AMERICAN HEALTH CONSULTANTS

The Physician's
Therapeutics & Drug Alert™

Volume 6, Number 3 Pages 17-24 October 2001

INSIDE

Threat of Biological Warfare Must Now be Recognized

By William T. Elliott, MD, FACP

The threat of biological warfare is suddenly on everyone's mind. Two of the biggest threats are **smallpox** and **anthrax**. Smallpox, which was officially declared eradicated from the planet in 1979, may represent the biggest threat. Samples of the virus were retained by the Soviet Union and the United States during the Cold War, but with the break up of the Soviet Union there is fear that some of the virus may have fallen into the hands of terrorists. British biotechnology company Acambis Plc has been developing a smallpox vaccine and announced in mid-September that it will begin clinical trials on the drug next year. The earliest that a smallpox vaccine could be in general usage is 2004, although the company is hoping that process may be accelerated. The US company BioPort is the sole manufacturer of anthrax vaccine. The company has just completed a major renovation of its manufacturing plant, which needs to be inspected and approved. Even with an accelerated manufacturing process, it is unlikely that the anthrax vaccine will be available to anyone except US military personnel in the foreseeable future. Meanwhile, the Centers for Disease Control (CDC) are focusing on treatment of anthrax. Last year the FDA approved **ciprofloxacin** as a treatment for anthrax and there are already reports that medical facilities and individuals are stocking up on the antibiotic.

Hepatitis C

Peginterferon plus **ribavirin** may become the new standard for treating chronic hepatitis C infections. **Interferon alfa-2b** plus ribavirin has been standard initial therapy for chronic hepatitis C, however, a new study suggests that a regimen of peginterferon and ribavirin produces higher sustained virologic response rates. Peginterferon is produced by attaching polyethylene glycol to interferon alfa-2b. The resulting compound has a longer serum half-life and may be given as a weekly injection, instead of daily, as is usually required for interferon alfa-2b. The study involved 1530 patients with chronic hepatitis C who were randomized to receive a standard interferon plus ribavirin or peginterferon plus ribavirin. Peginterferon was dosed at 1.5 µg/kg/wk, 1.5 µg/kg/wk for 4 weeks followed by 0.5 mg/kg/wk for the duration of study. At the end of 24 weeks, the high-dose peg interferon group had a significantly higher sustained virologic response rate than either the low-dose interferon group or the interfeon alpha-2b plus ribavirin group (54% vs 47%). The benefits were most apparent in patients with HCV genotype 1. Based on this study, Manns and colleagues suggest that peginterferon plus ribavirin will become the new

standard for treatment of hepatitis C (Manns MP, et al. *Lancet*. 2001;358:958-965).

Acute hepatitis C is an infrequently diagnosed condition that often progresses to chronic hepatitis C. A new study emphasizes the importance of recognizing acute hepatitis C since treatment with interferon is highly effective in preventing progression to the chronic form of the infection. German investigators identified 44 patients with acute hepatitis C between 1998 and 2001. Patients included men and women who had been infected via needlestick, IV drug use, sexual contact, medical procedures, or undetermined causes. All patients were treated with interferon alfa-2b subcutaneously daily for 4 weeks then 3 times a week for another 20 weeks. At the end of therapy, 42 of 43 patients who completed therapy had undetectable levels of HCV RNA and normal liver function tests. The *New England Journal of Medicine* will publish the full text of this study in November, however because of the importance of the findings, the abstract was posted on their web site on Oct. 1. The same group that reported these findings are also working on similar studies with peginterferon.

Influenza Vaccine

This year's **influenza vaccine** seems well matched to worldwide flu strains according to the US Centers for Disease Control. Two **influenza A** viruses and **1 B** virus have been found worldwide, but there have been few isolates in North America. Still, the CDC feels we will be well prepared once the vaccine is in general circulation. Production problems have slowed this year's vaccine, but more than half the nearly 80 million doses should be available at the end of this month, with the rest available in November and December.

Inhaled Glucocorticids

Premenopausal women on **inhaled glucocorticoids** may be at risk for osteoporosis according to a new study. Israel and associates from Harvard looked at 109 premenopausal women on inhaled triamcinolone for asthma. A dose-related decline in bone density at the hip, but not the spine, was found over the 3 years of the study. Even excluding women who required short courses of **oral steroids**, the number of puffs per year was associated with the decline in bone density. Bone density was assessed using dual photon absorbtiometry (Israel E, et al. *N Engl J Med*. 2001;345:941-947).

Statins

At a time when there is much public concern over side effects of **statins**, Astra-Zeneca is hoping to launch the most potent statin yet next year. **Rosuvastatin** (Crestor) is touted as being more effective at lowering LDL than **atorvastatin** (Lipitor), **simvastatin** (Zocor), or **pravastatin** (Pravachol). All this with a favorable side effect profile according to the company. Meanwhile, patients remain cautious about statin use following the well-publicized withdrawal of **cerivistatin** (Baycol) from the market. Cerivistatin, which was nearly 10 times more likely than other statins to cause **rhabdomyolysis**, was withdrawn in August. News reports frequently mentioned that all statins can cause muscle inflammation, but failed to point out the low overall risk.

ED

Several drugs for the treatment of **erectile dysfunction** are in various stages of the approval at the FDA. Icos' **tadalafil** (Cialis) has been accepted for review by the agency. Tadalafil is an oral phosphodiesterases inhibitor similar to **sildenafil** (Viagra). NexMed is in phase III trails with a topical formulation of **alprostadil** with the company's transdermal delivery technology. TAP's **apomorphine** (Uprima) is currently in limbo. The drug was being reviewed by the FDA when the application for approval was withdrawn. The drug is available in Europe. ■

Caspofungin—A New Antifungal Agent

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

Earlier this year, the fda approved the first in a new class of antifungal agents. Caspofungin represents the first of the echinocandine class, antifungal agents that inhibit fungal cell wall synthesis by inhibiting 1,3-beta-D-glucan synthase. Caspofungin exhibits in vitro antifungal activity against a wide range of fungi and yeast including Candida and Aspergillus spp, but is only currently approved for use against Aspergillus. The drug, which is given intravenously, is being marketed by Merck under the trade name Cancidas.

Indication

Caspofungin is indicated for the treatment of invasive aspergillosis in patients who are refractory to or intolerant of other antifungals.[1]

Dosage

The recommended dose is a single 70-mg loading dose

on day 1 and 50 mg daily thereafter. The duration of therapy should be dictated by the severity of the patient's underlying disease and clinical response.[1]

The drug should be given by intravenous infusion over about 1 hour. No dosage adjustment is needed in patients with mild hepatic impairment or renal impairment.[1]

Potential Advantages

Caspofungin provides a new antifungal with a different mechanism of action. About 50% of patients who had previously been refractory to, or intolerant of, other antifungals had a favorable response to caspofungin.[1] Its long elimination half-life (9-11 hours) permits once daily dosing. Caspofungin is generally well tolerated and similar to intraconazole.[2] It is better tolerated than amphotericin B. Caspofungin does not appear to interact with other drugs metabolized by the cytochrome P450 isoenzymes.

Potential Disadvantages

There are limited clinical data on caspofungin and no published clinical trials. Data to support FDA approval was a noncomparative open-label study involving 69 patients. The incidence of drug resistance is not known. The concomitant use of caspofungin and cyclosporine is not recommended as elevation of alanine transaminase 2 to 3 times the upper limits of normal has been reported.[1]

Comments

Caspofungin is a new class of antifungal agents that inhibits the formation of beta (1,3)-D-glucan by inhibiting glucan synthase. This mechanism differs from that of amphotericin B and azoles which affect ergosterol albeit in different ways. Beta (1,3)-D-glucan is found in the cell wall of many filamentous fungi (molds) but not in mammalian cells. Caspofungi is active in vitro against *Aspergillus fumigatus, A flavus, A terreus,* and many Candida species including both fluconazole susceptible and resistant species.[2-4] Candida species including *C albicans, C galabrata, C tropicalis, C krusei,* and *C lusitaniae.* It has limited activity against *Cryptococcus neoformans.*[5] Standardized testing for susceptibility of caspofungin has not been established and results of such testing may not correlate with clinical effectiveness. Caspofungin has been studied in various animal infection models, but data in humans is limited. Some degree of efficacy has been reported in oropharyneal and esophageal candidiasis and invasive aspergillosis,[6] however, it is only FDA approved for treating invasive aspergillosis refractory to or intolerant of other therapies.

Approval was based on an unpublished, open-label, noncomparative study in 69 patients. These patients had previously failed to improve or had disease progression despite at least 7 days of therapy with amphotericin B including lipid formulations, itraconazole, or an investigational azole with reported activity to *Aspergillus.* Some were also intolerant to previous therapy defined as doubling of serum creatinine or other side effects which may or may not be infusion-related.[1] About 50% of patients who received more than 7 days of therapy with caspofungin showed a favorable response.[1] This was defined as complete or partial response of all signs and symptoms and radiographic findings.[1]

The cost of caspofungin for a 14-day treatment course is about $4000 which is similar to intraconazole and less costly than lipid formulations of amphotericin ($7000 to $15,000).

Clinical Implications

Current antifungal therapies for aspergillosis include amphotericin B, azoles such as intraconazole, and lipid formulations of amphotericin (Abelcet, Ambisone). Renal toxicity has been associated with amphotericin B and some fungi have developed resistance to the azoles. Caspofungin provides another option if the patient is refractory to or intolerant of these standard therapies. Broader clinical experience will ultimately define the role of caspofungin. ■

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Nesiritide— A New Drug for the Treatment of CHF

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

The fda has approved nesiritide, a new drug for treating inpatients with acutely decompensated congestive heart failure (CHF). Nesiritide represents a new approach to treating CHF. It is a 32 amino

acid, recombinant B-type human natriuretic peptide that mimics the action of the endogenous counterpart. Its primary effects are a reduction in pulmonary capillary wedge pressure and systemic arterial pressure in patients with heart failure. Nesiritide is marketed under the trade name Natrecor by Scios Inc. of Sunnyvale, Calif.

Indications

Nesiritide is indicated for the treatment of patients with acutely decompensated CHF who have dyspnea at rest or with minimal activity.[1]

Dosage

The recommended dose is 2 µg/kg as an intravenous bolus followed by a continuous infusion of 0.01 µg/kg/min. There is limited experience with the use of nesiritide beyond 48 hours.[1] Nesiritide is eliminated in a manner proportional to body weight and the product is dosed accordingly. Nesiritide is incompatible with, and should not be coadministered with several other compounds including heparin (including heparin-coated catheters), insulin, ethacrynate sodium, bumetamide, enalaprilat, hydralazine, furosemide, and sodium metabisulfite.[1]

Nesiritide is available as 1.5 mg vials.

Potential Advantages

Nesiritide has been shown to reduce dyspnea in patients with decompensated CHF compared to placebo.[1,2] Improvement in pulmonary capillary wedge pressure, dyspnea, or fatigue was similar to that reported for others drugs such as dobutamine, nitroglycerin, dopamine, or amrinone.[2] In a comparative trial with nitroglycerin, the Vasodilation in the Management of Acute CHF (VMAC) trial, nesiritide caused fewer overall side effects.[3] Tachycardia or ventricular tachyarrhythmias has not been reported with nesiritide.[1] In the Prospective Randomized Evaluation of Cardiac Ectopy with Dobutamine or Nesiritide (PRECEDENT) study, dobutamine was associated with significantly greater incidences of ventricular ectopy and tachycardia.[5]

Tachyphylaxis has not been reported.[1]

Potential Disadvantages

Hypotension is the most common dose-related adverse effect. While the incidence of hypotension was similar between nesiritide and nitroglycerin, when it occurred, the intensity and duration of this effect was longer with nesiritide (2.2 hours vs 0.7 hours).[1] Blood pressure should be monitored closely during nesiritide administration. The use of other drugs, which may cause hypotension, must be done with caution. In some susceptible patients, those with severe heart failure, nesiritide may cause azotemia. Nesiritide can only be given intravenously and up to 48 hours. Following discontinuation of the drug, the effect (eg, pulmonary capillary wedge pressure) returns to within 10% of baseline within 2 hours.[1]

Comments

The natriuretic peptide family consist of 3 peptides: atrial natriuretic peptide, brain or B-type natriuretic peptide, and C-type peptide.[4] Nesiritide is B-type peptide produced by recombinant DNA technology using the *Escherichia coli* system and is identical to endogenous B-type peptide. Endogenous B-type peptide is released by the ventricular myocardium in response to such factors as stretching of the wall, volume overload, or pressure overload.[5] Levels are increased in patients with CHF and appear to be associated with the progression of clinical symptoms.[6,7] B-type natriuretic peptide has been proposed as a screening tool for left ventricular dysfunction.[8]

In CHF patients, nesiritide has been shown to improve clinical symptoms (eg, dyspnea), reduce pulmonary capillary wedge pressure, and suppression of the renin-angiotensin-aldosterone system. Improvement is generally seen within 15 minutes and reaches 95% of the 3-hour effect within 1 hour. In the clinical trials, the primary end points were changes in pulmonary capillary wedge pressure and improvement is dyspnea after 3 hours. The benefit dissipates within 2 hours after discontinuation. At doses higher than the currently recommended dose, 50-56% of patients who received nesiritide were rated as improved compared to 12% given placebo.[2] With the currently approved dose, the comparative rates were not reported by the manufacturer other than to indicate that they were statistically significant ($P = 0.034$; n = 489).[1] The FDA originally turned down the drug in April 1999 and a lower dose study was conducted at the FDA's request. The VMAC trial, which compared nesiritide with IV nitroglycerin or placebo, was designed to address the issues raised by the FDA such as safety and tachyphylaxis.[5]

No improvement in survival has been seen with nesiritide compared to other drugs such as nitroglycerin, dobutamine, nitroprusside, milrinone, amrinone, or dopamine.[1]

Nesiritide will cost about $800 (2 vials) for a 48-hour administration.

Clinical Implications

It is estimated that approximately 5 million Americans have heart failure, and decompensation is the most common reason for the hospitalization. The condition is characterized with symptoms of dyspnea and fatigue. Nesiritide has been shown to improve these symptoms rapidly and at least as effectively as currently available drugs with some potential advantages. Scios will develop a CHF patient registry, the Acutely Decompensated Heart Failure Registry (ADHERE)

and will launch a physician education program. The latter was at the request of the FDA advisory committee. ■

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Self-Medication Guidelines for Acute Diarrhea

Source: *Wingate D, et al. Aliment Pharmacol Ther. 2001;15: 773-782.*

Self-treatment of acute uncomplicated diarrhea is extremely common. However, guidelines for management of diarrhea have been confusing and contradictory. This paper is the product of an ad hoc advisory group that reviewed available evidence and reached consensus. Loperamide was deemed to be safe, effective, and less liable to produce unwanted side effects than older antidiarrheal drugs. In individuals who can successfully maintain oral fluid intake, oral rehydration solutions offer no additional advantages. Other than in certain situations related to travel and prior medical advice, the self-administration of antimicrobial drugs was not thought to be desirable. Medical intervention was urged for the frail, for severe diarrhea in the elderly (> 75 years), or the chronically ill, or for persistent diarrhea beyond 48 hours, or in situations with deterioration, distention, or dysentery (fever > 38.5° and/or bloody diarrhea).

Comment by Malcolm Robinson, MD, FACP, FACG

Guidelines for self-treatment of diarrhea in adults are extremely varied including recommendations for and against antidiarrheals, for and against probiotic treatment, and continuation of normal diet vs. use of clear liquids only. Recommendations for oral rehydration fluids in children have been extrapolated to apply to adults in the absence of any data suggesting that this approach would be at all useful. Although some physicians have refused to treat acute diarrhea, this distressing and uncomfortable symptom complex warrants intervention. There is absolutely no basis for withholding medication in acute diarrheal states. Some evidence suggests that older antidiarrheal drugs might worsen infectious dysentery, and this has been used to justify the avoidance of all antidiarrheal medication in the setting of fever and/or bloody stools. Probiotic agents have never been shown to improve acute diarrhea in adults and cannot currently be recommended. Adsorbents such as kaolin or charcoal provide minimal or no benefit and are clearly inferior to loperamide in acute diarrhea. Codeine and other opiates are excellent antidiarrheal drugs, but their abuse liability makes them less acceptable than loperamide. Bismuth subsalicylate is somewhat effective in travelers' diarrhea caused by Escherichia coli, but this effect is probably less than loperamide. Some poorly absorbed antimicrobials have been used for travelers' diarrhea including rifaximin. Neomycin, bacitracin, and erythromycin as sold in some Third World countries are not recognized as efficacious. Tetracycline, penicillins, and macrolides are no longer recommended due to problems with bacterial resistance. There may still be some role (albeit vanishing) for trimethoprim-sulfamethoxazole, and doxycycline also may occasionally be useful despite being a known photosensitizer (it does provide possible concomitant malaria prophylaxis). Quinolones have become increasingly popular for the treatment of acute travelers' diarrhea since they are generally effective and well tolerated. These recommendations seem quite sound and are helpful for our own use and for recommendations to our patients. ■

Dr. Robinson is Medical Director, Oklahoma Foundation for Digestive Research; Clinical Professor of Medicine, University of Oklahoma College of Medicine Oklahoma City, Okla.

Antibiotics and Respiratory Infection

Sources: *Gonzales R, et al. Eff Clin Pract. 2001;4:105-111; Sargent J, Welch HG. Eff Clin Pract. 2001;4:136-138.*

Gonzales and colleagues provide follow-up information on patient satisfaction after a study that documented the value of a patient education campaign on antibiotic prescribing.[1] The intervention led

to a drop in antibiotic prescriptions for acute bronchitis from 74% to 48% in outpatient clinics in the Kaiser Permanente system in Denver, Colo, during the winter of 1997-1998.

This study involved 2 clinics, both of which had an office-based program to reduce antibiotic prescribing that consisted of exam room posters, fact sheets, and a 1-hour educational session for clinicians. The intervention clinic also had the benefit of direct patient education with direct mailings to patients, refrigerator magnets, self-care guidelines, CDC brochures on antibiotic use, and a letter from the clinic director. The period under study was the winter of 1998-1999. No new direct patient contact was made, but there was some reinforcement of the prior messages through newsletters and another hour lecture for clinicians on how to say "No."

Records of patients seen at the clinic with a diagnosis of acute bronchitis were reviewed. Satisfaction was assessed with a telephone questionnaire, to which 416 patients responded. One hundred fifty patients were excluded because of missing data or a good reason to get an antibiotic because of another respiratory infection. Antibiotics were used less frequently in the "intervention" clinic, but the percentage receiving antibiotics rose to 64% from 48% the year before. Nonetheless, the control clinic remained higher, with 85% of patients receiving prescriptions.

Patients were interviewed within 4 weeks of evaluation. Sixty-nine percent in the intervention clinic and 63% in the control clinic indicated their level of satisfaction with care was "very good" or "excellent." Further analysis was done to determine satisfaction factors but only a limited correlation was found with age and duration of symptoms.

Comment by Alan D. Tice, MD, FACP

This is a follow-up study with some interesting observations and insight provided in the accompanying editorial. While patient satisfaction has not been reported to correlate with antibiotic prescriptions, physicians commonly report it as a reason why they prescribe antibiotics. This article again demonstrates satisfaction with care among those who did not get prescriptions compared with those who did. It is, however, the first to demonstrate no difference in satisfaction even though there was clearly a change in prescribing. In fact, there was a suggestion that there was a higher rate of satisfaction in the intervention clinic in which antibiotics were less frequently prescribed.

How important a factor patient satisfaction or demands are in the decision to prescribe antibiotics is up for debate. Certainly, time with a patient providing evaluation, education, and assurance correlate well with satisfaction with care. Beyond that, there appears to be little indication that patients feel they know more about antibiotic prescribing than the physician.

What is also interesting about the study is that more than half of the patients received an antibiotic for an illness in which such therapy is not indicated. Is that the fault of the physician or the patient?

As Sargent and Welch point out in the editorial, there are many factors responsible for antibiotic use besides the patient's wishes. A simple rule is not adequate for the complexity of factors that must be considered in evaluating an infection. Risks of therapy must be weighed against the possibility of serious disease that would easily respond to early therapy but not later on. The risk of a lawsuit for an infection that might have responded to an antibiotic not prescribed is far higher than one in which the drug was prescribed. The cumulative effect on antimicrobial resistance in society is a subtle one and not often appreciated by an ill person or even a physician who is trying to help. It is not an easy situation these days in this litigious society and creates a difficult choice between the individual and society with the rising tide of antimicrobial resistance.

In essence, the decision to prescribe an antibiotic lies with the physician, although the relationship with the patient is essential, and the desire of a patient to receive an antibiotic may be moderated by a careful evaluation, education, and assurance. ■

Dr. Tice is a member of Infections Limited, PS, Tacoma, Wash.

Reference

1. Gonzales R, et al. *JAMA.* 1999;281:1512-1519.

Acid Suppression in the Management of GERD

Source: *Jones R, Bytzer P. Aliment Pharmacol Ther. 2001;15: 765-772.*

H2-receptor antagonists (h2ras) continue to be widely prescribed for gastroesophageal reflux disease (GERD) despite the availability of substantially more effective proton pump inhibitors (PPIs).

Primary care physicians tend to consider GERD as a relatively benign disorder due to relatively low incidence of complications or other morbidity. Symptom "control" is deemed satisfactory rather than complete abolition of symptoms. Jones and Bytzer insist that GERD can indeed be an extremely serious illness, complicated by ulceration, stricture, Barrett's esophagus, and adenocarcinoma. This paper refers to the well known McMaster University meta-analyses that suggest a linear relationship between level of acid inhibition and healing of erosive esophagitis. They also cite many studies that support PPI use over H2RAs, including faster onset of relief and more complete relief and better maintenance of remission. There is brief discussion of the potential need for endoscopic assessment in GERD onset over age 45-55 or in the setting of any "alarm symptoms."

Data are cited for increasing use of PPIs in primary care, particularly as compared to new prescriptions for H2RAs. It was mentioned that lifestyle modifications were deemed of too low efficacy to warrant much attention by primary care practitioners for their patients. Issues related to attempted step-down therapy were raised, including the notion of therapy to half dose PPIs or perhaps to some form of "on demand" therapy with PPIs. It was concluded that the use of PPIs was preferable to initiation of H2RA therapy and that this could successfully be followed by one or another "step down" approaches.

Comment by Malcolm Robinson MD, FACP, FACG

This article, not at all surprisingly, was supported by "a grant from AstraZeneca." It is "party line" for this world leader in PPI distribution (Prilosec®, Nexium®)—and this approach to GERD therapy clearly will continue to result in huge profits for them. Most or all of the comparative studies cited were also supported by PPI-makers or their strong proponents. The enormous success of the H2RAs for many years cannot now be totally disregarded due to the emergence of an admittedly excellent new class of drugs, the PPIs. Patients who respond well to H2RA therapy need not have escalation of therapy to PPIs in every case, and I am not convinced by any broad-based data that PPIs are universally superior to H2RAs, especially in mild GERD as tends to be seen most often by primary care physicians. PPIs are unquestionably "addictive" by causing rebound acid hypersecretion after they are discontinued and perhaps otherwise. On-demand use of PPIs is extremely promising, but millions of patients have been quite satisfied with on-demand H2RA use, an unquestionably safe and inexpensive approach. Jones and Bytzer are well respected physicians in Europe, one in primary care and the other in gastroenterology. Nevertheless, I would urge readers to continue to regard their recommendations with appropriate skepticism and to use their own experience to guide them to properly individualized GERD therapy. ■

Therapeutics & Drug Briefs

BMD Response to Estrogen Replacement in Women

Source: *Villareal DT, et al. JAMA. 2001;286:815-820.*

The role of estrogen and progesterone replacement (HRT) for osteoporosis (OSPS) prevention is well established. Most data have accrued from relatively younger women, (ie, < 75 years old). Whether HRT provides equally beneficial OSPS effects for more senior women has not been well documented, since most data in older women is from observational studies.

In this placebo-controlled trial, Villareal and associates randomized 67 women who were considered especially high risk because of their relative frailty, to combination therapy with conjugated estrogens (0.625 mg QD) plus medroxyprogesterone acetate (5 mg QD for 13 consecutive days every third month) for 9 months. Bone mineral density (BMD) was measured at the lumbar spine and femur. Bone turnover markers were also measured. More than 90% of the women were osteopenic or osteoporotic at baseline.

BMD at the lumbar spine, and femoral neck, were statistically significantly improved in women who received HRT (eg, at the femoral neck) BMD increased 2.5%, as compared with a decrease in BMD in the placebo group. Bone turnover markers were similarly favorably affected. These data encouragingly support the concept that age should not be a barrier for consideration of HRT in at-risk menopausal women. ■

Doxazosin and Single-Drug Therapy in Hypertensive Patients

Source: *Martell N, Luque M. J Clin Hypertens. 2001;3:218-223.*

In middle age and beyond, both hypertension and benign prostatic hyperplasia (BPH) become increasingly common. Treatment of normotensive BPH patients can usually be accomplished using alpha-

blockers without problematic episodes of hypotension. For hypertensive BPH patients, there has been some concern that addition of doxazosin to the antihypertensive regimen might produce hypotension or other untoward effects. This study evaluated the effect of 2-4 mg QD doxazosin added to the regimen of patients who had a achieved a diastolic blood pressure < 95 on nonalpha blocker monotherapy.

Patients (n = 2363, Spanish men > age 40) were followed for 14 weeks, and evaluated by a quality-of-life scale, prostatism symptom scale, blood pressure measurement, and recording of adverse events.

Doxazosin treatment resulted in a mean blood pressure reduction of 10.7/6.1 over baseline treatment with an ACE inhibitor, calcium channel blocker, or diuretic. Favorable effects for prostatism scores were consistently seen. Symptoms of dizziness, vertigo, hypotension, or syncope were seen uncommonly (2.7%, 0.4%, 0.8%, 0.3%, respectively). Martell and Luque conclude that addition of an alpha-blocker to the treatment regimen of hypertensive BPH patients is generally effective and well tolerated. ■

The Therapeutics & Drug Briefs were written by Louis Kuritzky, MD.

Attention Readers

In the August 2001, issue on page 5 in the article, "Pioglitazone Improves Lipid Profiles More Effectively than Rosiglitazone," the sentence in the second paragraph, "Mean cholesterol, triglyceride, and low-density lipoprotein (LDL) cholesterol levels decreased in the pioglitazone group by 44.7%, 11.3%, and 7.3% but increased 8.4%, 38.4%, and 8.1%, respectively, in the rosiglitazone group," should have read ". . .cholesterol levels decreased in the pioglitazone group by 4.7%. . ." We regret any confusion this may have caused. ■

Readers are Invited. . .

Readers are invited to submit questions or comments on material seen in or relevant to *Physician's Therapeutics & Drug Alert*. Send your questions to: Robert Kimball, *Physician's Therapeutics & Drug Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. For subscription information, you can reach the editors and customer service personnel for *Physician's Therapeutics & Drug Alert* via the internet by sending e-mail to robert.kimball@ahcpub.com. ■

CME questions

Testing form inserted in the January 2002 issue

7. Which is *not* true about caspofungin?

a. It is given once a day orally.
b. It is approved for invasive aspergillosis.
c. It may be better tolerated than other antifungal agents.
d. It represents the first of a new class of antifungal agents.

8. Which statement is *not* true about nesiritide?

a. It is administered intravenously.
b. It may be used for up to a week.
c. Hypotension is the most common adverse effect.
d. The drug has not been shown to affect survival in CHF.

9. The ideal treatment for acute diarrhea in adults should include:

a. oral rehydration solution use, clear liquid diet, and a macrolide antibiotic.
b. loperamide for symptom control except in the presence of fever or bloody diarrhea.
c. keopectate® and prn use of low doses of codeine-containing products.
d. avoidance of all antidiarrheal agents to avoid prolongation of symptoms and possible worsening of infectious diarrhea.
e. self treatment with neomycin alone or in combination with bacitracin at the onset of diarrhea symptoms.

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