CME Digest

ANTIVIRAL THERAPY IN HIV INFECTION: PRACTICAL GUIDELINES

The latest data on treatments for human immunodeficiency virus (HIV) infection support the use of antiviral medication soon after a diagnosis of HIV infection has been made. Such an approach has been shown to have beneficial effects on immune function and to slow progression of HIV infection. Use of zidovudine in later-stage HIV disease has been shown to prolong healthy life. Despite the advances made with other antivirals, zidovudine still appears to be the best drug to initiate early treatment. But in starting any antiviral treatment, physicians should remember that these agents are only one part of a total health care plan.

In patients never treated with zidovudine, if the CD4 count is greater than 300/μL, zidovudine should be used alone. However, if the CD4 count is below 300/μL, zidovudine should be combined with dideoxycytidine (ddC). Dideoxycytidine can lead to peripheral neuropathy in a significant minority of patients. A combination of zidovudine and dideoxyinosine (ddI) may prove to be less toxic. A trial is currently underway examining four different treatment protocols: zidovudine alone, ddI alone, ddI plus zidovudine, and ddC plus zidovudine. Whenever any one of these potent antivirals is used in combination, the risk of side effects must be balanced against the therapeutic advantage. Combinations using three drugs are now being evaluated.

Among patients currently taking zidovudine or who have previously used the drug for more than 4 months, the major therapeutic dilemma is knowing when to switch or add drugs. The development of new viral assays may make that question easier to answer by indicating when the virus has become resistant to the current regimen.

Stable patients with CD4 counts above 300 should continue to take zidovudine. If the count drops below 300 and the HIV infection is progressing, they should be switched to ddI. The addition of ddI or ddC to the zidovudine regimen is also a possibility for these patients. Results from a recent trial suggest combination therapy is better than single-drug therapy for such patients with CD4 counts above 50.

Despite the moderate degree of success associated with these antivirals, their potency can lead to debilitating side effects—some so serious that drug withdrawal is the only solution. Zidovudine treatment can result in headaches, nausea, anemia, and neutropenia. Dideoxyinosine treatment can result in peripheral neuropathy and, occasionally, severe pancreatitis. The rate of pancreatitis and hyperamylasemia were about twice that seen in zidovudine-treated patients.

Dideoxyinosine has one other minor problem: the drug is destroyed by stomach acids and must be given with a buffer on an empty stomach.

Dideoxycytidine, besides causing peripheral neuropathy in 17% to 31% of patients who take it, can cause esophageal and oral ulcers, mild nausea, and abdominal pain. This drug does not cause bone marrow suppression.

New classes of anti-HIV drugs and combinations are now being tested in small trials. We hope these studies will provide promising new drugs in the near future.

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TREATING HYPERTENSION IN OLDER PATIENTS: SPECIAL CONSIDERATIONS

In patients 55 and older, the value of treating hypertension is now well established, regardless of race, sex, and blood pressure subgroups. There are, however, certain considerations to keep in mind when embarking on a course of antihypertensive drug therapy in an older patient.

In general, older patients tolerate active treatment well. For example, diuretics and beta blockers, when started in low doses, are safe and effective. The initial goal of therapy is to bring the systolic pressure down to less than 160 mm Hg in those whose pressure is over 180 mm Hg at the outset, and to lower the pressure by 20 mm Hg in those whose pressure is between 160 and 179. When isolated systolic blood pressure is 140 to 160, life-style modifications may be considered as either adjunctive or definitive therapy. If these lower pressures are well tolerated, it may be appropriate to reduce the blood pressure even further.

The goal of therapy for diastolic hypertension in older patients is similar to that of the general population, ie, less than 90 mm Hg.

POTENTIAL OBSTACLES TO TREATMENT

Certain physiologic changes occur with aging and should be considered when planning antihypertensive drug therapy in the elderly. With age, cardiac output falls, whereas total peripheral resistance rises and blood volume contracts. Renal and hepatic function falls off and the autonomic nervous system, particularly the baroreceptors, show a diminished response. There is a progressive loss of autonomic neurons with aging.

Pharmacodynamic profiles of antihypertensive drugs are different in the elderly because of diminished gastric emptying, decreased liver blood flow, a lower concentration of serum albumin, and a relative increase in body fat. These alterations can contribute to more drug-drug interactions and more side effects unless dosing is reduced appropriately. Concomitant disease such as diabetes, degenerative arthritis, congestive heart failure, coronary artery disease, cerebral and peripheral vascular disease, bronchospastic disorders, gout, and diminishing mental acuity are obstacles to the success of any drug program.

The overriding maxim for antihypertensive drug therapy remains "start low, go slow." In addition, always measure blood pressure in the standing and seated (or supine) positions. Antihypertensive drug therapy may exacerbate postprandial hypotension.

As the aggressive marketing of newer antihypertensive agents continues, it is important to keep in mind that, while all classes of antihypertensive drugs have been shown to be effective in lowering blood pressure in older patients, only diuretics and beta blockers have been used in controlled trials that have shown a reduction in cardiovascular morbidity and mortality.

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SUGGESTED READING

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