β-Agonists in LQTS Raises Cardiac Risks

BY BRUCE JANCIN
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CHICAGO — The use of β_2-agonists for bronchodilation in asthma patients with hereditary long QT syndrome doubles their risk of serious cardiac events, Princy Thottathil reported at the annual meeting of the American College of Cardiology.

That's the bad news. The good news is concomitant β-blocker therapy essentially neutralizes this increased risk, she said.

But while β-blockers are routinely recommended in patients with long QT syndrome (LQTS) to reduce sympathetic activation and decrease stimulation to the heart, they are underutilized for this purpose. Of 3,287 patients in the International LQTS Registry, only 49% were on a β-blocker. And in the subset of 101 registry participants on β_2-agonist therapy for asthma, only 66% were also on a β-blocker, said Ms. Thottathil, a medical student at the University of Rochester (N.Y.).

The risk was greatest during the first year after initiation of β-agonist therapy, when the patients were at an adjusted 3.5-fold increased risk of cardiac events.

"What we're suggesting is if a patient with LQTS has asthma and needs to be on a β_2-agonist, consider giving them a β-blocker," she said in an interview.

The problem with β_2-agonist therapy in patients with LQTS is that it results in costimulation of cardiac β_2-receptors, potentially resulting in prolonged repolarization and ventricular tachycardia, she explained.

The primary end point in her study of the International LQTS Registry population was the combination of syncope, aborted cardiac arrest, or sudden cardiac death through age 40. Patients on β-agonist therapy for asthma were at a twofold increased risk after adjustment for gender, history of asthma, QT interval, and other factors.

This risk was greatest during the first year after initiation of β-agonist therapy. During that first year, patients on a β_2-agonist were at an adjusted 3.5-fold increased risk of cardiac events. The risk dropped off subsequently, perhaps because of adaptation to the drug dosage, Ms. Thottathil said.

The combination of a β-agonist and a corticosteroid is often recommended in asthma patients, especially children. But the addition of a steroid further increased the risk of cardiac events; individuals with LQTS on this combination had a 3.7-fold increased risk of cardiac events, compared with those on neither drug. The explanation is probably that anti-inflammatory steroids can costimulate the β_2-receptor, she continued.

The elevated risk of the combined cardiac end point observed in LQTS patients on β-agonist therapy was reduced by 86% in patients on a β-blocker. ■

Statins Reduce BP, Even in the Normotensive

BY MARY ANN MOON
Contributing Writer

Statins reduced systolic and diastolic blood pressure, even in normotensive subjects and those with "prehypertension," in a secondary analysis of data collected in the University of California, San Diego, Statin Study.

Both simvastatin, the most lipophilic statin, and pravastatin, the most hydrophilic statin, were found to decrease blood pressure "substantially, although the mean absolute magnitude of the change was modest in this largely nonhypertensive sample receiving relatively low statin dosages," Dr. Beatrice A. Golomb and her associates at the university reported based on their analysis.

The investigators used data from the large 6-month UCSD Statin Study to assess the impact of the anticholesterol drugs on blood pressure because data from many small studies have suggested that statins improve hypertension.

However, these studies "have been correlational, uncontrolled, tested against other active drugs with uncertain impact on BP, unblinded, nonrandomized, or without assessment of statistical significance," they noted.

In contrast, the UCSD Statin Study randomly assigned 973 participants (about 68% men) to 20 mg/day simvastatin, 40 mg/day pravastatin, or placebo in a double-blind fashion and

assessed several factors, including blood pressure, at 1 month and 6 months, as well as at 2 months after the study was completed.

Blood pressure level was not a primary end point of the initial analysis.

The mean age of the placebo patients was nearly 58 years; the treated patient mean was nearly 57 years. More than 80% of the patients were white.

In the secondary analysis by Dr. Golomb and her associates, all of the participants, regardless of their blood pressure status at baseline, showed reductions in systolic and diastolic pressure after 1 month of statin treatment, though the difference between active therapy and placebo was nonsignificant at that point.

By 6 months, the participants in both of the statin groups showed significant reductions in blood pressure, compared with participants in the placebo group.

This refutes the findings of a previous study in which researchers suggested that statins decrease only high blood pressure.

For both drugs, the reductions in blood pressure ranged from 2.4 to 2.8 mm Hg for both systolic and diastolic blood pressure.

However, these differences had dissipated at follow-up assessment 2 months after the treatment was discontinued, reported Dr. Golomb and her associates (Arch. Intern. Med. 2008;168:721-7).

Statin-induced decreases in blood pressure, although they might be "modest," may well "contribute to reductions in transient ischemic attacks and stroke" that have been reported with statin therapy, they added.

Participants who had normal blood pressure, as well as those with "prehypertension," showed declines in blood pressure similar to those seen with hypertension, according to the findings of the analysis.

This refutes the findings of a previous study in which researchers suggested that statins decrease only high blood pressure, the investigators noted.

The current study excluded participants who had diabetes, known cardiovascular disease, and very high or very low LDL cholesterol levels, so the findings might not extend to those groups, the researchers added. ■