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Internal Medicine

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Vol. 42, Issue 4, February 29, 2020
ReliasMedia.com

ABSTRACT & COMMENTARY

Longer Antibiotic Courses for Pneumonia Do Not Improve Outcomes, Do Cause More Adverse Effects

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

SYNOPSIS: Excess antibiotic therapy did not improve mortality or morbidity outcomes, although each additional antibiotic day was associated with 3% increased odds of antibiotic-associated adverse drug events.

SOURCE: Vaughn VM, et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia: A multihospital cohort study. *Ann Intern Med* 2019;171:153-163.

In acutely ill patients with community-acquired pneumonia (CAP), multiple randomized, controlled trials have shown similar or improved patient outcomes with three- to five-day antibiotic courses compared to seven- to 14-day courses.[1] Although data are less prevalent for the duration of treatment for healthcare-associated pneumonia (HCAP), the last guidelines published in 2004 suggested a shorter duration of antibiotic therapy (seven to eight days).[2] However, a lack of explicit recommendations for using the shortest course of antibiotics possible for CAP and HCAP may affect antibiotic prescribing practices in the general medicine population. Vaughn et al performed a multicenter cohort study to examine the predictors of and outcomes associated with excess duration of antibiotics in CAP and HCAP across 43 hospitals in Michigan.[3]

Adult patients admitted to a general medicine service in one of 43 participating hospitals were included if they were admitted for CAP or HCAP treatment and were discharged from the hospital between January 2017 and April 2018. Those who were admitted to an ICU or were severely immunocompromised were not included. Approximately 60% of patients had severe pneumonia (pneumonia severity index class IV or V), with 55% having uncomplicated CAP, 19% having complicated CAP, and 27% having HCAP. Overall,

Financial Disclosure: *Internal Medicine Alert's* Physician Editor Stephen Brunton, MD, is a retained consultant for Abbott Diabetes, Acadia, AstraZeneca, and Boehringer Ingelheim; and he serves on the speakers bureau of AstraZeneca, Boehringer Ingelheim, Janssen, Lilly, and Novo Nordisk. Peer Reviewer Gerald Roberts, MD; Editor Jonathan Springston; Editor Jason Schneider; Editorial Group Manager Leslie Coplin; and Accreditations Manager Amy M. Johnson, MSN, RN, CPN, report no financial relationships relevant to this field of study.

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Internal Medicine Alert (ISSN 0195-315X) is published semimonthly by Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468. Periodicals postage paid at Morrisville, NC, and additional mailing offices. POSTMASTER: Send address changes to *Internal Medicine Alert*, Relias LLC, 1010 Sync St., Ste. 100, Morrisville, NC 27560-5468.

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67.8% of patients received excess antibiotics based on guideline recommendations. The median durations for both CAP and HCAP were eight days, with median excess durations of two days for CAP and one day for HCAP. In total, this resulted in 2,526 excess antibiotic days per 1,000 patients hospitalized with CAP or HCAP. The vast majority of these excess days (93.2%) occurred after hospital discharge, with an additional five days of treatment after discharge most common despite patients frequently needing zero or one additional day of therapy based on guideline recommendations. Patients from all hospitals were affected, with a range of patient discharges affected between 38.1% and 95.0%, depending on the hospital.

Variables associated with excess antibiotic treatment duration on multivariable regression analysis included positive respiratory culture result (predicted excess days per patient 3.2, adjusted rate ratio [aRR], 1.49; 95% confidence interval [CI], 1.33-1.68), each day of hospital stay (excess days, 0.2; aRR, 1.02; 95% CI, 1.02-1.02), receipt of high-risk antibiotics in the 90 days prior to admission (excess days, 2.9; aRR, 1.17; 95% CI, 1.10-1.25), and CAP diagnosis (excess days, 3.2; aRR, 1.43; 95% CI, 1.32-1.55). Documentation of total antibiotic treatment duration in the hospital discharge summary was predictive for excess antibiotic duration (aRR, 0.78; 95% CI, 0.70-0.87). Most outcomes were similar at 30 days between the appropriate duration and excess duration groups, including mortality (1.9% vs. 2.0%; adjusted odds ratio [aOR] per excess day, 1.01; 95% CI, 0.97-1.05), readmission (14.1% vs. 11.3%; aOR, 1.00; 95% CI, 0.98-1.03), and ED visit (11.4% vs. 10.9%; aOR, 0.98; 95% CI, 0.95-1.01). However, antibiotic-associated adverse drug events (ADEs) occurred more frequently in the excess duration group (3.4% vs. 4.8%; aOR, 1.03; 95% CI, 1.00-1.06).

■ COMMENTARY

Two-thirds of general medicine patients with pneumonia received excess antibiotic therapy, with 93.2% of the unnecessary duration occurring after hospital discharge. Although the reasons for these practices were not recorded, the authors hypothesized the most likely culprits affecting these durations were implied rather than explicitly stated recommendations for antibiotic durations in pneumonia guidelines, the wait for finalized culture results to be available, and a lack of national policy efforts focused on treatment durations. Since patient outcomes did not improve because of excess antibiotic durations, providers may be more comfortable aligning their treatment durations with more contemporary data for shorter courses. In fact, it may be possible to use one- to five-day antibiotic courses for CAP in many cases, which may allow for further reductions in antibiotic use.[4] Furthermore, each additional antibiotic day was associated with a 3% increased odds of an antibiotic-associated ADE. The most common ADE was diarrhea; however, the short study duration precluded the authors from evaluating the effect of antibiotic days on resistance development. In a recent study of more than 7,000 critically ill adults, researchers observed that each additional day of broad-spectrum beta-lactam therapy beyond day 3 was associated with a 4% increased risk of new resistance development.[5] Consequently, the long-term implications of excessive antibiotic durations in CAP and HCAP are uncertain and likely are worse than those reported in this study. A particular emphasis may be placed on leveraging the electronic health record to guide providers to an appropriate treatment duration based on days of therapy already received in the hospital and the treatment indication. This may help allay concerns about treatment duration while streamlining the discharge process. ■

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ABSTRACT & COMMENTARY

Fever of Unknown Origin Due to Cat Scratch Disease

By Stan Deresinski, MD, FACP, FIDSA, FESCMID

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

SYNOPSIS: Disseminated cat scratch disease may present as a fever of unknown origin.

SOURCE: Landes M, et al. Cat scratch disease presenting as fever of unknown origin is a unique clinical syndrome. *Clin Infect Dis* 2019; Nov 23. pii: ciz1137.

Landes et al analyzed data obtained from a national surveillance of cat scratch disease (CSD) in Israel from 2004-2017 to characterize cases presenting with fever lasting > 14 days without a cause identified. Of the approximately 2,800 patients with CSD, 126 reported a fever of unknown origin, but only 66 patients, 89% of whom were immunocompetent, were included in this study after various exclusions. The patients ranged in age from 3 to 88 years (median, 35.5 years); 83% reported contact with felines. The median duration of fever was four weeks. In 48%, the fever occurred daily, while in 52% it had a relapsing pattern. Loss of > 5% of body weight occurred in 37.5% of the patients.

The diagnosis was confirmed by serology in 65/66 patients, and *Bartonella henselae* DNA was detected in seven patients' tissue. Investigators found involvement of one or more organ systems in 39 patients: 23 with hepatic and/or splenic lesions, 12 with ocular disease, four with multifocal osteomyelitis, and three with pneumonitis. One patient each had pericarditis, pleuritis, meningitis, and sensorineural hearing loss.

Antibiotics with possible activity against *B. henselae*, mostly azithromycin and doxycycline, were administered to 46 patients for two days to 3.5 months. The mean duration of fever was four weeks regardless of whether antibiotics were taken. Nonetheless, symptoms eventually resolved in 56 of 59 patients with follow-up; the other three had ocular involvement with visual residua.

■ COMMENTARY

In classic CSD, characterized by regional lymphadenitis that is self-limited, fever may occur in up to 30% of patients, but it lasts a mean of only six days. The patients in the series described here lacked classic findings of CSD and had fever that lasted at least 14 days.

This syndrome has been described before, but it has been characterized more often as disseminated or simply named by the focal sites of infection identified, such as osteomyelitis. Such focal sites were identified in 59% of patients reported. One site of infection not included in this case series is heart valves; the diagnosis of *Bartonella* endocarditis often is quite difficult.

A finding of note in this series is the fact that the prolonged fever exhibited a relapsing pattern in approximately one-half of patients. The authors noted relapsing fever was characteristic of "trench fever," which is caused by *Bartonella quintana*, a louse-borne infection seen in modern times in people who are homeless in the United States and Europe. Of course, relapsing fever also may be caused by *Borrelia* (e.g., *Borrelia hermsii* in the western United States, *Borrelia persica* in Israel) or lymphoma, among other things.[1] ■

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ABSTRACT & COMMENTARY

The Risk of Endocarditis With Bacteremia

By Michael H. Crawford, MD

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

SYNOPSIS: Interrogation of the Danish National Patient Registry revealed bacteremia due to *Enterococcus faecalis* was most likely to be associated with infective endocarditis; thus, echocardiography is warranted in these patients.

SOURCE: Østergaard L, et al. Prevalence of infective endocarditis in patients with positive blood cultures: A Danish nationwide study. *Eur Heart J* 2019;40:3237-3244.

To decide which patients with bacteremia need an echocardiogram, knowledge of the risk of infective endocarditis (IE) with various blood stream infections is needed. Danish researchers interrogated the Danish National Patient Registry for patients with bacteremia typically associated with IE (*Enterococcus faecalis*, *Staphylococcus aureus*, *Streptococcus* spp., and coagulase-negative staphylococci [CoNS]) from 2010 to 2017.

The study outcome was a diagnosis of IE and a hospitalization of at least 14 days (unless the patients died earlier). The 69,021 patients identified were collected into four groups of two contiguous years. The highest prevalence of IE was in patients with *E. faecalis* (17%), followed by *S. aureus* (10%), *Streptococcus* spp. (7%), and CoNS (2%). The prevalence of IE in *E. faecalis* patients significantly increased over time (12% in 2011 vs. 19% in 2015; $P = 0.0005$) and in those with *Streptococcus* spp. (6% in 2010 vs. 8% in 2017; $P = 0.03$). Overall, the rates of IE were higher in men with *E. faecalis*, *Streptococcus* spp., and CoNS ($P < 0.0001$), but not for *S. aureus*. Also, all but *S. aureus* showed a higher prevalence of IE with advancing age ($P < 0.0001$). The authors concluded that the overall prevalence of IE was one in six for *E. faecalis* bacteremia, one in 10 for *S. aureus*, and one in 14 for *Streptococcus* spp. These results suggest echocardiographic screening for bacteremia caused by these three organisms is clinically warranted.

■ COMMENTARY

Considering the high in-hospital mortality of IE (about 20%), early identification of patients at high risk for IE is desirable. The four bacteria species investigated in this study account for 75-85% of cases of IE in reported series. Thus, assessing the prevalence of IE in patients with bacteremia from these organisms makes sense. Interestingly, all four are gram-positive bacteria, which are known to be superior at adhering to the endothelium.

The most surprising result of the study was the higher IE rate for *E. faecalis* than *S. aureus* (17% vs. 10%). However, the study also showed an increase in *E. faecalis* IE with age, which could be attributed to colon cancer and other diseases increasing the prevalence of *E. faecalis* bacteremia. The higher overall prevalence of *E. faecalis* IE probably is due in part to the aging of the population. At age 70-80 years, the *E. faecalis* IE rate was 20% vs. 12% for *S. aureus*. At age 40-50 years, the authors observed a rate of 13% for both. *E. faecalis* IE also is much more prevalent in men for reasons that are poorly understood, but may be due more to underlying epidemiologic characteristics than biologic ones.

Current major organizational guidelines recommend consideration of echocardiography, especially transesophageal echocardiography (TEE) for *S. aureus* bacteremia (class IIa). The results of this study suggest this recommendation should be extended to *E. faecalis*. However, the systematic application of echocardiography, especially TEE, for a disease with a ≤ 20% prevalence in the at-risk population may not be feasible or cost-effective. In most series, the use of echo is about 50-65%. Many have suggested using a risk score such as NOVA, PREDICT, VIRSTA, or AANDOC to cull the highest-risk bacteremia patients for echoes. The Duke score is not recommended because studies have shown that it is largely driven by the echo results. These scores are highly sensitive and carry a negative predictive value of > 95% (but specificity is lower). This may be acceptable for such a high mortality disease.

There were several limitations to the Østergaard et al study. First, as it was an administrative database study, there was limited clinical information, such as echo results. Second, the authors used ICD-10 codes to diagnose IE. Prior validation studies revealed this approach carried a positive predictive value of 90%. Third, the increase in the prevalence of IE over time may have been because of an increased use of echo and nuclear imaging. Fourth, echoes were not performed systemically; the estimates of IE rates may be conservative. Finally, the differences in the incidence rates for various organisms may vary geographically; these results may not reflect all areas in the world. I believe the main message of this paper is the increased prevalence of *E. faecalis* IE and the corresponding need to consider echoes earlier in the course of *E. faecalis* bacteremia. ■

SPECIAL FEATURE

CNS Agents Emerge as Frontrunners in FDA-Approved Treatments for Low Libido in Women

By Nicole Cirino, MD, CST, IF

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

Low libido is the most common sexual complaint, affecting up to 38.7% of women, with up to 12.3% also reporting significant distress associated with this condition.[1] Debate continues about how female desire disorders are characterized, diagnosed, and treated. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) categorized this common female condition in women as hypoactive sexual desire disorder (HSDD). HSDD is characterized by deficient or absent sexual fantasies and desire for sexual activity lasting at least six months. Women must report significant distress and no other identifiable cause for HSDD, such as substance abuse or general medical conditions (that may affect sexual function).[2]

HSDD occurs in 8-19% of women and is associated with lower health-related quality of life, psychosocial distress, depression, anxiety, and higher total healthcare expenditures.[3] In the updated DSM-5, HSDD has been removed and replaced with an amalgamation of female sexual arousal disorder diagnoses termed female sexual interest/arousal disorder (FSIAD).[3] However, even though HSDD has been removed from the updated DSM-5, FSIAD has failed to gain traction among the sexual medical community. HSDD remains the diagnosis used for studying new treatment modalities and developing algorithms of care. In the past five years, for the first time in history, we now have two FDA-approved medications specifically for treating HSDD in women. Thus far, FDA approval is for a specific population of HSDD: women who are premenopausal and have a generalized (vs. situational), acquired (vs. lifelong) form of the condition. Of note, both medications are central nervous system (CNS) agents. According to the FDA, both have pre- and postmenopausal designations, as is typical for sex steroids but atypical for CNS agents. The FDA Bone, Reproductive, and Urologic Drugs Advisory Committee (formerly Reproductive Health Drugs Advisory Committee), not a neuroscience committee,[4] approved the drug.

In fact, CNS-acting agents have emerged in sex-specific sexual medicine research as the newest treatment for this condition in women. The three main neurotransmitters in the brain implicated in sexual function are dopamine, serotonin, and norepinephrine. We have just recently begun to define how these neurotransmitters can inhibit or promote sexual desire. Generally, both dopamine and norepinephrine are considered pro-sexual, while serotonin has antisexual properties and is considered to be a "sexual satiety" agent.[5] Because they are CNS agents, caution must be used in prescribing them to women already taking CNS medications for psychiatric or neurologic conditions.

It is fairly universally agreed that interventions for low libido start with a full medical and psychosexual evaluation. The first line of treatment is office-based counseling, as well as addressing modifiable factors, such as untreated health conditions, medications, or relationship issues.[3] When this approach does not prove helpful, both physicians and patients alike start to wonder, "Is there a pill for this?" In 2020, it turns out, there are two (perhaps three). Although two novel CNS agents have captured the elusive FDA approval for HSDD, one longtime antidepressant with wide use has led to three possible options for patients with HSDD: flibanserin, bremelanotide, and bupropion.

In 2015, the FDA approved flibanserin for HSDD in premenopausal women with generalized, acquired HSDD. It came with both controversy (since it failed twice to be approved) and some trepidation, as it initially required a risk evaluation and mitigation strategies (REMS) certification and a black box warning limiting all alcohol consumption during the duration of the daily treatment because of concerns about hypotension and syncope. Recent updates have refined the limitation for alcohol and removed the REMS. Specifically, as of 2019, the boxed warning, contraindication, warnings and precautions, and adverse reactions sections of labeling are updated to reflect that women should discontinue drinking alcohol at least two hours before taking flibanserin at bedtime or skip the flibanserin dose that evening.[6]

Flibanserin is a CNS agent acting as a serotonin receptor agonist and antagonist that results in a transient decrease in serotonin with a downstream increase in dopamine and norepinephrine in certain regions of the brain. Initially, it was studied as a potential antidepressant. Although it was ineffective for depression, it appeared

to increase sex drive. The authors of a 2016 systematic review of flibanserin in pre- and post-menopausal women found five published and three unpublished studies that included 5,914 women. Overall, the quality of evidence for efficacy was rated as "very low." The mean differences in sexually satisfying events (SSE) involved a 0.49-point increase in SSE per month with flibanserin vs. placebo and a 0.27-point increase in Female Sexual Function Index desire domain (FSFI-D). Women's mean global impression of improvement scores indicated minimal improvement to no change.[7] Although serious adverse effects were rare, adverse events in pre- and post-menopausal women included dizziness, nausea, fatigue, and somnolence in 29.9% to 36.5% for flibanserin vs. 12.7% to 15.8% for placebo.[7]

The FDA approved bremelanotide, a melanocortin receptor agonist in June 2019 also for treatment of generalized, acquired HSDD in premenopausal women.[8] The medication is administered as a subcutaneous injection (1.75 mg) at least 45 minutes before anticipated sexual activity. Bremelanotide works as a premelanocortin, accidentally discovered by experimenting with self-tanning agents. Its mechanism of action is considered to be a downstream increase in dopamine in the CNS system.

Two randomized, Phase III trials involving 1,247 premenopausal women with HSDD showed that 24 weeks of bremelanotide compared with placebo resulted in more women with a meaningful increase in sexual desire using the FSFI-D (51% vs. 21%; $P < 0.001$) and improvement in sexual satisfaction using the Female Sexual Distress Scale desire/arousal/orgasm domain (FSDS-DAO; 57% vs. 26 %; $P < 0.001$). Women in the bremelanotide group showed an increase in FSFI-D scores of 0.35 points ($P < 0.001$) over placebo. Changes in the primary endpoint were observed at four weeks, which was the earliest evaluated time point. There was no statistically significant improvement in SSEs between treatment groups (bremelanotide 0.0 vs. placebo -0.1; $P = 0.630$) from baseline to the end of the study. The most common treatment-emergent adverse events, occurring in more than 10% of patients compared with placebo, were nausea, flushing, and headache.[9] Eighty-seven percent of participants rated administering the medication as "easy."[10]

Subsequently, the authors of a 52-week open label extension studied the safety and efficacy of bremelanotide. Researchers concluded no new safety signals were observed, and premenopausal women exhibited sustained improvements in HSDD with a higher reduction in distress over time (FSDS-DAO -1.7 and -1.4) from baseline to the end of open label testing, suggesting improvements in distress may lag behind improvements in desire.[11]

Bupropion is an antidepressant, known for a low sexual side effect profile, that has been used for depression and selective serotonin reuptake inhibitor-induced sexual dysfunction since its market release in 2006. Because it is widely used and has been on the market the longest, bupropion is cheaper and there are more safety profile data about it. Therefore, consider bupropion as an off-label CNS agent to treat HSDD. It is one of the few antidepressants that increases dopamine and norepinephrine.

For HSDD, there is a single, randomized, placebo-controlled trial of four months duration in nondepressed women with HSDD. There were 75 premenopausal participants, with an average age of 36.1 years. Statistically significant self-reported improvements in pleasure, arousal, and orgasm, according to the Changes in Sexual Functioning Questionnaire, occurred in the bupropion group.[12] Secondarily, blinded raters measured several sexual health variables, and although they showed improved "sexual responsiveness" in all rater-measured variables, many of them were not statistically significant. The effect was seen starting at 28 days of treatment.[12]

There are two FDA-approved medications and one off-label antidepressant that can be considered in treating the most common sexual complaint in women — low libido. On one hand, this is groundbreaking, as we are beginning to see more research on how CNS agents may be key in addressing sex-specific sexual dysfunction. However, each agent did not consistently show more than a modest improvement (if any) in the measurements used to assess sexual desire in their respective studies. For instance, flibanserin may increase SSEs by half an event a month, while no increase in SSEs was seen with bremelanotide. (SSEs were not studied with bupropion.)

Regarding the improvement in FSFI-D score, this was a statistically significant improvement in both the flibanserin and bremelanotide trials (0.27 points vs. 0.35 points). However, in the bremelanotide studies, this change in score did not transfer to significantly increase the women's global impression of improvement of their sexual function. While these medications may be options for some patients after behavioral approaches fail, it is unlikely current available medications for HSDD will change significantly the current landscape in the treatment of low libido. However, the press coverage (both positive and negative) these medications have received may bring the often-overlooked conversation on female sexual function back to the doctor's office to be addressed comprehensively. ■

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PHARMACOLOGY UPDATE

Icosapent Ethyl Capsules (Vascepa)

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

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

The FDA has approved icosapent ethyl as add-on therapy to reduce the risk of cardiovascular (CV) events in adults with elevated triglyceride. Icosapent ethyl is an ethyl ester of eicosapentaenoic acid, an omega-3 fatty acid derived from fish oil. It was approved in 2012 to treat severe hypertriglyceridemia. This new indication received a priority review. It is distributed as Vascepa.

INDICATIONS

Icosapent is an adjunct to maximally tolerated statin therapy to reduce the risk of coronary revascularization, myocardial infarction (MI), stroke, and unstable angina requiring hospitalization in adults with elevated triglyceride (≥ 150 mg/dL) and existing cardiovascular disease (CVD) or diabetes mellitus and two or more additional risk factors for CVD.[1] It was previously approved as an adjunct to diet to reduce triglyceride in patients with severe hypertriglyceridemia (≥ 500 mg/dL).

DOSAGE

The recommended dose is 4 g (4 × 500 mg or 2 × 1 g capsules) taken twice daily with food.[1] Icosapent is available as 500 mg and 1 g capsules.

POTENTIAL ADVANTAGES

Icosapent is the first drug approved to reduce the risk of CV events in patients with established CVD and hypertriglyceridemia on maximally tolerated statin therapy.[1,2]

POTENTIAL DISADVANTAGES

Icosapent was associated with a higher risk of atrial fibrillation or atrial flutter compared to placebo-treated subjects (3.1% vs. 2.1%; $P = 0.004$).[1,2] There is potential for allergic reaction to icosapent in patients with fish and/or shellfish allergies.[1] Bleeding risk has been associated with icosapent (12% vs. 10% for placebo), with serious bleeding 2.7% vs. 2.1% for placebo ($P = 0.06$).[1,2] The risk is higher in patients on anticoagulant/antithrombotic therapy.

COMMENTS

Icosapent's efficacy and safety were demonstrated in a randomized, double-blind, placebo-controlled trial in subjects (age ≥ 45 years) with established CVD (secondary prevention) or ≥ age 50 years with diabetes mellitus and at least one additional risk factor (primary prevention).[1,2] Eligible subjects had fasting triglyceride between 150 and 499 mg/dL and LDL-cholesterol between 41 and 100 mg/dL. A total of 8,179 subjects were randomized to icosapent or placebo. The median age was 64 years, 71% were male, 90% were white, 71% were on a secondary prevention, 62% were on a moderate-intensity statin, 30% were on a high-intensity statin, 60% recorded triglyceride levels ≥ 200 mg/dL, and 58% presented with type 2 diabetes. The primary efficacy endpoint was a composite of CV death, nonfatal MI, nonfatal stroke, coronary revascularization, or unstable angina. The median follow-up was 4.9 years.

Events occurred in 17.2% of those randomized to icosapent vs. 22% randomized to placebo (hazard ratio, 0.75; 95% confidence interval, 0.69-0.83; $P < 0.001$). The key secondary composite endpoint of CV death, MI, and stroke was reduced by 26%. Other secondary endpoints (fatal or nonfatal MI, emergent or urgent coronary revascularization, fatal or nonfatal stroke, and

hospitalization for unstable angina) also declined significantly (range, 20-32%). Those on secondary prevention, younger subjects (< age 65 years), and those with baseline triglyceride ≥ 200 mg/dL and HDL cholesterol ≤ 35 mg/dL tended to benefit more. Death from any cause was not significantly different between treatment groups (6.7% vs. 7.4%). The timing of the benefit appears to begin after two years of treatment. After one year, there was an 18.3% reduction in triglyceride levels vs. 2.2% in the placebo group (median baseline, 216 mg/dL). LDL-cholesterol increased by 3.1% vs. 10.2%, respectively (median baseline, 74 mg/dL).

CLINICAL IMPLICATIONS

Icosapent is the first FDA-approved treatment to reduce the risk of CV events in patients with elevated triglyceride when added on to maximally tolerated statin therapy. There have been numerous studies that have attempted to show the benefit of omega-3-fatty acids supplementation (generally with combined eicosapentaenoic and docosahexaenoic acids) for reducing the risk of CV events, particularly in secondary prevention, but results have been mixed.[3] A Cochran review and a meta-analysis of 10 randomized trials (n = 47,803) did not show clear CV benefit.[4,5] The American Heart Association recommends omega-3 fatty acid supplements as secondary prevention for CVD death for patients with prevalent coronary heart disease as well as prevalent heart failure with reduced left ventricular function.[3] Icosapent has shown efficacy in patients with hypertriglyceridemia, established CV diseases, and those on moderate- to high-intensity statin therapy. The cost for icosapent is $397 (4 × 1 g/day) or $465 (8 × 0.5 g/day) for a 30-day supply. ■

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CME QUESTIONS

1. Newer data suggest the prevalence of infective endocarditis is highest in bacteremia caused by:
a. coagulase-negative staphylococci.
b. *Enterococcus faecalis*.
c. *Streptococcus* spp.
d. *Staphylococcus aureus*.

2. Which is true about hypoactive sexual desire disorder (HSDD)?
a. All current treatments are dosed on an as-needed basis before sexual activity.
b. Bupropion is an FDA-approved treatment for HSDD.
c. The neurotransmitter serotonin is considered to have prosexual properties in women.
d. The shared mechanism of action for all FDA-approved medications for HSDD is believed to be an increase in dopamine in the central nervous system.

3. In the study by Vaughn et al, which outcome occurred more commonly in the group that received an excess duration of antibiotics compared to an appropriate duration?
a. Antibiotic-associated adverse drug event
b. Development of a new resistant pathogen
c. ED visit
d. Hospital readmission

4. Which is correct regarding patients with cat scratch disease considered by Landes et al to have fever of unknown origin?
a. Approximately one-half had daily fever.
b. A relapsing fever pattern was not observed.
c. Focal sites of infection were absent.
d. Antibiotic administration was associated with a dramatically reduced duration of fever.