ASCOT-LLA Trial

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Methods

Of the 19,342 patients with hypertension (aged 40 to 79 years with at least three other cardiovascular risk factors) randomized to one of two antihypertensive regimens in the Anglo-Scandinavian Cardiac Outcomes Trial–Lipid Lowering Arm (ASCOT-LLA), 10,305 patients with non-fasting total cholesterol concentrations ≤ 6.5 mmol/L were randomly assigned additional atorvastatin, 10 mg, or placebo. These patients formed the lipid-lowering arm of the study.

A followup was planned for an average of five years, the primary end point being nonfatal myocardial infarction and fatal coronary heart disease. Data was analyzed with the intention to treat.

Results

Treatment was stopped after a median followup of 3.3 years. By that time, 100 primary events had occurred in the atorvastatin group, compared with 154 events in the placebo group.

This benefit emerged in the first year of followup. There was no significant heterogeneity among prespecified subgroups.

Fatal and nonfatal stroke, as well as total cardiovascular events were reduced in the atorvastatin-treated group.

Total serum cholesterol and coronary events were also significantly lowered. There were 185 deaths in the atorvastatin group, compared to 212 in the placebo group.

Dr. Lin's comments

In 1948, the Framingham Heart Study started and, in 1961, cholesterol and hypertension were found to be contributory to heart attacks. Since then, the last three decades have been spent proving that treating hypertension and cholesterol is beneficial.

Many trials have looked at the benefits of treatment versus no treatment in specific populations. Patients with the highest risks were studied first and, when the therapies proved successful, other, less ill patients, were studied.

The ASCOT study put two big risk factors together in one trial—hypertension and cholesterol. Before the study began, it was already well-established that hypertension needed to be treated; the question remained, were new drugs better than old ones? To answer this, patients were randomized to beta blockers and diuretics versus calcium channel blockers and angiotensin-converting enzyme inhibitors. This part of the study is still ongoing.

The cholesterol question, however, was different. It was known patients with high cholesterol needed treatment, so they all received therapy in the trial. The real question was should patients with cholesterol levels < 6.5 mmol/L be treated?

All the patients in this part of the study had hypertension, along with three other cardiac risk factors. Half of these individuals were given atorvastatin and the rest were given placebo. The primary end point was cardiac events.

This part of the study was stopped prematuely because of the overwhelming benefit of treatment. It became unethical to continue to withhold treatment from the 5,000 people in the placebo arm.

The study was designed for five years, but after 3.3 years, it was clear that treatment with the statin was superior. The main end point of cardiac events was reduced by 36% in the atorvastatin-treated group. More striking, however, was the reduction in strokes by 27%.

It can be concluded that in patients with hypertension, like those in the ASCOT trial, reducing cholesterol is paramount.

About the author...
Dr. Lin is the past medical director, University of Toronto Health and Wellness Centre at Scarborough, Scarborough, Ontario.