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INSIDE

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Diarrhea vs Death: You Decide

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

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

Dr. Phillips is a consultant for Cephalon, and serves on the speakers bureaus for Resmed and Respironics.

Synopsis: *Early antibiotic administration was associated with reduced likelihood of death, mechanical ventilation, and readmission (but increased risk of* Clostridium difficile *infection) among patients hospitalized for acute exacerbations of COPD.*

Source: Rothberg MB, et al. Antibiotic therapy and treatment failure in patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease. *JAMA* 2010;303:2035-2042.

THIS REPORT IS THE RESULT OF A RETROSPECTIVE, NONRANDOMIZED chart review of 312 hospitals over a 2-year period. The hypothesis was probably that use of antibiotics in patients who were hospitalized for chronic obstructive pulmonary disease (COPD) exacerbations would improve outcomes.

Participating hospitals were primarily small-to-medium-sized nonteaching hospitals located in urban areas. The investigators were able to collect and review extensive data for the patients included in this study, including age, sex, race, marital and insurance status, principal diagnosis, comorbidities, self-reported race, and specialty of the attending physician. In addition, they were able to determine which tests and treatments patients received. They were also able to distinguish between those elements of patient management that were guideline-recommended and those that were not. Patients were included if they were at least 40 years of age and had a principal diagnosis of an acute exacerbation of COPD or emphysema, or if they had respiratory failure coupled with a secondary diagnosis of COPD

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exacerbation. Patients were excluded if they had another indication for antibiotics, a length of stay shorter than 2 days, a secondary diagnosis of pulmonary embolism or pneumothorax, a recent hospital discharge, or an attending physician who was not an internist, family physician, hospitalist, pulmonologist, or intensivist.

Antibiotic treatment was defined as a minimum of 2 consecutive days of an antibiotic, initiated on hospital day 1 or 2, including time spent in the emergency department. Antibiotics that were "counted" included first-, second-, and third-generation cephalosporins, quinolones, macrolides, tetracyclines, trimethoprim-sulfamethoxazole, and amoxicillin with or without clavulanic acid. Patients receiving other classes of antibiotics or who received only a single day of treatment on hospital day 1 or 2 were excluded from the analysis. For the analysis, all antibiotics were considered equivalent, regardless of class, dose, duration, or route of administration. Patients whose antibiotic treatment started later than hospital day 2 were grouped with those who were not treated. The primary outcome was a composite measure of treatment failure, defined as the initiation of mechanical ventilation after hospital day 2, in-hospital mortality, or readmission for COPD within 30 days of discharge. Secondary outcomes included hospital costs and length of stay, as well as allergic reactions, diarrhea, and antibiotic-associated diarrhea, defined as treatment with either metronidazole or oral vancomycin initiated after hospital day 3 or readmission within 30 days for diarrhea and *Clostridium difficile*.

The sample used for the analysis included 84,621 patients whose median age was 69 years; 61% were women and 71% were white. Ninety percent of patients had a principal diagnosis of obstructive chronic bronchitis with acute exacerbation and 10% had respiratory failure. The most common comorbid conditions were hypertension, diabetes mellitus, and congestive heart failure. Twenty-eight percent had been admitted at least once in the preceding 12 months. In-hospital mortality was 1.2%, while 10% of patients experienced the composite measure of treatment failure (initiation of mechanical ventilation after hospital day 2, in-hospital mortality, or readmission for COPD within 30 days of discharge). Mean length of stay was 4.8 days.

Most (79%) patients received at least 2 consecutive days of antibiotic treatment beginning on day 1 or 2 of hospitalization, usually with a quinolone (60%), a cephalosporin (37%), or a macrolide (38%). Compared with patients not receiving antibiotics in the first 2 days, antibiotic-treated patients were less likely to receive mechanical ventilation after the second hospital day (1.07% vs 1.80%), had lower inpatient mortality (1.04% vs 1.59%), had a lower incidence of treatment failure (9.77% vs 11.75%), had lower costs, and subsequently had lower rates of readmission for acute exacerbations of COPD (7.91% vs 8.79%). Although antibiotic-treated patients had somewhat fewer allergic reactions (0.13% vs 0.20%), they had a higher incidence of readmissions for *C. difficile* diarrhea (0.19% vs 0.09%). After adjustment for the severity of illness, the beneficial effects of antibiotics were still evident. Buried in the fine print, however, was the revelation that the antibiotic group had higher costs than the non-antibiotic group, after adjustment.

Most hospitals had rates of antibiotic prescribing between 65% and 95%. When individual patients were assigned a probability of initial treatment with antibiotics equal to the hospital rate where they received care, each 10% increase in the hospital rate of treatment (e.g., from 70% to 80%) was associated with a 5% reduction in the odds of treatment failure, and this relationship was strengthened by removing patients with asthma plus COPD with acute exacerbation from the calculation.

There were some differences between those patients whose physicians ordered early antibiotics and those who did not in this nonrandomized trial. Compared with patients who did not receive initial treatment with an antibiotic, treated patients were younger and had fewer comorbidities and prior recent admissions. They were more likely to have private insurance and to be white. They were also more likely to be from hospitals that were smaller, southern, rural, and nonteaching.

In general, those patients who received early antibiotics were more likely to be treated according to published guidelines, including receiving steroids and bronchodi-

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Questions & Comments
Please call **Paula Cousins**, Senior Managing Editor, at (404) 262-5488.

lators. They were also, however, more likely to receive some treatments not recommended by guidelines, such as methylxanthine and mucolytic agents and chest physiotherapy. They were less likely to receive loop diuretics, morphine, and non-invasive positive pressure ventilation. The authors determined several factors that increased the propensity for antibiotic use early on; after adjustment for the "propensity score" of antibiotic prescription, those who were prescribed antibiotics early on were still more likely to be white, rural, insured by Medicare, and to have heart failure, diabetes, or renal failure. They also were more likely to receive methylxanthines, bronchodilators, steroids, morphine, and diuretics. They also underwent more diagnostic testing, but the differences were small.

■ **COMMENTARY**

Although its prevalence has begun to fall as tobacco consumption falls, COPD remains prevalent, and is the fourth leading cause of death in the United States.[1] COPD exacerbations drive much of the cost of care for COPD patients, and are responsible for more than 600,000 hospitalizations annually, resulting in direct costs of more than $20 billion.[2] Respiratory infections are probably the commonest cause of COPD exacerbation,[3] and several COPD treatment guidelines recommend antibiotic treatment for patients with purulent sputum and either an increase in sputum production or an increase in dyspnea.[2,4,5] As is true for many expert guidelines, these recommendations are largely based on older (albeit randomized) trials. The current report, while retrospective and unrandomized, comes from a large national sample of hospitals, and assessed outcomes in addition to mortality and respiratory failure. In this sample, fewer than 80% of patients received antibiotics in the first 2 days of hospitalization, perhaps because current guidelines recommend antibiotics only for patients with purulent or increased sputum production. What is new here is that the results of this analysis do not support restriction of antibiotics to COPD patients (experiencing exacerbation) with purulent sputum, increased sputum production, or dyspnea. The authors conclude that since "… all patient groups seemed to benefit from therapy and that harms were minimal, … all patients hospitalized with acute exacerbations of COPD should be prescribed antibiotics." Compared to lots of other things we do for patients who have a very high probability of winding up in the ICU, this does not seem to be such a far-fetched conclusion. ■

References

1. National, Heart, Lung, and Blood Institute. Take the first step to breathing better. Learn more about COPD. Available at: www.nhlbi.nih.gov/health/public/lung/copd. Accessed June 7, 2010.
2. Snow V, et al; Joint Expert Panel on Chronic Obstructive Pulmonary Disease of the American College of Chest Physicians and the American College of Physicians-American Society of Internal Medicine. Evidence base for management of acute exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 2001;134:595-599.
3. Rosell A, et al. Microbiologic determinants of exacerbation in chronic obstructive pulmonary disease. *Arch Intern Med* 2005;165:891-897.
4. Celli BR, MacNee W; ATS/ERS Task Force. Standards for the diagnosis and treatment of patients with COPD: A summary of the ATS/ERS Task Force. *Eur Respir J* 2004;23:932-946.
5. Rabe KF, et al; Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176:532-555.

To Drive or Not to Drive? That Is the Question

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD, MA

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

Synopsis: *Patients with dementia and their physicians face the difficult decision to cease driving with little solid evidence to guide them.*

Source: Iverson DJ, et al. Practice parameter update: Evaluation and management of driving risk in dementia: Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010;74:1316-1324.

The American Academy of Neurology has issued a new practice parameter that updates the literature on the risk of demented patients driving. The authors reviewed articles from 1970 through 2006. They identified 6000 studies and selected 422 for full review. An additional 80 references were added after secondary bibliography search. Successfully completing an on-road driving test (ORDT) was chosen as the gold standard for safe driving. The parameter addressed 5 questions:

1. How strongly are global measures of dementia severity associated with decreased driving ability? The Clinical Dementia Rating (CDR) can identify patients at increased risk for unsafe driving.[1] However, many patients identified by CDR will pass ORDT. The Folstein Mini-Mental State Examination (MMSE) was not designed to identify unsafe drivers and performs poorly when used to do so. A score ≤ 24 may identify an individual at risk.

2. To what extent are patients and their caregivers able to assess driving ability and risk? Not very. Patients with Alzheimer's dementia who identify themselves as "safe drivers" more often than not fail ORDT. A caregiver's opinion may be helpful if it is negative.

3. Which elements of the driving history are associated with decreased driving ability? A history of a crash in the last 5 years, a traffic citation in the last 2-3 years, self-imposed reduced driving mileage, self-reported avoidance of unsafe conditions (nighttime driving, driving in the rain, etc.), and aggressive or impulsive personality traits are possibly useful in identifying patients with decreased driving ability.

4. What neuropsychological tests provide additional prognostic information? No comprehensive neuropsychological assessment has yet been devised to reliably evaluate driving risk in patients with dementia; they can help determine the severity of the dementia.

5. Are there interventions that reduce driving risk? No beneficial interventions have been demonstrated for patients with dementia. This includes licensing restrictions and driver's training.

The authors offer an algorithm that incorporates the CDR and historical risk factors such as those listed above to estimate the driving risk and recommend that physicians reevaluate patients who continue to drive every 6 months. They conclude with the recommendation for more research into this subject.

■ COMMENTARY

Let's put this into perspective. If you were 24 when Ronny and the Daytonas recorded "GTO" in 1964, immortalizing the Pontiac model of the same name, you would be staring 70 in its face and maybe, just maybe, be wondering whether your memory and your reaction times are what they once were. The baby-boom generation embraced the automobile and the freedom and mobility it provided. We are not going to let go easily. Because this population is aging and because physicians are expected to advise their patients and their caregivers on this topic, there has been a flurry of articles about the at-risk driver in the literature lately. The *Journal of the American Medical Association* recently published a similar article in its "Care of the Aging Patient" section.[2] It covers much the same ground and evidence, but also includes a vignette that has a patient, his spouse, and his physician reflecting on the difficulty of terminating a patient's driving privileges. It also includes some resources that primary care physicians may find useful: the website for the Association for Driver Rehabilitation Specialists,[3] a patient handout on driving and dementia from the American Academy of Family Physicians,[4] and a guide on state licensing requirements and reporting laws from the American Medical Association.[5]

To whom is the physician responsible in this situation? The patient or the public? As Eby and Molnar point out in their editorial, there is a wide expanse of gray landscape between premature cessation of driving privileges that isolates the patient and places additional responsibilities on the caregiver and continued driving that places the patient and others in harm's way.[6] Additionally, there are inconsistent legal requirements for physicians to report unsafe drivers. They note that 22 states encourage reporting and 12 require it. However, only 25 states provide immunity to physicians from civil lawsuits that result from reporting and only 19 protect the identity of reporting physicians.

The determinants of unsafe driving are more than just dementia. Poor eyesight, poor hearing, distractibility, and arthritis all play a role. Sometimes, physicians add to the problem by prescribing medications that exacerbate cognitive decline. A new tool that considers crash history, family concerns, clinical condition, and cognitive functions may be a useful marker to identify at-risk elderly drivers,[7] but as a Cochrane review states, "Driving legislation and recommendations from medical practitioners require further research that addresses these outcomes in order to provide the best outcomes for both drivers with dementia and the general public."[8] ■

Reference

1. Regional Geriatric Program of Toronto. Available at: http://rgp.toronto.on.ca/. Accessed June 5, 2010.
2. Carr DB, Ott BR. The older adult driver with cognitive impairment: "It's a very frustrating life." *JAMA* 2010;303:1632-1641.
3. Association of Driver Rehabilitation Specialists. Driving and Alzheimer's/Dementia. Available at: www.driver-ed.org/i4a/pages/index.cfm?pageid=104. Accessed June 5, 2010.
4. American Academy of Family Physicians. Driving and dementia: What you should know. Available at: www.aafp.org/afp/2006/0315/p1035.html. Accessed June 5, 2010.
5. American Medical Association. State licensing and reporting requirements. Available at: www.ama-assn.org/ama1/pub/upload/mm/433/chapter8.pdf. Accessed June 5, 2010.

6. Eby DW, Molnar LJ. Driving fitness and cognitive impairment: Issues for physicians. *JAMA* 2010;303:1642-1643.
7. O'Connor MG, et al. The 4Cs (crash history, family concerns, clinical condition, and cognitive functions): A screening tool for the evaluation of the at-risk driver. *J Am Geriatr Soc* 2010 May 7; Epub ahead of print.
8. Martin AJ, et al. Driving assessment for maintaining mobility and safety in drivers with dementia. *Cochrane Database Syst Rev* 2009;(1):CD006222.

Does the Estimated GFR Cause Us to Cry Wolf with Chronic Kidney Disease?

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Synopsis: *An analysis of more than 1 million persons in Alberta, Canada, showed that laboratory reporting of estimated glomerular filtration rate (GFR) beginning in 2004 resulted in more referrals to nephrologists, but no apparent improvement in outcomes.*

Source: Hemmelgarn BR, et al. Nephrology visits and health care resource use before and after reporting estimated glomerular filtration rate. *JAMA* 2010;303:1151-1158.

The estimated glomerular filtration rate (eGFR) came into widespread use in 2004 and is based on the serum creatinine (Cr) with minor adjustments using the patient's age, race, and gender. The eGFR is often reported along with the serum Cr in chemistry panel results.

A study group from the University of Calgary, Alberta, Canada, and the Alberta Kidney Disease Network looked at a community-based cohort of 1,135,968 persons before and after the reporting of eGFR starting in October 2004. The rate of first nephrologist visits went up substantially after the onset of eGFR reporting. Among patients with an eGFR < 30 mL/min/1.73 m^2, there was a 95% increase in referrals. There was no evidence of an increase in the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) for chronic kidney disease (CKD). The authors conclude that eGFR reporting increases the rate of first visit to a nephrologist without any apparent improvement in outcomes.

■ COMMENTARY

There is a shortage of nephrologists in the United States and globally.[1] An estimated 31 million Americans (16% of the population) have a form of CKD and 506,000 Americans are being treated for ESRD.[2] Should the estimated 8300 nephrologists in the United States see every patient with CKD? What is the role of primary care?

According to the National Kidney Foundation, a normal GFR is between 90 and 130 mL/min (stage 1). Kidney damage with mild decrease in kidney function (stage 2) is between 60 and 90 mL/min. Moderate decrease in kidney function (stage 3) is between 30 and 60 mL/min. Severe decrease in kidney function (stage 4) is between 15 and 30 mL/min with kidney failure (stage 5) being a GFR < 15 mL/min.[3]

Before the addition of the eGFR, primary care physicians had been used to evaluating kidney function based on the serum BUN and Cr. Serum levels of Cr < 1.5 mg/dL have generally been considered normal or benign. The National Library of Medicine lists a normal Cr as 0.8-1.4 mg/dL.[4] Yet, the eGFR for me, a 59-year-old non-African-American male, with a Cr of 1.4 would be 52 mL/min, or Stage 3 CKD! If I were age 79, my eGFR with a serum Cr of 1.4 mg/dL would be 48 mL/min. A 79-year-old male (not African-American) with a Cr of 1.2 mg/dL has an eGFR of 58 mL/min, still stage 3. The eGFR causes us to call patients previously thought of as normal as having moderate CKD.

It is understandable that most primary care physicians would refer to a nephrologist any patient with stage 3 CKD. Most of these referrals would not have been triggered by a serum Cr < 1.5 mg/dL. The eGFR has changed that and puts the number < 60 mL/min in front of us with many patients. More compulsive or conscientious physicians (based on your point of view) might refer anyone with stage 2 disease or an eGFR < 90 mL/min. This would be most people with a serum Cr ≥ 1.2 mg/dL. What would the nephrologist do with these patients? One would hope that without too many other tests, they would be counseled on the control of their hypertension and diabetes, and would be followed. Primary care physicians can do that.

There is a convenient online calculator of eGFR available from the National Kidney Foundation.[5] Using the eGFR calculator, a level of 30 mL/min (severe disease) begins to occur at a serum Cr > 2 mg/dL. The limited number of nephrologists in the United States should be focusing on the care of these patients. Prevention of severe CKD and failure is the work of primary care physicians, and we should become more knowledgeable in managing patients with mild-to-moderate disease. We do this with hypertension, diabetes, and asthma. The prevention and management of CKD should become more common in our continuing education and clinical work, and the use of eGFR underscores this need. Assuming the eGFR is an accurate reflection of GFR, it may be time to rethink the classification of CKD and to put out more recognized guidelines for the management of these patients in primary care. ■

References

1. Field M. Addressing the global shortage of nephrologists. *Nat Clin Pract Neprol* 2008;4:583.
2. Bizzozero J. Understanding the nephrologist shortage: Is there a nephrologist in the house? *Renal Business Today*. Sept. 30, 2009. Available at: www.renalbusiness.com/articles/understanding-nephrologist-shortage.html. Accessed June 4, 2010.
3. National Kidney Foundation. Glomerular Filtration Rate (GFR). New York; 2010. Available at: www.kidney.org/kidneydisease/ckd/knowgfr.cfm. Accessed May 30, 2010.
4. Medline Plus. Creatinine — blood. National Library of Medicine, National Institutes of Health; 2009. Available at: www.nlm.nih.gov/medlineplus/ency/article/003475.htm. Accessed May 30, 2010.
5. National Kidney Foundation. Calculators for Health Care Professionals. Available at: www.kidney.org/professionals/KDOQI/gfr_calculator.cfm. New York; 2009. Accessed May 30, 2010.

Pharmacology Update

Naproxen and Esomeprazole Delayed-Release Tablets (Vimovo®)

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 relationship to this field of study.

A COMBINATION OF A NONSTEROIDAL ANTI-INFLAMMATORY agent and a proton pump inhibitor has been approved by the FDA. Naproxen and esomeprazole (NAP/ESO) is marketed as a delayed-release tablet as Vimovo™ by AstraZeneca.

Indications

NAP/ESO is indicated for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis, and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers.[1]

Dosage

The recommended dose is one tablet twice daily. The dose should be based on the lowest effective dose. NSAIDs are not recommended for patients with moderate or severe renal dysfunction or severe hepatic dysfunction.

NAP/ESO is available as 375 mg/20 mg and 500 mg/20 mg delayed-release tablets.

Potential Advantages

NAP/ESO reduced the cumulative incidence of gastric ulcers compared to enteric-coated naproxen alone.[1]

Potential Disadvantages

NAP/ESO is more expensive than taking generic naproxen and omeprazole separately. Esomeprazole is the active isomer of omeprazole and is currently not available in the generic form.

Comments

The effectiveness of NAP/ESO in preventing gastric ulcers was based on two randomized, double-blind trials.[1] Adult patients with a documented history of gastric or duodenal ulcers that required daily NSAIDs were randomized to NAP/ESO 500 mg/20 mg twice daily (n = 428) or enteric-coated naproxen 500 mg twice daily (n = 426). The cumulative incidences of gastric ulcers at 6 months were 4.1% compared to 24.3%, respectively. A higher percent of subjects discontinued naproxen than NAP/ESO (12% vs 4%). The efficacy of NAP/ESO was shown in two 12-week randomized, placebo-controlled trials in subjects with osteoarthritis.[1]

Clinical Implications

Gastrointestinal complications associated with NSAID have been well documented. The risk is enhanced in patients who have a history of previous GI events, are age > 65 years, take high doses of NSAID, and those who concurrently use aspirin, anticoagulants, or corticosteroids.[2,3] *Helicobacter pylori* infection increases the risk of peptic ulceration; therefore, testing and eradication should be considered. The Practice Parameter Committee of the American College of Gastroenterology recommends NSAID plus misoprostol or a PPI in patient with moderate GI risk and low cardiovascular risk.[2] Naproxen + misoprostol or a PPI is recommended for patients with low or moderate GI risk but high CV risk (low-dose aspirin is required). In patients with high GI and CV risk, NSAIDs should be avoided. In those with high GI risk but low CV risk, a COX-2 inhibitor with a PPI or misoprostol is recommended. NAP/ESO provides a NSAID/PPI combination in a single tablet. However, the use of generic versions of naproxen and omeprazole is less expensive. The cost of a 30-day supply of Vimovo is $106.06 com-

pared to $88.44 for generic versions of naproxen 500 mg and omeprazole 40 mg taken separately.[4] ■

References

1. Vimovo Prescribing Information. Wilmington, DE: AstraZeneca; April 2010.
2. Lanza FL, et al. Guidelines for prevention of NSAID-related ulcer complications. *Am J Gastroenterol* 2009;104:728-738.
3. Lazzaroni M, Porro GB. Management of NSAID-induced gastrointestinal toxicity: Focus on proton pump inhibitors. *Drugs* 2009;69:51-69.
4. Latimer N, et al. Cost effectiveness of COX 2 selective inhibitors and traditional NSAIDs alone or in combination with a proton pump inhibitor for people with osteoarthritis. *BMJ* 2009;339:b2538; doi:10.1136/bmj.b2538.
5. RxUSA. Available at: http://rxusa.com/html. Accessed May 26, 2010.

CME Questions

28. Early antibiotic treatment in patients admitted with a COPD exacerbation is associated with:
a. no effect on treatment failure.
b. reduced treatment failure.
c. increased treatment failure.
d. reduced costs.

29. Choose the one *incorrect* statement regarding driving risk and dementia.
a. The Mini-Mental State Examination is a poor tool for identifying at-risk drivers.
b. If a patient declares that he is a safe driver, his physician should believe him.
c. Aggressive or impulsive personality traits are possibly useful in identifying patients with decreased driving ability.
d. No comprehensive neuropsychological assessment has yet been devised to evaluate driving risk in patients with dementia.
e. There are no interventions that reduce driving risk for patients with dementia.

30. A 59-year-old white male has a serum creatinine of 1.4 mg/dL. His estimated glomerular infiltration rate (eGFR) will indicate that his kidney function is:
a. normal (stage 1).
b. mild decrease in kidney function (stage 2).
c. moderate decrease in kidney function (stage 3).
d. severe decrease in kidney function (stage 4).

Answers: 28. b, 29. b, 30. c.

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.

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

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For type 2 diabetes, after metformin, what next?

Source: Phung OJ, et al. Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. *JAMA* 2010;303:1410-1418.

In the absence of contraindications, metformin is the preferred initial treatment for most patients with type 2 diabetes (DM2). Unfortunately, monotherapy is unlikely to maintain adequate glycemic control, requiring additional treatment. Although the addition of insulin to metformin is an appropriate next step, and has been labeled Tier 1 in the most recent guidelines published by the American Diabetes Association, some patients are reluctant to use insulin, and the considerable weight gain experienced by some insulin users, as well as risk of hypoglycemia, is problematic.

Among the non-insulin therapeutic choices, there is a great degree of variation in tolerability issues, such as amount of weight gain and frequency/severity of hypoglycemia that may help guide treatment decisions. Phung et al analyzed data from 27 randomized controlled trials (n = 11,198), most of which were 6 months or less in duration, to compare weight changes and hypoglycemia when non-insulin agents were added to metformin.

As might be anticipated, when TZDs, sulfonylureas, and glinides were added to metformin there was a 1.8-2.1 kg weight gain. GLP-1 mimetics, alpha-glucosidase inhibitors, and DPP-4 inhibitors were either weight-neutral or associated with minimal weight loss. Sulfonylureas were associated with higher rates of hypoglycemia.

Of course, progressive treatment of DM2 must be individualized, and should include consideration of characteristic tolerability issues such as weight gain and hypoglycemia. ■

Suicide risk with anticonvulsants

Source: Patorno E, et al. Anticonvulsant medications and the risk of suicide, attempted suicide, or violent death. *JAMA* 2010;303:1401-1409.

Although the term "anticonvulsant" is indicative of a therapeutic class, pharmacologically the class is diverse. Despite dissimilarities, an analysis by the FDA (2008) discerned a relative doubling of suicide behavior/ideation in those receiving anticonvulsants compared to placebo, resulting in a change in labeling.

The HealthCore Integrated Research Database provides data with which to assess the relative risk for suicidal acts in persons receiving a variety of anticonvulsant agents. During a 5-year interval (2001-2006), almost 300,000 new prescriptions for various anticonvulsants were documented in this population. When compared to treatment with either topiramate or carbamazepine (reference drugs), important distinctions emerged in reference to suicidal acts and violence. For instance, the hazard ratio for suicidal acts was 1.42 for gabapentin, 1.84 for lamotrigine, and 1.65 for valproate, compared to topiramate.

The mechanism by which some anticonvulsants incur an increased suicide risk is not known, despite the recognition that anticonvulsants can have impact upon mood. The first 2 weeks after initiation is recognized to be a higher risk period. Clinicians should be vigilant for behavior or mood changes in patients treated with anticonvulsants, and note the lesser apparent risk for topiramate or carbamazepine. ■

Best use of home BP monitoring

Source: Pickering TG, et al. When and how to use self (home) and ambulatory blood pressure monitoring. *J Am Soc HTN* 2010;4:56-61.

The largest body of information guiding treatment of hypertension (HTN) is based upon office BP management. Nonetheless, home BP monitoring (HBPM) is documented to be a better predictor of CV risk than office BP. For instance, patients with high office BP but low HBPM are recognized to be at substantially lower risk than office BP predicts; similarly, high HBPM pressures compared to office BP portends greater risk than indicated by office BP alone. Simply the fact that HBPM offers the opportunity for many more BP readings than is readily accessible in clinical care provides both a more comprehensive and consistent BP profile.

Recording HBPM twice daily (morning and evening), when averaged over 1 week, provides a sufficient BP profile to help guide management. By HBPM, HTN is > 135/85 mmHg and normotension is < 125/75 mmHg. Borderline HBPM (125-135/75-85 mmHg) merits consideration of 24-hour ambulatory BP monitoring for further clarification. The authors, writing on behalf of the American Society of Hypertension, provide a list of validated home BP monitoring devices at: www.dable-educational.org/. ■

In Future Issues:

Some Antibiotics May Increase the Risk of Upper GI Bleed in Anticoagulated Older Patients

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