In-Hospital Initiation of Lipid-Lowering Therapy for Patients With Coronary Heart Disease
The Time Is Now

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In the last 2 decades, in-hospital mortality for acute coronary syndromes and percutaneous and surgical revascularization has decreased markedly. To continue to make progress and to meet the goal set by the American Heart Association (AHA) of reducing coronary heart disease (CHD) and stroke by 25% by 2010, the focus of treatment in patients hospitalized with CHD must evolve from treating symptoms of the disease to treating the underlying disease process of atherothrombosis. Although dietary therapy is recommended for all patients with CHD, the recommendations for when to initiate lipid-lowering drug therapy have not been as clear, partly because of a lack of data on the benefits, risks, and costs of immediate initiation of therapy versus delayed initiation after a trial of diet and lifestyle modification.

Numerous studies have shown that the conventional practice of delaying lipid-lowering medications simply does not work as well as algorithm-guided in-hospital initiation of treatment in regard to patients’ being started on therapy, remaining on therapy for the long-term, and achieving target low-density lipoprotein cholesterol (LDL-C) levels. Is there now enough evidence to adopt in-hospital initiation of lipid-lowering therapy in CHD patients as the standard of care?

Despite clinical trials demonstrating that lipid-lowering medications reduce mortality in patients with established CHD and national guidelines calling for their use, study after study has demonstrated that these therapies continue to be underused. Studies of treatment rates for patients discharged after cardiac hospitalization show a large number of high-risk patients are not receiving lipid-lowering treatment. An analysis of 138,001 patients from 1470 US hospitals in the National Registry of Myocardial Infarction 3 revealed that only 31.7% of patients hospitalized with acute myocardial infarction (MI) were discharged on lipid-lowering therapy. 4 Similarly, among the 8515 patients hospitalized with an acute coronary syndrome and enrolled in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial, only 25.1% were discharged on lipid-lowering therapy. 5

In the outpatient setting, this treatment gap persists. The Quality Assurance Project analyzed treatment rates in 48,586 outpatients with CHD from 140 medical practices (80% cardiology). 6 Only 39% of these patients were treated with lipid-lowering medications and only 11% were documented to have LDL-C levels <100 mg/dL. In the third National Health and Nutrition Examination Survey (NHANES III), lipid-lowering medication was used in an estimated 11% of participants with CHD. 7 In the Lipid Treatment Assessment in Practice (L-TAP) study, only 18% of outpatients with CHD treated for hyperlipidemia had LDL-C levels <100 mg/dL. 7 This was not due to a lack of provider knowledge, because 95% of the surveyed physicians reported that they were knowledgeable on the National Cholesterol Education Program guidelines and 65% reported that they follow the guidelines on most patients. The American College of Cardiology Evaluation of Preventive Therapeutics (ACCEPT) study, which evaluated 6875 patients from 55 US centers, showed that at 6 months after cardiac hospitalization, despite prospective monitoring, only 28% of patients were at goal for LDL-C. 8 These studies demonstrate that conventionally guided management leaves a large number of CHD patients untreated and undertreated.

Institution of lipid-lowering therapy in the inpatient setting has a number of potential advantages. Measurement of lipid levels can be systematically integrated into the diagnostic testing performed during cardiac hospitalization through the use of preprinted orders and care maps. It has been demonstrated that measuring lipoprotein levels on admission for acute coronary events or within 24 hours provides a reasonable estimate of baseline lipoprotein levels. 9 The structured setting within the hospital can facilitate the initiation of lipid-lowering treatment though the use of physician prompts and reminders, such as preprinted order sets, discharge forms, and involvement of other healthcare professionals. Studies have demonstrated that treatment rates for aspirin and β-blockers in patients with acute MI can be significantly improved through the use of hospital-based programs. 10 Such programs would be expected to be similarly effective in improving the use of lipid-lowering medications in hospitalized CHD patients.

The Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP) was one of the first programs to demonstrate that a treatment algorithm focused on initiating lipid-lowering medications and other secondary prevention measures before hospital discharge could be a more effective

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way of initiating therapy. This program, which was initiated in a university hospital setting in 1994, focused on the initiation of aspirin, statin (titrated to achieve LDL-C ≤100 mg/dL), β-blocker, and angiotensin-converting enzyme (ACE) inhibitor therapy in conjunction with dietary and exercise counseling in patients with established CHD before hospital discharge. Preprinted orders, care maps, discharge forms, physician/nursing education, and treatment use reports were employed to facilitate program implementation. Lipid-lowering medication use at the time of discharge increased from 6% before initiation of the program to 86% after CHAMP was implemented (P<0.001). Improved use of aspirin, β-blockers, and ACE inhibitors was also observed. These improved treatment rates at the time of discharge have been sustained over a 7-year period. More recently, a pharmacy-based program that included placing lipid treatment reminders on the charts of patients hospitalized with CHD demonstrated an increase in treatment rates to 77% at the time of discharge. These and other programs have demonstrated that high rates of lipid-lowering treatment initiation can be achieved with a hospital-based system.

In-hospital initiation of lipid-lowering therapy compared with delayed outpatient initiation has several intrinsic advantages to enhance longer-term treatment use and patient compliance. Treatment is started when patients and their family are focused on the patient’s cardiovascular risk. The expertise of inpatient nurses and pharmacists is applied, facilitating patient education on lipid-lowering therapy. Hospital-based initiation of therapy may also help alleviate patient concerns about monitoring, medication tolerability, and side effects. Creating a link between the initiation of lipid-lowering medication (and other secondary-prevention measures) and the patient’s cardiac hospitalization strengthens the perception that this therapy is essential for the prevention of recurrent events and is an essential part of the patient’s long-term treatment. Hospital initiation of treatment may help facilitate the coordination of lipid care between cardiologists and primary care physicians by inclusion in the discharge summary with a follow-up plan.

In-hospital initiation of lipid-lowering therapy was recently demonstrated to be associated with marked improvement in longer-term treatment rates and patient compliance. With CHAMP, 1 year after hospital discharge, 91% of CHD patients were treated with statins and 58% were documented to have LDL-C levels <100 mg/dL; these rates were 10% and 6%, respectively, before CHAMP was implemented (P<0.01). This improved use of lipid-lowering medications, along with other cardioprotective therapies, was associated with a significant reduction in clinical events the first year after discharge: the rate of death and nonfatal MI decreased from 14.8% to 7.3% (odds ratio, 0.43; P<0.01). Further evidence comes from an analysis of 600 patients with angiographic evidence of CHD. Although only 18% of patients were discharged on statin treatment, long-term compliance (>2 years) was significantly improved in these patients compared with the 46% who started statin treatment on an outpatient basis (77% versus 40% remaining on treatment; P<0.0001). In addition, patients who had in-hospital initiation of statins had lower mortality during long-term follow-up (6% versus 12%; P = 0.05).

Another compelling argument for initiating therapy before discharge is that the early benefit in reducing cardiovascular events may be missed by delayed outpatient initiation. In an analysis of almost 20,000 patients in the Swedish Registry of Cardiac Intensive Care, the 1-year unadjusted mortality rate in patients who received statins at or before discharge was 4.0%, compared with 9.3% in patients who were not discharged on statins. After adjustment for confounding factors and a propensity score based on likelihood of receiving statin therapy at discharge, early initiation of statin therapy was associated with a 25% reduction in relative risk for mortality at 1 year (P = 0.001). In the Lipid-Coronary Artery Disease (L-CAD) study, patients randomized to immediate (average of 6 days after acute MI and/or angioplasty) initiation of pravastatin, alone or in combination with cholestyramine and/or niacin, given as necessary to reduce LDL-C to ≤130 mg/dL, had angiographic benefit at both the 6-month and 24-month follow-up. At 24 months, significantly fewer had clinical events: only 23% when compared with 52% of patients randomized to usual care (P = 0.005; odds ratio, 0.28; confidence interval, 0.13 to 0.60).

In the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) study, 3,086 patients hospitalized for unstable angina or non–Q-wave MI were randomized within 24 to 96 hours of admission to receive atorvastatin 80 mg or placebo. Although patients with total cholesterol >270 mg/dL were excluded, there was no lower limit for total cholesterol or LDL-C, and mean LDL-C was only 124 mg/dL. In the brief follow-up of only 4 months, there was a 16% relative risk reduction in cumulative ischemic events (14.8% versus 17.4%, P = 0.048), with the majority of benefit due to a reduction in worsening angina with new objective evidence of ischemia requiring urgent rehospitalization (6.2% versus 8.4%, P = 0.02).

One potential argument against in-hospital initiation of lipid-lowering drug therapy in patients with recent events is that there may be a higher risk of adverse events than in “stable” patients. In the MIRACL study, however, there were no cases of rhabdomyolysis with aggressive lipid-lowering therapy, and the incidence of elevated liver transaminases >3 times the upper limit of normal on 2 occasions (2.5% with atorvastatin versus 0.6% with placebo) was no different than that observed in previous outpatient trials of patients without CHD.

Another concern about initiating drugs in the hospital is the unnecessary use of drugs in patients who may respond to diet. In an angiographic trial of CHD patients with mildly to moderately increased LDL-C, only 1.5% of the 402 patients with baseline LDL-C ≥130 mg/dL achieved LDL-C ≤100 mg/dL after 8 weeks on an AHA diet, despite an average weight loss of 3 lbs (C.M. Ballantyne, MD, unpublished data, 1997). For the individual with an exceptional reduction in LDL-C after the initiation of concomitant lifestyle changes and drug therapy, a “step-down” approach could be offered with a reduction in drug dose or possibly cessation of drug therapy, as is done with antihypertensive therapy. Ongoing clinical trials should provide answers on the optimal LDL-C.
level for the patient with CHD and the LDL-C threshold (if any) for initiating drug therapy.

In summary, a review of the evidence from recent trials and clinical studies provides a compelling argument for implementing lipid-lowering drugs in the hospital, not in lieu of other interventions but as part of a systematic approach to address the issues of diet, exercise, and aspirin, β-blocker, ACE inhibitor, and statin therapy in all patients before discharge.10 An essential element of the new AHA program “Get With The Guidelines” is the use of protocols to encourage in-hospital initiation in all CHD patients of lipid-lowering medications and other secondary-prevention measures proven to save lives. The marked improvement in the achievement and maintenance of LDL-C targets for the long term, coupled with potential early benefits and low risks of therapy, are compelling enough to make in-hospital initiation the standard of care. Now is the time to ensure treatment is initiated before discharge in each and every appropriate CHD patient, close the national treatment gap in secondary prevention, and prevent pain, suffering, and death from CHD.

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