Mealtime therapy can fit into latitude 37.104, longitude -119.318.

Higher Losartan Dose Better for Heart Failure

BY MITCHEL L. ZOLER

ORLANDO — A 150-mg/day dosage of losartan was better for preventing events in heart failure patients than was the conventional, 50-mg/day dosage in a randomized comparison involving nearly 4,000 patients followed for more than 4 years. The finding immediately created a new, standard losartan dosage for these patients, experts said.

The higher dosage also led to no significant increase in patients’ stopping therapy because of adverse events, compared with the lower dosage.

“In patients with heart failure, reduced left ventricular ejection fraction, and angiotensin converting enzyme inhibitor intolerance, incremental value is derived from up-titrating angiotensin receptor blocker doses,” Dr. Marvin A. Konstam said at the annual scientific sessions of the American Heart Association.

“If a clinician is using losartan to treat patients with heart failure, he or she must know that if you up-titrate to 150 mg/day you’re going to get better outcomes,” he said.

Experts agreed that the finding should be applied in practice immediately.

“All [heart failure] patients on losartan today need to be reevaluated and probably up-titrated to the high dose,” said Dr. Karl Swedberg, professor of medicine at Göteborg (Sweden) University, who was not involved in the study. “Symptom improvement is not a surrogate for life prolongation. There is no way around it; if you want to give the best care for a patient you should up-titrate the dose.”

This message was viewed as especially important because many heart failure patients receive inappropriately low doses of the drugs that inhibit the renin-angiotensin system: ACE inhibitors and angiotensin-receptor blockers (ARBs).

“Physicians now do not prescribe anything close to the target doses” of ACE inhibitors and ARBs, said Dr. Milton Packer, professor of medicine at the University of Texas Southwestern Medical Center in Dallas.

“In the study [reported by Dr. Konstam], the biggest difference [from the higher, 150-mg/day dosage] appeared to be in the patients with class I or II heart failure. These are the very patients in whom we don’t up-titrate the doses” right now, said Dr. John G.F. Cleland, a professor of medicine at the University of Hull, England.

The Heart Failure Endpoint Evaluation of Angiotensin II Antagonist Losartan (HEAAL) trial enrolled patients with symptomatic, New York Heart Association class II-IV heart failure who had a left ventricular ejection fraction of 40% or less. All enrolled patients had to have known intolerance to ACE inhibitors. Patients enrolled at 255 sites in 30 countries during November 2001–March 2005. Their average age was 66 years, 70% were men, 60% were white and 22% were Asian. Patients had to be on a stable drug regimen, and most were on current standard therapy, including 72% on a beta-blocker and 38% on an aldosterone blocker; 70% had class II heart failure and 30% had class III. Randomization assigned 1,921 patients to the 150-mg/day dosage and 1,913 to the 50-mg/day regimen.

After a median follow-up of 4.7 years, the incidence of the primary end point, death or hospitalization for heart failure, occurred in 43% of patients on the higher dose and 46% on the lower dose, a 3% absolute difference that was statistically significant, reported Dr. Konstam, professor of medicine and director of the cardiovascular center at Tufts University in Boston. Concurrently with his re-
Indication
Humalog (insulin lispro injection [rDNA origin]) is for use in patients with diabetes mellitus for the control of hyperglycemia. Humalog should be used with longer-acting insulin, except when used in combination with sulfonylureas in patients with type 2 diabetes.

Important Safety Information
Humalog is contraindicated during episodes of hypoglycemia and in patients sensitive to Humalog or one of its excipients.

Humalog differs from regular human insulin by its rapid onset of action as well as a shorter duration of action. Therefore, when used as a mealtime insulin, Humalog should be given within 15 minutes before or immediately after a meal.

Due to the short duration of action of Humalog, patients with type 1 diabetes also require a longer-acting insulin to maintain glucose control (except when using an insulin pump). Glucose monitoring is recommended for all patients with diabetes.

The safety and effectiveness of Humalog in patients less than 3 years of age have not been established. There are no adequate and well-controlled clinical studies of the use of Humalog in pregnant or nursing women.

Starting or changing insulin therapy should be done cautiously and only under medical supervision.

Hypoglycemia
Hypoglycemia is the most common adverse effect associated with insulins, including Humalog. Hypoglycemia can happen suddenly, and symptoms may be different for each person and may change from time to time. Severe hypoglycemia can cause seizures and may be life-threatening.

Other Side Effects
Other potential side effects associated with the use of insulins include: hypokalemia, weight gain, lipodystrophy, and hypersensitivity. Systemic allergy is less common, but may be life-threatening. Because of the difference in action of Humalog, care should be taken in patients in whom hypoglycemia or hypokalemia may be clinically relevant (eg, those who are fasting, have autonomic neuropathy or renal impairment, are using potassium-lowering drugs, or taking drugs sensitive to serum potassium level).

For additional safety profile and other important prescribing considerations, see accompanying Brief Summary of full Prescribing Information.

Please see full user manual that accompanies the pen.

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