Perioperative β-Blockade May Raise Stroke Risk

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Perioperative β-blockers may reduce the risk of myocardial infarction after noncardiac surgery, but they confer a doubling in the risk of disabling strokes, especially among lower-risk patients, according to a meta-analysis of 33 randomized controlled trials.

In light of these findings, the guideline committee of the American College of Cardiology, which recommends the drugs for patients undergoing noncardiac surgery, "should soften their stance on perioperative β-blockade until definitive evidence shows clear benefit," Dr. Sripal Bangalore wrote in an article published online in The Lancet (doi:10.1016/S0140-6736(08)61560-3). "β-Blockers should not be routinely used for perioperative treatment … unless patients are already taking them for clinically indicated reasons."

Trials including high-risk patients drove the beneficial effects of β-blockers, while trials with low- or intermediate-risk patients drove the risks.

The risks associated with β-blockers were most apparent in trials that included low- to intermediate-risk patients, particularly the recent Perioperative Ischemic Evaluation (POISE) trial, which is considered a landmark study (Lancet 2008;371:1839-47). POISE, which included more than 8,300 patients randomized to extended-release metoprolol succinate or placebo before surgery, found a doubling in the risk of stroke among those in the active group.

The drugs also were associated with significant increases in other cardiac problems, wrote Dr. Bangalore of Brigham and Women's Hospital, Boston, and his colleagues. "For the overall cohort, we estimate that treatment of 1,000 patients with β-blockers results in 16 fewer nonfatal myocardial infarctions in survivors, but at the expense of three disabling strokes, 45 patients with clinically significant perioperative bradycardia, 59 with hypotension, and potentially increased mortality."

The 33 trials included in the meta-analysis comprised 12,300 patients: 6,300 randomly assigned to β-blockers and 6,000 given placebo. The trials varied with regard to the drug used, the dosage, and the timing and duration of administration.

Overall, β-blockers did not result in any significant decrease in the risk of all-cause mortality, cardiovascular mortality, or heart failure. There was a 35% decreased risk of nonfatal heart attack (number needed to treat [NNT]: 63), and a 64% decreased risk of myocardial ischemia (NNT: 16). But the investigators also found a 116% increased risk of nonfatal stroke (number needed to harm [NNH]: 275), based on trials with low- or intermediate-risk patients.

β-Blockade also resulted in a tripling of the risk of perioperative bradycardia (NNH: 8), as well as a 70% increased risk of perioperative hypotension (NNH: 17).

When the researchers examined outcomes according to the risk level of patients in each trial, trials including high-risk patients drove the beneficial effects of β-blockers, while trials with low- or intermediate-risk patients drove the risks.

In high-risk trials, the investigators found no increased risk of all-cause mortality, an 81% decreased risk of nonfatal MI (NNT: 15), and a 69% decreased risk of MI (NNT: 9), although there were no significant benefits for cardiovascular mortality or heart failure.

Trials conducted using low- or intermediate-risk patients found a 28% increased risk of all-cause mortality (NNH: 164), and a 116% increased risk of nonfatal stroke (NNH: 275), with a 28% decreased risk of nonfatal MI (NNT: 80), a 59% decreased risk of myocardial ischemia (NNT: 23), and no reduction in rates of cardiovascular mortality or heart failure.

The POISE trial carried the most statistical weight among lower-risk trials, while a 1999 study drove the findings among high-risk trials. That study randomized 59 high-risk patients to perioperative bisoprolol or standard care. Nine patients in the standard-care group and two in the bisoprolol group died of cardiac causes during the perioperative period (N. Eng. J. Med. 1999;341:1789-94).

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