Data Alert #7

MIRACL: Very early statin therapy not guided by cholesterol levels is beneficial in acute coronary syndromes

Dear Colleague:

Final results of the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) trial have been published and confirm that treatment with atorvastatin 80 mg/d early during an acute coronary syndrome (ACS) reduces the risk of early recurrent events, primarily recurrent symptomatic ischemia during hospitalization. MIRACL closes a treatment gap, because previous trials of statin therapy have excluded patients with recent unstable angina or acute MI. It is within the early period after an acute coronary syndrome that patients experience the highest rate of death and recurrent ischemic events.1

Addressing the treatment gap

The MIRACL trial (an international, randomized, placebo-controlled, double-blind trial) was initiated to examine if early, rapid, and intensive reduction in serum lipids with high-dose atorvastatin would reduce early recurrent ischemic events in patients with unstable angina and non-Q-wave MI.

Trial design

The benefits seen with MIRACL were significant. Earlier work has shown that lipid-lowering therapy appears to stabilize plaque, decrease local inflammation, and can render the lesion potentially less thrombotic, which decreases coronary events and lengthens longevity.  

MIRACL was not planned to be able to detect differences between treatment groups in the individual components of the primary composite outcome. Although death, nonfatal MI, and cardiac arrest tended to occur less frequently in the atorvastatin group than in the placebo group, the difference in these outcome events was not statistically significant. Most of the intergroup differences in the combined primary outcome resulted from a reduction in recurrent symptomatic myocardial ischemia and emergency rehospitalization.

16% reduction to first ischemic event

26% reduction in worsening angina requiring repeat hospitalization


Role of statin therapy in the discharge plan

The MIRACL results for both outcomes and safety add statin therapy to the physician’s armamentarium for reducing CV risk in acute myocardial infarct patients. Using data from the National Registry of Myocardial Infarction 3, Fonarow and co-workers found that lipid-lowering medications were part of the discharge regimen in only 31.7% of the patients. There is also potential for improving compliance. Muhlestein and fellow investigators studied patients who had an angiographic diagnosis of CAD. The investigators found that a prescription of appropriate statin therapy at the time of hospital discharge improved long-term statin compliance versus patients not discharged with a statin prescription, 77% vs 40%, respectively.

Implications for clinical practice

Several retrospective analyses have recently demonstrated the benefits of early cholesterol reduction after an acute coronary syndrome: MITRA 1 & 2, PRISM, and the Frankfurt Stent Study. Using data taken from the GUSTO IIb and PURSUIT trials, Aronow and co-workers have shown that early lipid lowering therapy was associated with reduced death and MI after all types of ACS. The Swedish Register of Cardiac Intensive Care, a prospective cohort study, found that early initiation of statin treatment in patients with AMI was associated with reduced 1-year mortality. These nonrandomized data support the conclusions found in the randomized MIRACL trial.

In MIRACL, the reduction of primary ischemic events by atorvastatin did not appear to depend on the baseline level of LDL cholesterol. This observation suggests that the decision to begin intensive lipid-lowering therapy after an ACS should not necessarily be influenced by serum lipid levels at the time of the event.

Early and intensive lipid-lowering therapy is safe. In MIRACL, there were no documented cases of myositis. Levels of serum transaminases exceeding 3 times the ULN were detected in 2.5% of atorvastatin treated patients and 0.6% of placebo-treated patients.
From the apparent clinical benefit and the lack of early adverse side effects of significance, the MIRACL trial results suggest no reason why early treatment with lipid-lowering therapy should not be implemented. Initiating lipid-lowering therapy prior to discharge offers the opportunity not only to reduce the risk of recurrent CV disease but to improve long-term therapeutic compliance.

Sincerely,

Carl J. Pepine, MD
REFERENCES


