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INSIDE

Congress Quashes Drug Reimportation Mandate

By William T. Elliott, MD, FACP

Forget reimportation of drugs from other countries as a way to control drug costs. Congress has failed to reverse a mandate barring **drug reimportation** proposed by Tommy Thompson, secretary of Health and Human Services. Pharmacies and pharmacy benefit management companies (PBMs) had hoped to purchase American-made drugs in Canada or Mexico where prices are substantially lower, then reimport them here for sale. Secretary Thompson, under strong pressure from the pharmaceutical industry, cited safety concerns for his ban, especially the risk of counterfeit drugs. However, patients in border states are not banned from purchasing drugs in Canada and Mexico where the prices are often 50% less than those in neighboring pharmacies across the border.

Deep Venous Thrombsis (DVT)

Oral anticoagulation for the treatment of DVT may be safely discontinued after 3 months according to Italian investigators. In this study, 267 patients with a first episode of idiopathic proximal DVT were randomized to oral anticoagulant for 3 months or 12 months. Most cases of **recurrent thromboembolic events** occurred in the first year after discontinuing the medication, but the rate of recurrence was the same regardless of the duration of treatment. After 2 years of follow-up, there was no difference in the rate of recurrent thromboembolic events between the 3- or 12-month treatment group. There were 4 nonfatal major hemorrhages in the 12-month group. This study implies that recurrent thromboembolic events after DVT are delayed, but not prevented, by prolonged treatment with an oral anticoagulant (Agnelli G, et al. *N Engl J Med*. 2001;345:165-169).

Lipids

The FDA has issued an approvable letter for a new **lipid-lowering drug** that combines **lovastatin** and **niacin**. The drug will be marketed under the name Advicor and is indicated for mixed dyslipidemia where either niacin or a statin alone may not be effective. Formal approval of the drug awaits the expiration of the exclusivity patent for Merck's lovastatin, which is expected later this fall.

Antidepressants for Headache Treatment

Tricyclic **antidepressants** (TCAs) have been a mainstay of **headache prophylaxis**. Now there is good evidence that **selective serotonin reuptake inhibitors** (SSRIs) may work as well as TCAs with fewer side effects. A large meta-analysis

going back more than 30 years revealed that antidepressants in general are highly effective in preventing both migraine and tension headaches, and the effect was similar with all classes of antidepressants. Specifically, SSRIs were as effective in preventing headaches as tricyclics, generally with less side effects (Tomkins G, et al. *Am J Med*. 2001;111:54-63).

Pulmonary Emboli

Patients with **massive pulmonary emboli** (PE) represent a therapeutic dilemma. Should these patients receive **thrombolytic therapy** or **standard heparin therapy**? A new French study suggests that although short-term clinical markers may be improved with thrombolysis, long-term outcomes are worse. Davidson and colleagues performed a retrospective review of 128 patients with massive PE with evidence of right ventricular dysfunction, but normal hemodynamics. Half of these patients received heparin and half received thrombolytic therapy. The patients given thrombolytic therapy had a marked, rapid, improvement in lung perfusion compared to heparin patients, as has been shown in other studies. Despite this, all patients in the heparin group survived, while 4 patients in the thrombolytic group died, 2 from cerebral bleeding, 1 from shock following the thrombolytic infusion, and 1 from recurrent PE. Davidson et al conclude that patients with massive PE and normal hemodynamics will not benefit from thrombolytic therapy. Patients in shock or who are hemodynamically unstable should continue to be evaluated for thrombolytic therapy (Davidson B, et al. *Chest*. 2001;120:6-8).

Urinary Tract Infection (UTI)

Women with a history of **UTIs** can accurately diagnose and treat themselves according to a new study from the University of Washington. In this study, 172 women with a history of recurrent UTIs were followed. None had recently been pregnant and women with chronic diseases were excluded. During the study period, 88 women self diagnosed 172 cases of UTI. All were then treated with antibiotics after a urinalysis and culture was done. Only 5% of women had no **pyuria** or **bacteriuria**. Cure was achieved in more than 90% of women, and there were no adverse outcomes. Gupta and colleagues conclude that women with a history of UTI can accurately self diagnose and treat UTI, thus avoiding an office visit (Gupta K, et al. *Ann Intern Med*. 2001;135:9-16).

Oxycodone given "Black Box" Warning

The FDA has taken the unusual step of adding a "Black Box" warning to OxyContin, Purdue Pharma's brand of **oxycodone**, a long-acting **Schedule II narcotic**. The warning is intended to help prevent diversion of the drug, which has a become a popular drug of abuse. Nicknamed "Oxy" on the street, the drug sells for an average of $1/mg or $40 for a 40-mg pill. Abuse has become a particular problem in rural America as described in an article in the July 29 *New York Times*. Several deaths have been reported associated with misuse of the drug, which is commonly crushed and injected or snorted. The Black Box warning stresses the problems of abuse and diversion hoping that awareness will reduce the likelihood of inappropriate prescribing. Last May, Purdue withdrew the 160 mg strength, the highest dose form of OxyContin, because of increasing reports of abuse.

Prozac's Patent Expires

After more than a decade of immense popularity and astounding sales, Lilly's **fluoxetine** (Prozac) has seen its patent expire, opening the door for generic forms of the drug. Barr Laboratories, the first generic manufacturer to develop a generic, prevailed in more than 5 years of lawsuits with Lilly. Barr shipped their generic fluoxetine on Aug. 2, and will likely retain 180 days of exclusivity as the first generic filed under the Hatch-Waxman act. The cost of fluoxetine to consumers is expected to plummet. Lilly posted more than $2.5 billion sales of Prozac last year. ■

Almotriptan (Axert—Pharmacia Corporation) For Migraine

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

The fda has approved pharmacia's almotriptan malate for the treatment of migraine with or without aura in adults. The drug is touted as being as effective as other triptans, but with a favorable side effect profile, especially cardiovascular side effects. Almotriptan will be marketed by Pharmacia under the trade name "Axert."

Indications

Almotriptan is indicated for the acute treatment of migraine with or without aura in adults.

Dosage

The recommended dose of almotriptan is 6.25 mg or 12.5 mg initially. If the headache returns, the dose may be repeated after 2 hours. No more than 2 doses should be taken within a 24-hour period. The safety of using almotriptan for more than 4 headaches in a 30-day period has not been established. Patients with impaired renal or hepatic function should take an initial dose of 6.25 mg.[1]

Almotriptan is supplied as 6.25 mg and 12.5 mg tablets.

Potential Advantages

The incidence of chest pain associated with almotriptan in preclinical studies was lower than that reported for sumatriptan in premarketing studies.[2] Single doses from 12.5 mg to 50 mg did not have a significant effect on the electrocardiography of healthy volunteers while doses of 25 mg and 50 mg had a small dose-related increase in systolic and diastolic blood pressure up to 4 hours postdose (2.78 and 4.17 mg Hg and 3.77 and 6.11 mg Hg, respectively).[3] Animal studies also suggest a more favorable cardiovascular safety profile than sumatriptan.[4] In a comparative assessment of almotriptan and sumatriptan, patients reported they were more satisfied with the side effects profile of almotriptan.[5] Subjects were asked "how bothered" they were by any side effects of the study medication. No differences were reported in terms of pain relief, functional status, or health-related quality of life. Almotriptan, as with naratriptan, does not appear to interact with propranolol as some patients may be taking the latter for migraine prophylaxis.[6]

Potential Disadvantages

As with other 5-HT 1B/1D agonists, almotriptan is contraindicated in patients with documented ischemic heart disease or symptoms consistent with ischemic heart disease.[1] Cerebrovascular (eg, stroke), vasospastic-related events (eg, colonic ischemia), and increases in blood pressure have been reported with 5-HT1 agonists.

Almotriptan is metabolized by monamine oxidase and, to a lesser degree, cytochrome P450 3A4 and 2D6. Inhibitors of MAO and CYP 3A4 are expected to reduce the elimination of almotriptan. Coadministration with SSRIs has been reported, albeit rarely, to cause weakness, hyperflexia, and incoordination.[1]

Comments

Almotriptan is a 5-HT 1B/1D receptor agonist similar to other triptans such as sumatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan. These drugs are thought to act on the receptors in meningeal arteries and trigeminovascular nerve endings.[7] The newer agents have better oral bioavailability compared to sumatriptan. Their efficacy and recurrence rates appear to be similar with the possible exception of a lower efficacy with naratriptan and a lower recurrence rate and a faster onset with rizatriptan.[8] Almotriptan is priced the same for either strength, about $11 per tablet.

Clinical Implications

Almotriptan provides another alternative for the oral management of migraine. While differences among the triptans appear small, there may be a greater interpatient difference in response and tolerance.[7] Premarketing clinical studies suggest that almotriptan may have a low incidence of chest symptoms compared to what has been reported with sumatriptan. Chest symptoms have been reported as a frequent occurrence with sumatriptan, but are rarely significant.[9] There are no comparative studies among the triptans specifically assessing differences in chest pain. Some difference may be attributed to variations in subject inclusion and a wider definition of chest pain. Until there are data to clearly differentiate among the triptans, they are all contraindicated in patients with suspected or documented ischemic heart disease. ■

References

1. Axert Product Information. Pharmacia Corporation. May 2001.
2. Dodick DW. *Headache*. 2001;41(5):449-455.
3. Boyce M, et al. *J Cardiovasc Pharmacol*. 2001;37(3): 280-289.
4. Gras J, et al. *Eur J Pharmacol*. 2000;410(1):53-59.
5. Colman SS, et al. *Clin Ther*. 2001;23(1):127-145.
6. Fleishaker JC, et al. *Clin Pharmacol Ther*. 2000;67(5): 498-503.
7. Deleu D, Hanssens Y. *J Clin Pharmacol*. 2000;40(7): 687-700.
8. Tfelt-Hansen P, et al. *Drugs*. 2000;60(6):1259-1287.
9. Visser WH, et al. *Cephalalgia*. 1996;16(8):554-559.

Yasmin— A Novel New Oral Contraceptive

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

The fda has approved berlix's "yasmin," a unique new monophasic oral contraceptive. The product contains ethinyl estradiol and drospirenone—a new progestogen. Drospirenone is an

analog of spironolactone, an aldosterone antagonist, and like spironolactone, drospirenone has antimineralocorticoid activity. As such, its antiandrogenic and antimineralocorticoid actions are closer to progesterone than to other progestogens such as desogestrel or levonorgestrel. Drospirenone is also being touted as a more "natural" progestogen.

Indications

Ethinyl estradiol/drospirenone (DRSP/EE) is indicated for the prevention of pregnancy in women who elect to use an oral contraceptive.[1]

Dosage

DRSP/EE is taken once daily. It may be started the first day of the menstrual period or on the first Sunday after the onset of the menstrual period. Each blister pack contains 21 active tablets and 7 inert tablets. Each active tablet contains 30 mcg of ethinyl estradiol and 3 mg of drospirenone.

Potential Advantages

In addition to its antiandrogenic activity which reduces symptoms such as acne, seborrhea, and hirsutism, drospirenone also has antimineralocorticoid activity that reduces ethinyl estradiol-induced sodium and water retention.[2]

Potential Disadvantages

Drospirenone in Yasmin is comparable in its antimineralocorticoid activity to 25 mg of spironolactone.[1] It has the potential to cause hyperkalemia and should not be used in patients at risk for this condition. These include patients with renal insufficiency, adrenal insufficiency, and hepatic dysfunction. DRSP/EE must be used with caution in patients taking medication that may cause elevation of serum potassium (eg, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, potassium sparing diuretics, and NSAIDs). Drospirenone increases the concentration of plasmin renin activity and plasma aldosterone.[3]

Comments

DRSP/EE has been shown to be an effective contraceptive with good cyclic control compared to ethinyl estradiol/desogestrel.[4] Drospirenone is an analog of spironolactone and its pharmacologic profile closely resembles that of progesterone.[2]

DRSP/EE is an oral contraceptive that may slightly reduce body weight and blood pressure and improve preexisting acne and seborrhea.[2-4] In addition, it does not adversely affect lipid or carbohydrate metabolism.

DRSP/EE costs about $27 per cycle.

Clinical Implications

Yasmin is a new monophasic oral contraceptive with unique properties. Since weight gain has been cited as a concern in patients who discontinue the use of oral contraceptives,[5] DRSP/EE provides an alternative to other oral contraceptives in patients with a tendency to gain weight due to water retention. In addition, DRSP/EE is an alternative to the use of a progestogen with a low androgenic potential (eg, norgestimate or low-dose norethindrone) in patients with acne. ■

References

1. Yasmin Product Information. Berlix Laboratories. May 2001.
2. Krattenmacher R. *Contraception*. 2000;62:29-38.
3. Oelkers W. *Eur J Contracept Reprod Health Care*. 2000;5(Suppl 3):17-24.
4. Foidart JM. *Eur J Contracept Reprod Health Care*. 2000;5(Suppl 3):25-33.
5. Mansour D. *Eur J Contracept Reprod Health Care*. 2000;5(Suppl 3):9-16.

NCEP Guidelines and Implications for Cerebrovascular Disease

Source: *NCEP Expert Panel. JAMA. 2001;285:2486-2497.*

The third report on the evaluation and treatment of elevated cholesterol in adults was released in May 2001. The Adult Treatment Panel III (ATPIII) promotes a much more aggressive stance than its predecessors, particularly with regard to statin therapy in patients with only mildly elevated lipids.

As with previous National Cholesterol Education Program (NCEP) reports, the key lipid component for prevention of atherosclerotic disease is the LDL subfraction. This emphasizes the importance of carrying lipid testing beyond total cholesterol alone. As shown in the Table, among patients with coronary artery disease (CAD), LDL cholesterol should be below 100 mg/dL. If this cannot easily be achieved with diet, then lipid-lowering therapy with a statin agent should be implemented. Patients with symptomatic carotid artery disease are also to be placed in this top category.

Table

NCEP Cholesterol Management Guidelines

Risk Category	LDL Goal (mg/dL)	LDL Level— Lifestyle change needed	LDL Level— Drug therapy to be initiated
1) Coronary artery disease (or 10-year risk > 20%)*	< 100	‡100	‡130; (100-129, optional)
2) ‡2 risk factors** (10-year risk £ 20%)	< 130	‡130	a) 10-year CAD risk 10-20%; ‡130 b) 10-year CAD risk < 10%; ‡160
0-1 risk factors	< 160	‡160	‡190; (160-189, optional)

*10-year risk of coronary artery disease is determined using Framingham Point Scores (calculated on the basis of age, sex, blood pressure, tobacco use, and cholesterol levels)

**Major risk factors are: tobacco use, hypertension, low HDL-cholesterol levels (< 40 mg/dL), family history of premature CAD, and age (men ‡45, women ‡55)

In contrast to prior NCEP guidelines, all patients with diabetes mellitus are considered to have a "coronary artery disease risk equivalent," placing them automatically in the top category. The ATPIII also puts increased emphasis on the effects of elevated cholesterol in women and the elderly. While the majority of early data on statin therapy focused on only middle-aged men, recent studies have indicated the benefit of these agents across a wider range of age and gender.

The ATPIII also argues that patients with a distinct "metabolic syndrome" may gain benefits from statin therapy beyond merely lower cholesterol. This syndrome encompasses a spectrum of abdominal obesity, insulin resistance, atherogenic dyslipidemia (elevated triglyceride, small LDL particles, and low HDL cholesterol) as well as prothrombotic or proinflammatory states. Regression of atherosclerosis in these patients may be promoted with statin therapy. Treatment for hyperglycemia and the use of aspirin may be complementary.

Comment by Alan Z. Segal, MD

Perhaps the most striking aspect of the NCEP report is the unfortunate absence of any reference to stroke. Indeed, the NCEP panel does not include a neurologist and the Member Organization list does not include the American Stroke Association (ASA) or National Stroke Association (NSA).

This leaves neurologists who treat patients with stroke wondering: where does this leave me? If stroke is a vascular disease, can the recommendations as made here for heart disease be followed in parallel? How should prior stroke be factored in among other markers of atherosclerotic disease?

Most information regarding the use of statin therapy for patients with stroke derives from the cardiac literature (patients with CAD). Specific data regarding stroke patients are lacking. Certain forms of stroke, such as those caused by atrial fibrillation or cardiac embolism, may not bear a relation to cholesterol levels. The risk of other forms of stroke such as intracerebral hemorrhage may actually be magnified by low cholesterol.

Stroke is, nevertheless, a vascular disease. For this reason, neurologists should err on the side of caution. Lowering of LDL cholesterol to Category I goals (< 100 mg/dL) or at least Category IIa (< 130 mg/dL) is recommended until more disease-specific data are available. ■

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Pioglitazone Improves Lipid Profiles More Effectively than Rosiglitazone

Source: *Gegick CG, Altheimer MD. Endocr Pract. 2001;7:162-169.*

The objective of this study was to compare short-term glycosylated hemoglobin (HbA1c), lipid, weight, tolerability, and hepatic effects after switching patients with type 2 diabetes from troglitazone to either pioglitazone or rosiglitazone treatment.

A total of 144 and 125 patients met the criteria for comparison of HbA1c and lipids, respectively. HbA1c decreased 0.08% for each treatment group, after a mean

Table

Lipid Changes After Changing From Troglitazone

Lipid	Before mg/dL	After mg/dL
Pioglitazone		
Total Cholesterol	190.6	181.6
Triglycerides	208.5	184.9
HDL	46.7	47.9
LDL	104.6	97.0
Rosiglitazone		
Total Cholesterol	180.0	195.0
Triglycerides	178.7	247.4
HDL	44.1	41.3
LDL	100.0	108.1

3.2 months of observation. 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. Mean high-density lipoprotein (HDL) increased 2.6% with pioglitazone and decreased by 6.3% with rosiglitazone.

Patients receiving a statin concomitantly when switched to rosiglitazone treatment had a 51.9% increase in mean triglyceride levels vs. a 25.7% increase in those not receiving a statin, whereas the patients switched to pioglitazone therapy had respective decreases of 14.2% and 6.2%. Both drugs were generally well tolerated and had similar slight weight increases and no hepatic dysfunction.

Switching to pioglitazone caused a trend toward lipid profile improvement, but switching to rosiglitazone therapy caused a significant increase in all lipids, except HDL, which was lowered. Patients receiving statins when switched to rosiglitazone had particularly notable triglyceride worsening. Whether these effects will lead to changes in cardiovascular outcome or will be maintained over a longer period of time remains to be established.

Comment by Ralph R. Hall, MD, FACP

Despite the short-term nature of this study and the lack of patient randomization, these are remarkable changes in risk patterns. Further, this is how it happens in our practices. Other medications such as metformin, monotherapy with troglitazone, sulfonylurea treatment, and others were similar for each group of patients.

The changes seen in HDL cholesterol and triglycerides suggest that the patients switched to rosiglitazone had an increase in the more atherogenic small dense LDL. With these changes and the availability of pioglitazone, it would be difficult to maintain treatment with rosiglitazone until more safety and long-term studies were completed.

One other item of note is that these patients had been treated for their HbA1c and lipid goals prior to the change from troglitazone to the other thiazolidinediones. The study also demonstrates that the national goals for HbA1c and lipids can be met in clinical practice. ■

Dr. Hall is Emeritus Professor of Medicine, University of Missouri-Kansas City School of Medicine, Kansas City, Mo.

Combined Bisphosphonate and Hormone Treatment

Source: *Harris ST, et al. J Clin Endocrinol Metab. 2001;86: 1890-1897.*

Harris and colleagues report the results of a multicenter, 1-year, double-blind, placebo-controlled study of the effect on bone mineral density of risedronate (5 mg daily) combined with conjugated estrogens (0.625 mg daily) compared with estrogen alone in a total of 524 women. Forty-eight percent of the patients also received medroxyprogesterone (5 mg) in a sequential regimen. At the end of 1 year, both treatment groups increased bone mineral density. (*See Table*).

The only differences that achieved statistical significance were those in the femoral neck and midshaft radius. Bone biopsies in a subset of patients demonstrated normal bone structure and mineralization in both groups. After 1 year, there were 4 new vertebral fractures (2.6%) in the hormone-only group and 3 (1.8%) with the combined treatment; however, this study had insufficient

Table

Gain in BMD with Treatment

Lumbar	Femoral spine	Midshaft neck	Radius
Hormone therapy alone	4.6%	1.8%	0.4%
Combined risedronate & hormone therapy	5.2%	2.7%	0.7%

power to detect meaningful differences in fractures.

Comment By Leon Speroff, MD

There is growing recognition that not all postmenopausal women respond to treatments aimed at the prevention of bone loss. Clinicians have rapidly assumed that the solution is to combine treatments. There are 2 important questions:

1. Will a slightly better gain in bone density mean better protection against fractures?
2. Will a poor responder to 1 treatment respond to an alternative treatment?

Adding alendronate or risedronate to postmenopausal hormone therapy produces a gain in bone density that is about 1-2% greater than with single treatment, indicating that each works through a different mechanism. There is no doubt that both lack of bone loss and a gain in bone mineral density correlate with a reduction in fractures. However, that does not mean that a 7% gain protects against fractures better than a 5% gain. One piece of evidence that suggests a difference in bone density is not the whole story is the fact that raloxifene produces a smaller increase in vertebral bone density compared with estrogen and alendronate, yet the 3 agents are associated with essentially identical reductions in vertebral fractures. No study, thus far, has had a sufficient number of patients followed long enough to provide reliable fracture information with combined therapy compared to single agent treatment.

The percentage of postmenopausal women who respond poorly to single agent treatment varies from 5-20% in various studies. This is a substantial number, and underscores the recommendation to screen 65-year-old women with bone density measurements even if they are on osteoporosis prevention treatment. This would detect the poor responders and provide the opportunity for intervention. However, studies of this group of women have yet to appear in the literature. At this time we can only provide the proper intervention, follow the patient, and learn from the patients.

Recommended Evaluation and Intervention for Poor Responders:

1. Rule out other causes of osteoporosis.
2. Make sure calcium and vitamin D supplementation is adequate.
3. Make sure compliance with the treatment is appropriate.
4. Add another antiresorptive agent to the treatment regimen.
5. After 2 years, assess bone density response.

The bone world has expressed concern that combining 2 agents that both inhibit bone resorption might over time interfere with the dynamics of bone remodeling and ultimately yield more fragile bone. This is speculation at the present time, and the biopsy results in this study indicating normal bone morphology and mineralization are reassuring. This has also been reported with combined alendronate and estrogen treatment.[1] In addition, tetracycline labeling appeared in the biopsy specimens indicating that the necessary bone turnover to repair microdamage was taking place.

At the present time, it is premature to assume that combined agent therapy will yield better fracture protection. We need evidence from bigger studies with longer follow-up. ■

Reference

1. Bone HG, et al. *J Clin Endocrinol Metab*. 2000;85: 720-726.

Race and the Response to Carvedilol

Source: *Yancy CW, et al. N Engl J Med. 2001;344:1358-1365.*

The best study showed a poor response to the beta-blocker bucindolol in black individuals.[1] Also, the SOLVD studies showed lack of efficacy of the angiotensin-converting enzyme inhibitor enalapril in blacks with reduced left ventricular (LV) function, with or without overt heart failure.[2] Thus, the report of Yancy and colleagues for the US Carvedilol Heart Failure Study Group is of interest. Of the 1094 patients with symptomatic heart failure and LV ejection fraction (EF) < 35% despite maximal therapy with conventional therapy, 217 (20%) were black. The end points of LVEF, clinical status, and major cardiac events were retrospectively compared in this randomized, placebo-controlled trial between the blacks and nonblacks. The combined end point of death or hospitalization for any reason was reduced 48% in blacks and 30% in nonblacks (P = NS) by carvedilol vs. placebo. Clinical progression of heart failure was also significantly reduced by carvedilol in both groups (relative risk [RR] in blacks 0.46 and 0.49 in nonblacks). LVEF increased in both groups on carvedilol (10% in blacks, 8% in non-

blacks; $P < 0.001$ for both). During the 2-week open-label carvedilol therapy period, the number of blacks who discontinued therapy was similar to nonblacks (5% vs 7%, respectively) as was withdrawal for adverse events throughout the study. Yancy et al concluded that the response to carvedilol added to conventional therapy in patients with symptomatic heart failure due to systolic dysfunction is of similar magnitude in blacks and nonblacks.

Comment by Michael H. Crawford, MD

The results of this analysis of the Carvedilol Study Group pooled data is encouraging for the treatment of heart failure in blacks, since they are known to have a higher incidence of heart failure compared to nonblacks, and have more rapid progression of heart failure once diagnosed. The reason heart failure is more common in blacks may be due to their higher incidence of hypertension and diabetes, or environmental factors such as restricted access to health care. Thus, heart failure in blacks is a major public health problem.

The major criticism of this study is that it was not a prospective, randomized trial of response in different racial groups. In fact, the nonblack group included those of European, Asian, and Native American descent. So the results could be just due to vagaries of patient selection. However, the blacks in this study had similar characteristics to the blacks in other heart failure trials, namely a higher incidence of hypertension and less ischemic heart disease.

Why blacks did better on carvedilol than the results reported for bucindolol may be due to the alpha-blocking properties of carvedilol. Interestingly, labetolol, a combined alpha-beta-blocker, has been shown to be superior to propranolol in blacks with hypertension.[3] Also, alpha blockade may improve insulin sensitivity and serum lipids in patients on a beta-blocker, which may be especially important in blacks with vascular disease. Whatever the mechanism, until further data are forthcoming, blacks with heart failure who are treated with beta-blockers should probably receive carvedilol. ■

References

1. BEST Investigators. *N Engl J Med*. 2001;344:1659-1667.
2. Exner DV, et al. *N Engl J Med.* 2001;344:1351-1357.
3. Flammenbaum W, et al. *J Clin Hypertens*. 1985;1:56-69.

CME questions

Testing form inserted in the January 2002 issue

1. **The bucindolol vs. placebo for heart failure treatment showed:**
   a. no difference in all-cause mortality.
   b. increased cardiovascular death.
   c. reduced ejection fraction.
   d. equal efficacy in black patients.
2. **Which one of the following statements is *false*?**
   a. The change in HDL cholesterol was more favorable with pioglitazone than with rosiglitazone.
   b. The increase in triglycerides that occurred is probably not important.
   c. Hepatic dysfunction was not a problem with either pioglitazone or rosiglitazone.
   d. The rise in triglycerides and the fall in the HDL lipoproteins in the rosiglitazone group is consistent with a change to small dense LDL cholesterol, which is more athergenic.
3. **The following statements are true regarding osteoporosis prevention therapy *except*:**
   a. Bisphosphonate and estrogen treatment produce comparable effects on bone density.
   b. It is worthwhile to try to gain as much bone density as possible.
   c. All the currently approved agents for the prevention of osteoporosis produce comparable effects on reduction of vertebral fractures.
   d. There is concern that long-term follow-up of treated patients will yield different results than short-term bone density studies.

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