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INSIDE

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Everything You Ever Wanted to Know About Sex (in the Elderly), But Were Afraid to Ask

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

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

Synopsis: *Sexuality is an important aspect of life for older Americans.*

Source: Lindau ST, et al. A study of sexuality and health among older adults in the United States. *N Engl J Med.* 2007;357:762-774.

Lindau and colleagues sampled Americans aged 57 to 85 years, living independently in 2004 to learn about their sexual habits. A total of 1550 women and 1455 men were interviewed. The interviews were conducted at home in English or Spanish, as appropriate, and a basic physical examination was performed and blood, salivary, and vaginal mucosa specimens were obtained for laboratory analysis. Items of interest included marital history, recent sexual partnerships, sexual activity, sexual problems, physical health, and whether sex had been discussed with a physician since turning 50 years of age. The correspondents were grouped by sex and age (57-64, 65-74, and 75-85 years). They were predominantly Caucasian and increasingly so as the age of the subgroups increased, reaching 86% by age 75-85 years. More than half had at least some college education. Eighty percent were married or widowed with a greater percentage of men being married than women in every age group. The majority rated their health status as good to excellent. At all ages, men were more sexually active than women. The percentage of individuals engaging in sexual activity dropped with increasing age. The frequency of sexual activity also declined with age, but even in the 75-85 years group, more than half were having sex at least two or three times a month. Rating one's health more favorably was associated with a

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greater likelihood of sexual activity for both sexes, but, here again, healthy men were more likely than healthy women to be sexually active. Of the individuals who were in a relationship, very few reported it to be homosexual (3 of 1198 men and five of 815 women). Being in a relationship was highly associated with being sexually active in the previous year. Sexual activity for both sexes included masturbation, vaginal intercourse, and oral sex. Sexual problems were common. For men they included difficulty in achieving or maintaining an erection, lack of interest in sex, climaxing too quickly, anxiety about performance, and inability to climax. The problems that women experienced included lack of interest in sex, difficulty with lubrication, inability to climax, finding sex not pleasurable, and pain. Chronic diseases (in particular diabetes mellitus) were associated with less frequent sexual activity. Discussions about sex with a physician were infrequent: 38% of men and 22% of women.

COMMENTARY

With the possible exception of frequency of sexual activity, the results of this survey are not too surprising. We are not comfortable talking about sex. Rent the movie Kinsey for an insightful portrayal of our reluctance. We physicians are really uncomfortable discussing sex with our elderly patients. However, sexual activity is an important component of quality of life in the elderly.[1,2,3] Additionally, sexually transmittable diseases (including HIV/AIDS) are a problem in our older population. While the estimated number of HIV/AIDS cases remained stable among persons 65 years and older in 2005, they increased among persons aged 55-59 and 60-64 years.[4] There is a price to be paid for our disinclination to speak about sex. We owe it to our older patients to develop our communication skills in this area. ■

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Aliskiren and Valsartan for Hypertension

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

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

Dr. Crawford is on the speaker's bureau for Pfizer.

Synopsis: *Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomized, double-blind trial.*

Source: Oparil S, et al. Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomized, double-blind trial. *Lancet.* 2007;370:221-229.

ALISKIREN IS A NEW CLASS OF DRUGS THAT directly inhibit renin and is approved in the

USA for the treatment of hypertension. Valsartan is the best-selling antihypertensive medication in the world. Little is known about the combination of these 2 drugs on blood pressure. Thus, Oparil and colleagues conducted a double-blind, placebo-controlled parallel group, dose escalation study at 312 centers in the USA, Spain, and Germany in 1797 patients with hypertension, but no severe cardiovascular disease. Patients were given once-daily oral aliskiren 150 mg or valsartan 160 mg or the combination or placebo for 4 weeks. Then they were force titrated to double the dose of each agent for 4 weeks. The primary end-point was a change in mean sitting diastolic blood pressure from baseline to week 8. Secondary end-points included systolic blood pressure measurements, the 4-week results and plasma levels of renin, renin activity and aldosterone. Overall 11% of the patients withdrew early from the study mostly because of inadequate blood pressure control.

Premature discontinuation was least common in the combination therapy group and most common in the placebo group. Both mean sitting blood pressure and mean 24-hour ambulatory blood pressure decreased most on combination therapy and less but equally on both monotherapies. All 3 active drug groups decreased significantly vs placebo. Mean sitting systolic blood pressure decreased 4.6 mmHg on placebo, 13 mmHg on each monotherapy, and 17.2 on combination therapy. Plasma renin levels were increased by all 3 active therapies, but most by aliskiren. Plasma renin activity was reduced by aliskiren alone or in combination, but was elevated by valsartan monotherapy. Aldosterone levels were not changed on aliskiren monotherapy, but were reduced by valsartan and combination therapy. Adverse events occurred in 2-3% of patients in each group. Potassium levels >5.5 mmol/L occurred in 2-4% of patients more in the combined therapy group. The authors concluded that the combination of aliskiren and valsartan in maximum recommended doses results in greater blood pressure lowering than does monotherapy with either agent in patients with hypertension. Also, combination therapy exhibited a low adverse event rate that was similar to monotherapy.

COMMENTARY

It is unusual to see pharmacologic treatment studies that combine maximum doses of 2 drugs. Most are done with less than maximum doses, leaving the question of what would happen if one drug was increased maximally, rather than adding another drug. The major rationale for using multiple drugs at low doses is to avoid adverse effects that may be seen at higher doses of one drug. This assumes that the added drug is from a different class of agents with a different adverse effect profile. Although this theory sounds good, it has never been convincingly proved in clinical trials. In fact, some studies have shown the opposite, that adverse effects tend to increase in frequency the more drugs you give. Thus, this study was interesting because all these issues were challenged. Maximum doses were used as monotherapy and in combination, and the 2 agents chosen had similar adverse-effect profiles. The results showed that combination therapy with aliskiren and valsartan was superior to monotherapy with either drug, with a similar adverse effect frequency.

One strength of the study was the use of an 8-hour ambulatory blood pressure recording to weed out the white coat hypertensives. This is important because they tend to get better over time, which results in greater placebo effects. Also, 24-hour ambulatory blood pressure measures were done and correlated well with the mean sitting blood pressure results. The major adverse effect observed was an increase in creatinine, which was seen in 4 patients on combination therapy (0.9%), 2 on valsartan, one on aliskiren and none on placebo. However, this was not accompanied by an increase in blood urea nitrogen and serum potassium levels > 5.5 mmol/L, and were not significantly different between the 4 groups (3% placebo, 2% aliskiren, 2% valsartan and 4% combination). None of these patients had events that lead to study drug discontinuation.

The biochemical results are also interesting. Plasma renin levels increased in all 3 therapeutic groups as might be expected from drugs that block its activity downstream. However, only aliskiren and combination therapy reduced renin activity. What, if any, effects elevated renin and renin activity have in patients on angiotensin receptor blockers (ARB) is unknown, but blocking renin's effect with aliskiren did further reduce blood pressure. Perhaps the observed inconsistent effect of adding an ARB to an ACE inhibitor on blood pressure is due to increased renin activity. Also, combination therapy and ARB monotherapy reduced aldosterone levels which would be expected to help reduce blood pressure. Thus, this may be an especially potent drug combination for favorably altering the renin angiotensin aldosterone system. ■

A Prospective, Randomized Trial of Clear Liquids vs Low-fat Solid Diet as the Initial Meal in Mild Acute Pancreatitis

ABSTRACT & COMMENTARY

By Malcolm Robinson MD, FACP, FACG

Emeritus Clinical Professor of Medicine, University of Oklahoma College of Medicine, Oklahoma City

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

Synopsis: *Patients with mild acute pancreatitis probably can be fed solid food with results as good as those seen with initial feeding with the traditional clear liquid diet.*

Source: Jacobson Brian C, et al. *Clin Gastroenterol and Hepatol.* 2007;5:946-951.

There are almost 250,000 cases of pancreatitis annually in the United States. Most are classified as mild disease and resolve within a few days. Management of pancreatitis has traditionally entailed IV hydration, pain control, and elimination of oral feeding (NPO). The NPO status is presumed to avert early and potentially deleterious pancreatic stimulation. Once re-feeding is deemed appropriate, clear liquid diet has been the usual starting point. Diet is then advanced slowly and as tolerated. These authors hypothesized that re-feeding with a low fat solid diet (LFSD) would be as well tolerated as a clear liquid diet (CLD). It was hoped that the more advanced initial diet might lead to a shorter hospital stay. The study was well powered to detect a difference in length of hospital stay between groups receiving initial CLD vs LFSD. Out of a total of 1,355 patients at Brigham and Women's Hospital admitted with pancreatitis between 1999 and 2005, 121 patients with clear-cut mild pancreatitis were ultimately randomized into this non-blinded study. Those excluded were mostly ineligible on the basis of pancreatic enzymes that were not > 3 times normal or > twice normal with clear CT evidence of pancreatitis or eliminations for comorbidities. The primary prospective endpoint of this study was to have been a reduction in length of hospitalization (LOH). Analysis of data included the elimination of patients who had been fed less than 6 hours prior to eating. Even in this fine hospital, some study patients received the wrong initial meal. In any case, there was no difference in LOH between the CLD and LFSD groups. There were 113 patients in the per protocol evaluation group. Despite the failure to demonstrate a change in LOH, first meal and first day caloric intake and fat intake were higher in the LFSD group than in CLD patients. The authors thought that the lengths of stay in study patients might have been impacted by factors that were not related to diet. For example, a number of patients had extended hospitalizations for additional diagnostic studies. Previous studies elsewhere also have shown solid diet toleration in pancreatitis patients although they too failed to demonstrate decreased LOH. The authors conclude that early initiation of solid food intake is certainly worth considering in patients who are hospitalized with mild acute pancreatitis.

COMMENTARY

As was mentioned in an accompanying editorial, this paper raises more questions than answers.[1] There is little justification in the concept that restriction of oral feeding is beneficial in many cases of pancreatitis. The inflamed pancreas probably doesn't respond normally to stimulation, and some patients, even those with relatively severe pancreatitis, might have no problems with initiation of feeding early in their course. We know little or nothing about the relative effects of any particular dietary constituents on the inflamed pancreas. The editorial writer mentions the potentially parallel notion that nasogastric tubes were deemed indispensable after many forms of gastrointestinal surgery, especially surgery with fresh intestinal anastomoses. This concept has been disproved, and most modern surgeons now dispense with the routine use of nasogastric suction in such cases. The whole concept of graduated diets in most hospitalized patients is either invalid or very poorly validated. In particular, the classical progression from clear liquid diet to the so-called full liquid diet seems especially ridiculous. Full liquids are mostly dairy-based, and large numbers of people in the general population are dairy intolerant for any of several reasons (especially lactose intolerance). Such individuals would almost certainly do better with initiation of a general diet. It has always seemed to me that the diets of hospitalized patients should be individualized. Patients who are doing well and who really want to try a particular food or beverage often should be accommodated. I would urge that patients with pancreatitis who have been able to reduce their requirements for opiate-based analgesic therapy could have pro-active dietary advancement. If a larger study were to be performed, I am quite confident that this hypothesis would be upheld and that shortened hospital stay would be demonstrable. Meanwhile, we already have evidence that dietary advancement in patients with mild pancreatitis is generally safe and tolerable. ■

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Influenza — 2007/2008

Special Report by Carol Kemper, MD, FACP

Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center.

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

Source: MMWR June 29, 2007, www.cdc.gov.mmwr/preview/mmwrhtml

GUIDELINES FOR THIS YEAR'S influenza season are now available, with important recommendations to hospitals and clinics. The 2007/2008 trivalent vaccine contains A/Solomon Islands/ 3/2006 (H1N1-like), A/Wisconsin/ 67/2005 (H3N2-like), and B/Malaysia/ 2506/2004-like antigens. The A/Solomon Islands component, which is a recent antigenic variant of the former A/Caledonia, is a new addition to the vaccine, while the other 2 antigens remain unchanged. While H1 viruses were more common during the peak season in February 2007, H3 viruses were more frequently identified later in the season in March through May. A few Influenza B viruses were also identified.

Vaccine coverage still falls below 50% for children, health care personnel, pregnant women, and adults with risk factors for influenza complications.

The target groups for vaccination have not changed. But the ACIP is re-emphasizing the following:

• Administration of 2 doses of vaccine to all children aged 6 months to 8 years;

• If children received only one dose in previous years, they should receive 2 doses this year. If they received two doses last year, then one dose this year is sufficient;

• Anyone who requests vaccine should receive it; in other words, anyone wishing to reduce their risk of influenza, even if they do not fall into a risk category, is a candidate for vaccination;

In addition, the ACIP strongly recommends:

• Health care facilities should offer immunization clinics throughout the flu season;

• Health care facilities should consider the level of vaccination among health care workers a patient safety quality measure.

• Health care facilities should implement policies such that health care workers refusing vaccination shall sign a declination. ■

Pharmacology Update

Lidocaine Powder Intradermal Injection System (Zingo™)

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

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

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

THE FDA HAS APPROVED A PRODUCT FOR TOPICAL anesthesia prior to venous access procedures such as venipuncture or peripheral intravenous cannulations in children. The device is a needle-free single-use helium-powered intradermal delivery system containing 0.5 mg of lidocaine hydrochloride monohydrate. It is marketed by Anesiva as Zingo.

Indications

Lidocaine intradermal injection system is approved to provide local analgesia prior to venous access procedures in children ages 3 to 18 years of age.[1]

Dosage

One dose from the intradermal delivery system is delivered one to three minutes prior to needle insertion. The procedure should be completed within 10 minutes after administration.[1]

Potential Advantages

The system provides a needle-free delivery dose of local anesthetic with effect observed if given one to three minutes prior to venous access.1 Typically topical anesthetics such as lidocaine/prilocaine emulsion (EMLA), lidocaine liposomal cream (ELA-Max) lidocaine/tetracaine patch (Synera) requires administration 20 to 60 minutes prior to the procedure.[2,3,4]

Potential Disadvantages

Adverse events are local in nature. The most frequent are erythema (53% vs 27% for placebo), petechiae (44% vs 5%), and edema (5% vs 3%).[1]

Comments

This is a novel delivery system for lidocaine. Efficacy was shown in 2 randomized, double-blind, parallel-arm,

sham placebo controlled trials (n = 1,109).[1] The system reduced pain, compared to placebo, when administered one to three minutes prior to venous access. Administrations were to the back of the hand or the antecubital fossa. Pain was assessed using a 6-point categorical scale using faces to reflect the degree of pain ranging from "no hurt" to "hurt worst." The adjusted means difference between groups was statistically significant, but modest (-0.33 to -0.39), representing a 16% to 22% reduction compared to placebo. The upper limit of the 95% confidence interval ranged from -0.58 to -0.65 or about 2/3rd of a point on a 6 point scale. Currently there are no comparative studies between the lidocaine intradermal system with other topical anesthetics such as EMLA, ELA-Max, Synera or administration of lidocaine using a needle-free device such as J-Tip. The administration of 0.25 ml of a buffered 1% lidocaine solution using this device one to three minutes before insertion has been shown to be significantly more effective than EMLA (mean of 69 minutes) in reducing pain associated with intravenous catheter insertion.[5] The cost of Zingo was not available at the time of this review. The cost has been estimated to be $12 to $16 per injection.[6]

Clinical Implications

Needle insertion is regarded as a frightening and bothersome procedure for children.[7] There has been an increase in the reported use of topical or local anesthetics for venipuncture.[8] The slow onset of existing products is problematic in certain practice settings such as the emergency room. The onset of action of Zingo is certainly an attractive feature. However, it is not clear how effective the analgesic effect really is without an active control. ■

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CME Questions

49. Choose the one incorrect answer. In a recent survey of sexuality in the elderly:
a. males were more sexually active than females.
b. good general health was associated with more frequent sexual activity.
c. masturbation, oral sex, and vaginal intercourse were common.
d. diabetes mellitus was associated with less frequent sexual activity.
e. sex was frequently discussed at visits to the doctor.

50. More rapidly advancing the diets of most patients with mild pancreatitis achieves which of the following goals?
a. Patients can leave the hospital in fewer days.
b. caloric intake and fat intake can be increased on the first day of solid food intake.
c. re-hospitalizations during the subsequent 20 days can be decreased
d. Fewer patients have recurrences of pancreatitis.
e. Nausea and vomiting after feeding is statistically greater in the low fat solid diet group.

Answers: 49 (e); 50 (b)

CME Objectives

The objectives of *Internal Medicine Alert* are:
- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances;
- to describe cost-effective treatment regimens;
- to describe the pros and cons of new screening procedures.

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville
Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Benefits of Calcium and Vitamin D: A Meta-analysis

In an era of multiple randomized controlled trials that have documented the efficacy of antiresorption agents (eg, alendronate, risedronate, ibandronate, raloxifene) both to enhance bone mineral density (BMD) and reduce osteoporotic fractures, there remains some uncertainty about the efficacy of calcium supplementation, vitamin D supplementation, or the combination. Even meta-analysis on the topic have been inconsistent.

The impact of supplementation is especially important to clarify since in developing nations, which are beginning to share the same "graying" demographics as America, the cost of preventive treatments is critical.

Tang, et al performed a meta-analysis on all recorded randomized clinical trials of persons over 50 (n=29), comprised of 52,625 participants. The trial selection process can provide greater assurance than earlier meta-analysis, because they did not include any observational trials.

Overall, calcium or calcium plus vitamin D were associated with a 12% relative risk reduction in fracture risk (p=0.0004) in a time span of approximately 3.5 years. Beneficial effects are greatest in the highest risk, elderly, slender population who have low calcium intake at baseline, but is still beneficial in the over-50 population as a whole. Comparing various doses of calcium, more benefit was seen with doses over 1200 mg/day of calcium. Although in the large category of "any" supplementation with vitamin D, no measurable benefit was seen over calcium supplementation alone. When higher doses of vitamin D were used, there was additional benefit. Outcomes were similar regardless of gender. The authors suggest that calcium and vitamin D, when given at doses of at least 1200 mg/d and 800 IU/d respectively, improves BMD and reduces fractures in persons over 50. ■

Tang BMP, et al. Lancet. 2007;370:657-66.

ARBs and Inflammatory Markers in Type 2 Diabetics

Discussions about the role of inflammation in generating endothelial dysfunction, atherosclerosis, and cardiovascular (CV) endpoints continue to generate interest. Antibiotic therapy has not improved CV outcomes, nor has modulation of homocysteine or antioxidants. NSAIDs, despite being prototypically anti-inflammatory, remain under a dark CV cloud. Perhaps, though, the method by which inflammation is reduced is pertinent. To address this concept further, a study of diabetic hypertensives was performed comparing one year of atenolol (ATN) therapy with valsartan (VAL).

At baseline, inflammatory markers (cytokines, chemokines, and adhesion molecules) were measured in both groups; additionally, a group of nonhypertensive subjects was included for comparison.

Compared with non-hypertensive controls, inflammatory markers were 2-4 fold higher in diabetic hypertensives at baseline. During treatment, glucose and lipid levels did not change, hence any variation in inflammatory markers would not be attributable to enhanced management of diabetes or dyslipidemia.

ATN and VAL lowered blood pressure to a similar degree, but there was disparity in effects upon inflammation: VAL reduced all three categories of inflammatory markers, but only cytokine IL-18 was reduced by ATN.

Treating diabetic hypertension with VAL provides broad reductions of inflammatory markers compared to atenolol. Whether modulation of inflammation will ultimately impact the CV outcomes of hypertension remains to be seen. ■

Touyz RM, et al. J Am Society of Hypertens. 2007;1(3):189-199.

When Oral Therapy Fails in Type 2 Diabetes

One might assume that the proliferation of tools to manage type 2 diabetes (2DM) would augur well for levels of diabetic control. Unfortunately, that appears to not be the case. The progressive nature of the disease, hesitance of clinicians to advance therapy, reluctance to employ parenteral agents, and growing burden of obesity and sedentary lifestyle all contribute. Thiazolidinediones (TZDs, ie, pioglitazone, rosiglitazone) have shown promise as potent agents to reduce glucose. In the recently published ADOPT trial, durability of glucose control with rosiglitazone monotherapy was found to be superior to other comparators; at 5 years, the failure rate was lowest with rosiglitazone (15%), next lowest with metformin (21%), and greatest with sulfonylurea (34%).

Riedel assessed retrospectively the time to loss of control after adding a TZD to a regimen of either metformin or metformin plus sulfonylurea in a managed care population of diabetics (n=579).

Several interesting insights are provided by this examination of a "real world" (as opposed to data from a randomized clinical trial) patient population. First, the addition of a TZD did enable the majority to achieve a goal of < 7.0%. Second, the mean time to failure was 1.3 years. Finally, the addition of TZD to metformin provided more durable glucose control than adding sulfonylurea to metformin. Clinicians must remain vigilant for early treatment failure of oral hypoglycemic agents. It happens very quickly in some patients. ■

Riedel AA, et al. Am J Manag Care. 2007;13:457-463.

Bradycardia with a Cause

By Ken Grauer, MD, *Professor, Department of Community Health and Family Medicine, University of Florida.*
Dr. Grauer is the sole proprietor of KG-EKG Press, and publisher of an ECG pocket brain book.

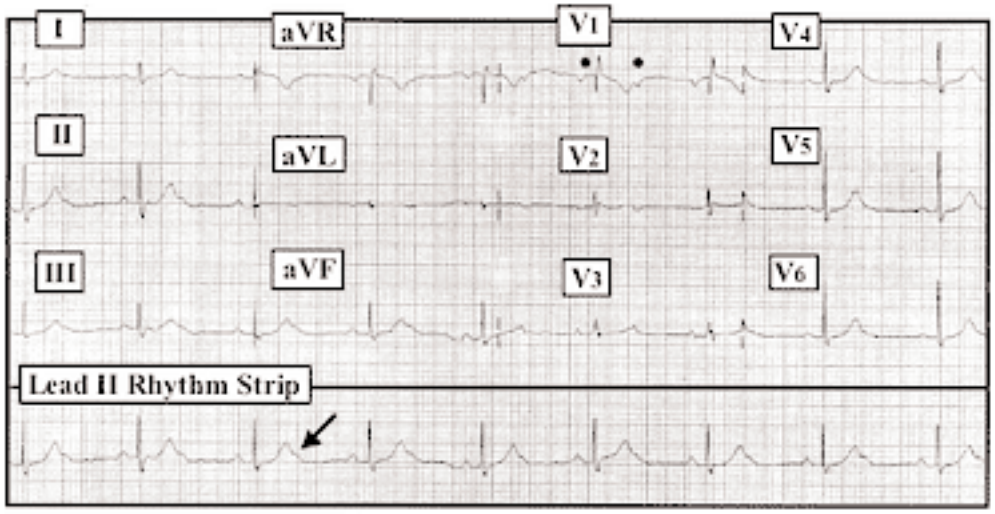

Figure: 12-lead ECG obtained from a 81-year old man with bradycardia.

Clinical Scenario:

There is a cause for the slow ventricular rate that is seen in this 12-lead ECG, obtained from an 81-year-old man. What is the cause likely to be?

Interpretation/Answer:

The rhythm appears to be sinus bradycardia at a rate of just over 50 beats/minute. Clearly, an upright sinus P wave with a fixed and normal PR interval is seen to precede each QRS complex in the Lead II rhythm strip at the bottom of the tracing. However, this is not the cause of the slowed ventricular rate. Instead, close inspection of selected leads on this 12-lead ECG suggest the presence of additional atrial activity. This is perhaps best seen in lead V1 (dots in this lead). Despite the artifactual baseline wander seen in this lead, a regularly occurring negative P wave at a rate of 100/minute is seen. That there is an underlying, regular atrial rate at 100/minute is further suggested by the presence of a subtle but real "extra shoulder" (See arrow) on the terminal portion of the T wave in each of the inferior leads, as well as a slight peak to the T wave in lead V3. Confirmation that the rhythm is 2° AV block with 2:1 AV conduction was forthcoming on subsequent tracings, when further slowing of the atrial rate resulted in clearly discernable separation of the extra P wave from the end of preceding T wave. Otherwise, there is IRBBB (incomplete right bundle branch block), and minimal non-specific ST segment flattening on the ECG, but no acute changes.

An important point to emphasize is that at times, definitive diagnosis of the rhythm is simply not possible from a single tracing. As was the case here, subsequent tracings may be needed for clarification. Our suspicion that additional P waves were "hiding" in the terminal part of the T wave could only be confirmed by additional tracings after the heart rate had slowed. ■

In Future Issues: **Randomized Controlled Trial of Esomeprazole**

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Stopping Statins in At-Risk Patients — Just Too Risky

In this issue: *Make sure your patients don't stop statins after a stroke or surgery; MRSA is becoming more resistant to mupirocin; new asthma treatment guidelines; and FDA approvals and warnings.*

Stopping statins, even briefly, after stroke or cardiovascular surgery increases vascular complications according to 3 new studies. Spanish investigators looked at 89 patients who were on chronic statin therapy and were admitted with acute stroke. Half were randomized to statin withdrawal for the first 3 days after admission, while the other half immediately received atorvastatin 20 mg/day. After 4 days, the statin withdrawal group was also started on atorvastatin. The primary outcome was death or dependence after 3 months as defined by modified Rankin scale of 2 or more. After 3 months, 60% of those in the statin withdraw group were disabled to the point of dependence compared with 39% of those that continued statin therapy (P = 0.043). Early neurologic deterioration was also far greater in the statin withdrawal group (65.2% versus 20.9%; $P < 0.0001$). Statin withdrawal patients also had greater infarct volume (P = 0.002). The authors conclude that statin withdrawal in the first few days after stroke is associated with a markedly increased risk of death or dependency at 90 days; hence, treatment should continue the acute phase of an ischemic stroke (*Neurology* 2007; 69:904-910).

In another study, researchers in Italy looked at stroke patients who discontinued statins after discharge from the hospital. The study population included 631 stroke patients (322 men, 309 women) without evidence of heart disease. All patients were discharged on a statin, but 38.9% discontinued the drug within 12 months. In the 12 months of follow-up, 116 patients died. After adjustment for all confounders and interactions, the hazard ratio for mortality in patients who quit a statin was 2.78 (95%CI, 1.96-3.72; P = 0.003) or nearly 3 times higher risk of death (*Stroke* 2007, published online ahead of print 8/30/07).

Another study from the Netherlands looked at a brief interruption in statin therapy associated with major vascular surgery. Nearly 300 patients on statins underwent major vascular surgery, and statin therapy was interrupted in the perioperative period in 70 patients for mean duration of 3 days. An association was observed between statin discontinuation and an increase risk of postoperative troponin release (HR 4.6) and the combination of MI and cardiovascular death combined (HR 7.5). Because many surgical patients are NPO and unable to take oral statins, and there's no intravenous statin available, the only extended release statin was tried on a subset of patients preoperatively. Patients receiving extended-release fluvastatin had fewer perioperative cardiac events compared to other statins (*Am J Cardiol* 2007; 100:316-320). The message of these studies is that statin interruption, even for a brief period during hospitalization, may lead to serious adverse events in patients at risk.

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Mupirocin Less Effective Against MRSA

Mupirocin (Bactroban) is becoming less and less effective against MRSA, even in hospitals with low levels of mupirocin use. Researchers from Washington University in St. Louis performed nasal swab cultures for MRSA in all patients admitted to their surgical intensive care unit (SICU) on admission, weekly during hospitalization, and at discharge. Of the 302 positive MRSA isolates, 13.2% were resistant to mupirocin, with 8.6% having high-level resistance. Patients with mupirocin-resistant MRSA were more likely to be older, have a history of a previous admission in last year, and had higher in-hospital mortality. The authors conclude that patients carrying mupirocin-resistant MRSA acquired it through contact with the health-care system; the strains were probably not acquired in the SICU (*Clin Infect Dis* 2007; 45:541-547). Mupirocin is commonly used to decolonize patients who are *staph aureus* carriers or have nasal colonization with MRSA. With resistance patterns increasing nationwide, this strategy may need to change.

New Guideline for Asthma Diagnosis/Management

The National Asthma Education and Prevention Program has issued an update to their clinical practice guidelines for diagnosis and management of asthma (Expert Panel Report 3 [EPR-3]). The new guideline emphasizes the importance of asthma control and highlights 4 areas of emphasis including assessment and monitoring, patient education, control of environmental factors and other asthma triggers, and pharmacotherapy. The new guideline recommends continued use of a stepwise approach to asthma control in which medication doses or types are stepped up or down as needed based on asthma control. Recommendations now are based on 3 age groups, 0-4 years, 5-11 years (a new category), and 12 years and older.. The new age group was added because of evidence that children respond differently to medications than adults. The entire guideline can be found at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf .

FDA Actions

The FDA announced on August 14 that manufacturers of rosiglitazone (Avandia) pioglitazone (Actos), and other combination medications containing the 2 drugs will be required to add a "black box" warning to their labeling to reflect the risk of heart failure associated with the 2 drugs. Both drugs have been associated with reports of significant weight gain and edema, and some cases continuation of therapy has lead to poor outcomes including death. The black box warning advises health-care professionals to carefully observe patients taking these drugs for signs and symptoms of heart failure including rapid weight gain, shortness of breath, edema. The warning also recommends not starting either drug in patients with a history of congestive heart failure. The agency continues to review rosiglitazone for the possible increase risk of myocardial infarction associated with use of the drug.

The FDA has approved a new indication for zoledronic acid (Reclast) as a once-a-year treatment for postmenopausal osteoporosis. Reclast is administered as an annual 15-minute intravenous infusion. The drug is a bisphosphonate similar to oral bisphosphonates such as alendronate and risedronate.

Anesiva has received approval to market lidocaine topical powder intradermal injection system (Zingo) to provide local analgesic prior to venipuncture or peripheral intravenous cannulation in children ages 3-18. Zingo is a single-use helium powered system that is administered 1-3 minutes prior to needle insertion. The system is also being studied in trials of adults.

The FDA has approved a new combination of carbidopa, levodopa, entacapone (50 mg/200 mg/200 mg) for the treatment of Parkinson's disease. The new preparation helps reduce the pill burden for Parkinson's patients on multiple medications. Carbidopa/levodopa/entacapone will be marketed by Orion Corporation as Stalevo.

Omrix Biopharmaceuticals has received approval to market human thrombin (Evithrom) to promote blood clotting and control bleeding during surgery. Evithrom is the first human thrombin approved since 1954 and the only product currently available for this indication. It is applied to the surface of bleeding tissue during surgery and may be used in conjunction with absorbable gelatin sponge. Other thrombins currently on the market are derived from cattle plasma.

Nursing mothers who were taking codeine may put their babies at risk of morphine overdose if they are "ultra-rapid metabolizers of codeine," a condition that may affect up to 28% of the population. Codeine is generally recommended for nursing mothers as a cough suppressant and pain medication; however, ultra-rapid metabolizers quickly convert codeine to morphine and excrete it in breast milk. At least one infant death has been associated with this condition. The FDA has issued warning regarding codeine use by nursing mothers, recommending that mothers observe their infants closely while taking the medication for signs of morphine overdose including sleepiness, difficulty breast feeding, breathing difficulties or limpness. ■