in and out of sync with the conventional sleep-wake schedule. Common complaints include insomnia, difficulty waking in the morning, and excessive daytime sleepiness. The effectiveness of tasimelteon was evaluated in two randomized, placebo-controlled studies. In the first study, totally blind subjects (n = 82) were randomized to 20 mg of tasimelteon or placebo taken 1 hour before bedtime for up to 6 months. Efficacy endpoints were the total sleep time at night and daytime nap duration based on 25% of nights with the least nighttime sleep and 25% of days with the most daytime naps. Data were captured via patient-recorded diaries. In the first study, diaries were recorded for an average of 88 days during screening and 133 days during randomization. Tasimelteon improved nighttime sleep duration by 50 minutes (baseline 195 minutes) compared to 22 minutes for placebo. Daytime naps were reduced by 49 minutes (baseline 137 minutes) compared to -22

minutes for placebo. The second study was for 12 weeks. Subjects were treated for 12 weeks with tasimelteon and those with calculated time of peak melatonin level occurring at approximately the same time of day were randomized to continue with tasimelteon or placebo. Those randomized to tasimelteon showed a 7-minute decrease in nighttime sleep time and a 9-minute decrease in daytime nap time compared to -74 minutes and +50 minutes with placebo.[1] Less than one-third of subjects treated were considered as responders, defined as at least 45 minutes increase in nighttime sleep and ≥ 45 minutes reduction of daytime nap time.

Clinical Implications

Approximately 50% of blind people are affected by non-24 disorder.[2] Within non-24, there appears to be significant physiological presentation. Current treatment includes the combination of good sleep hygiene, structured daily schedules, and low-dose melatonin (0.5 mg).[3] Tasimelteon offers the first FDA-approved pharmacological treatment with about 30% of users achieving meaningful improvement. There are no published comparative studies between melatonin and tasimelteon. The cost for tasimelteon was not available at the time of this review. ■

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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.

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CME Questions

1. **Using elastic compression stockings in patients with first-time proximal DVT resulted in:**
   a. prevention of post-thrombotic syndrome.
   b. decrease in mortality from pulmonary embolism.
   c. no impact on post-thrombotic syndrome incidence.
   d. increase in mortality from pulmonary embolism.

2. **Biondo and colleagues deemed the following groups ineligible for outpatient management for acute diverticulitis, *except*:**
   a. patients with symptomatic improvement in the ED.
   b. patients who were immunosuppressed.
   c. patients with recent antibiotic use.
   d. patients who were pregnant or breastfeeding.

3. **Which of the following is correct?**
   a. Coadministration of erythromycin with a calcium-channel blocker such as nifedipine can result in a 500% increase in serum concentrations of erythromycin.
   b. Exposure to excessive concentrations of calcium-channel blockers may lead to renal dysfunction as a result of such concentrations causing elevated blood pressure.
   c. Coadministration of clarithromycin with a calcium-channel blocker such as nifedipine results in an increased risk of diarrhea due to elevated serum concentrations of the antibiotic.
   d. Coadministration of clarithromycin with a calcium-channel blocker such as nifedipine is associated with an increased risk of acute kidney injury, hospitalization because of hypotension, and all-cause mortality.

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.

Treatment to Reduce Genital HSV Shedding

Source: Wald A, et al. *N Engl J Med* 2014;370:201-210.

Patients burdened with genital herpes often desire treatments to reduce the frequency of viral shedding, hoping to reduce the rate of transmission. Several antivirals are currently available to reduce viral shedding, each of which has demonstrated some efficacy, but none of which totally eliminates viral shedding.

Herpes simplex virus type 2 (HSV-2) comprises a substantial share of the causes of genital herpes infection. Although two decades ago HSV-2 was responsible for the vast majority of genital herpes infections, the prominent role of HSV-1 in genital herpes has been increasingly recognized since 2006. Clinically, outbreaks are indistinguishable, although nuances of difference between HSV-1 and HSV-2 do exist (e.g., frequency of outbreaks and severity of outbreaks being modestly less with the former).

Pritelivir (PRT) is the first member of a new class of antiviral agents active against both HSV-1 and HSV-2. The mechanism of action — inhibition of the viral helicase-primase complex — differs from currently available nucleosidase analogues.

Wald et al performed a double-blind, placebo-controlled trial among adults (n = 156) with a clinical history of genital herpes and confirmed HSV-2 seropositivity. Subjects performed daily self-swabbing for HSV PCR testing, as well as reporting on occurrences of HSV outbreaks (which had to be confirmed within 24 hours by clinic personnel).

Over the 28-day duration of the study, study subjects who received daily doses of PRT of 25-400 mg/day experienced a significant reduction in the number of days of viral shedding (43-87% reduction, depending on dose). Clinical outbreaks were also dramatically reduced (87% reduction). PRT was well tolerated, with no serious drug-attributable adverse effects. It is uncertain if and when PRT will find clinical utility because animal trials disclosed skin and hematologic abnormalities, albeit at much larger relative doses than used in humans. ■

The Continuing Saga of Vitamin D: Who, When, and Why Should We Use It

Source: Reid IR, et al. *Lancet* 2014;383: 146-155.

The greying of the population assures a continued prominence for osteoporosis and its consequences. The "story line" of vitamin D in relation to osteoporosis is fairly straightforward: As vitamin D levels decline to suboptimal levels (actual number of what constitutes "suboptimal" is still hotly debated), secondary hyperparathyroidism develops, resulting in accelerated bone loss. To date, clinical trials have not confirmed a fracture reduction benefit from vitamin D supplementation, and even the relationship between vitamin D status and bone mineral density (BMD) is plagued with inconsistencies. To further clarify the question of the relationship between vitamin D and BMD, Reid et al performed a meta-analysis of clinical trials that evaluated the effects of vitamin D on BMD.

The clinical trial results (23 studies, n = 4082) were quite mixed, with some showing BMD benefit, some detriment, and some neutral. In essence, the net small benefit suggested by some trial data was of dubious clinical significance. These results should be distinguished from data on vitamin D in combination with calcium supplementation; since many trials provide vitamin D in combination with calcium (calcium does increase BMD), it has been sometimes misconstrued that each component of the vitamin D/calcium combo contributed to better BMD. The authors suggest that vitamin D would be best suited for persons with vitamin D insufficiency, rather than for all persons at risk for osteoporosis. ■

Antidepressants and New Onset Diabetes

Source: Wu CS, et al. *J Clin Psychiatry* 2014;75:31-38.

The relationship between antipsychotic medication and diabetes has been well demonstrated and is widely recognized by clinicians. Unfortunately, the relatively limited selection of antipsychotics sometimes requires that in order to achieve symptom control, new-onset diabetes must be accepted as a consequence.

The population of individuals treated with antidepressants far eclipses those treated with antipsychotics. The earliest commonly used antidepressants, tricyclics, were associated with weight gain due to activity and the post-synaptic histamine receptor site, which of course could be diabetogenic.

Wu et al report on a case-control study based on the Taiwan National Health Insurance Research Database. Over the 1998-2009 interval, they compared use of antidepressants among patients with diabetes (n = 47,885) and controls (n = 95,770).

Overall, persons treated with antidepressants for at least 2 years were 20% more likely to develop diabetes. In particular, younger individuals were adversely affected: Persons < 44 years of age had more than a doubling of risk for new onset diabetes.

The mechanism(s) by which antidepressants impart increased risk for diabetes are not clear. For instance, the above-mentioned weight gain with tricyclic antidepressants was not reflected in a greater incidence of diabetes than that seen with newer antidepressants (e.g., SSRIs, SNRIs). Recent studies have shown that other commonly used medications are associated with increased risk for new onset diabetes, including statins and thiazide diuretics. The frequency of prescription of antidepressants merits enhanced clinician vigilance for the development of diabetes. ■

Group Beating from AV Wenckebach?

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.

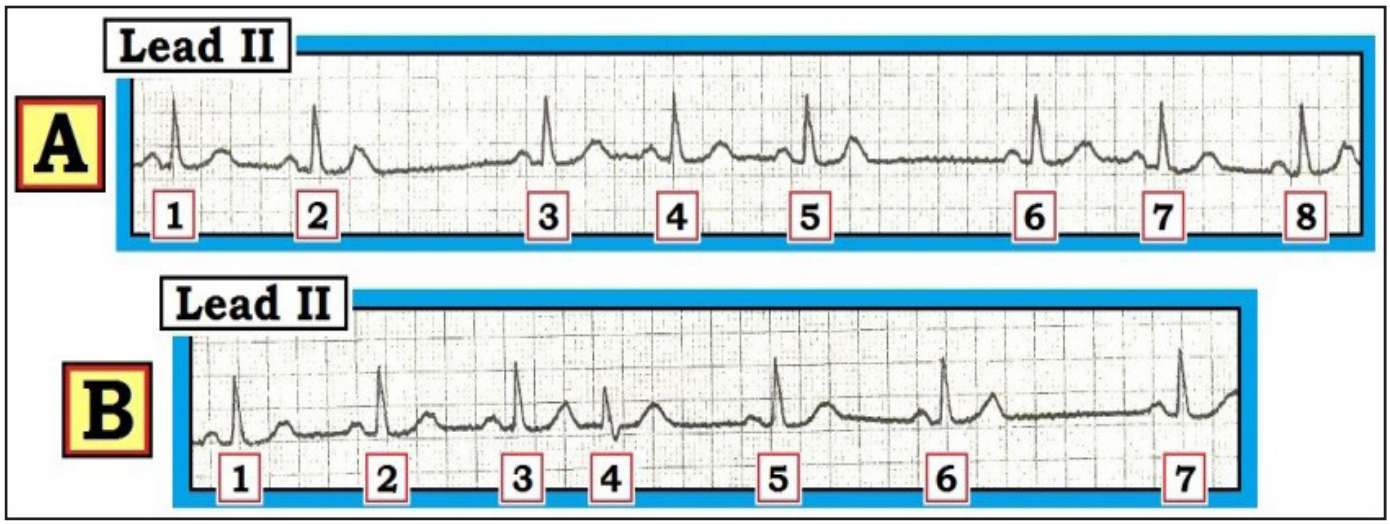

Figure — Sequential tracings obtained from the same patient a few minutes apart. Is the group beating in the top tracing the result of AV Wenckebach?

Scenario: The two tracings above were obtained from the same patient a few minutes apart. There is group beating in the top tracing. Does this represent second degree AV block of the Mobitz I type (AV Wenckebach)?

Interpretation: Recognition of the phenomenon of *group beating* should always suggest the possibility of a Wenckebach conduction disorder. That said, this case presents a wonderful example of why group beating does not always mean that a Wenckebach block is present.

Knowing that the two rhythm strips in the Figure were obtained from the same patient is helpful in our interpretation because findings present in one tracing will often be present later on. So it is here. The lower tracing clearly shows the underlying rhythm to be sinus arrhythmia. Beat #4 is early in this lower tracing. Note definite peaking of the T wave preceding beat #4 that is not seen in the much smoother T waves of beats #1, #2, and #5. This peaking in the T wave of beat #3 in the lower tracing is due to a PAC (premature atrial contraction) that is hidden within. The reason for the slightly different QRS morphology of beat #4, is that this early-occurring PAC is conducted with aberration.

Note the slight (1.6 second) pause at the end of the lower tracing (between beats #6-7). The commonest cause of a pause is a blocked PAC. T wave peaking of the T wave at the onset of this pause (in the T wave of beat #6) indicates that a blocked PAC is indeed the reason for this relative pause in the rhythm at the end of the lower tracing.

A similar phenomenon occurs repetitively in the top tracing. Despite group beating, the top tracing does not represent AV Wenckebach. This is because: 1) the atrial rhythm is not regular as it should be with a conduction disturbance due to AV block, and 2) the PR interval is not progressively increasing within groups of beats. Instead, there is subtle-but-real peaking of the T wave at the onset of each of the relative pauses in this top tracing. In the context of the lower tracing, it becomes much easier to appreciate that the T waves of beats #2, #5, and probably #8 in the top tracing are all taller than the T waves of beats #1, #3, #4, #6, and #7 that do not contain PACs within them. Thus, there is sinus arrhythmia with frequent PACs on these two sequential tracings. PACs are either non-conducted or conducted with aberration. ■

In Future Issues:

Curcumin Comparable to Fluoxetine for Treatment of Major Depressive Disorder