EDITORIALS

Medication Adherence After Myocardial Infarction: A Long Way Left To Go

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Coronary heart disease (CHD) remains the leading cause of death in the USA and other developed countries and may soon become the leading cause of death in the developing world as well.[1,2] More than 1 million Americans have an acute myocardial infarction (MI) every year.[3] In 2006, CHD is estimated to have accounted for more than $140 billion in direct and indirect health care costs.[3]

Medications for the treatment and prevention of CHD-related events have been subject to rigorous evaluation in trials involving hundreds of thousands of patients, and practice guidelines recommend that post-MI patients receive treatment with a beta-blocker, a lipid lowering agent, an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker, and aspirin,[4] unless a contraindication exists. Taken in combination, these drugs have been estimated to reduce the relative risk of CHD mortality by 80% as compared to placebo.[5]

Despite the evidence supporting their use, the under-prescribing of preventive therapies after MI has been well documented. Only 10 years ago, less than half of post-MI patients received beta-blockers at hospital discharge.[6] In response, large-scale efforts, such as the American Heart Association's Get With the Guidelines Program[7] and the American College of Cardiology's Guidelines Applied in Practice Initiative,[8] have actively promoted effective post-MI prescribing, and credentialing bodies such as the National Committee for Quality Assurance (NCQA) and Joint Commission on Accreditation of Healthcare Organizations have included appropriate post-MI medication use as a quality measure.[9] The result is that now, some 25 years after the first trial demonstrating the value of beta-blockers after MI was published,[10] more than 90% of patients discharged from hospital receive beta-blockers (and other essential preventive medications) and, accordingly, the NCQA has very recently retired this quality measure.[11] ACE inhibitor prescribing for post-MI patients with left ventricular dysfunction has also improved, but rates still remain somewhat suboptimal.[9]

Unfortunately, prescribing appropriate medications to post-MI patients at hospital discharge is only part of the battle. Long-term, often life-long, persistence with these treatment regimens is essential to reap the maximum benefits from these proven therapies. Non-adherence (or non-compliance) and non-persistence are not recently recognized phenomena—academic investigators have documented their existence for almost 50 years.[12] However, in this issue of the *Journal*, Ackincigil et al.[13] give us a sobering sense of how much work we have left still to do. Using medical and pharmacy claims from patients discharged from hospital after an acute MI who received their benefits through a large health insurer, they measured the proportion of patients who discontinued beta-blocker or ACE inhibitor therapy (defined as having a 60-d gap without medication). Of those patients prescribed these medications after hospital discharge, only 50% of the patients were still using them 2 years later.

The results reported by Ackincigil are very much in keeping with findings of numerous other investigators. Despite these analyses being conducted in a variety of different health plan structures and countries and involving patients with different conditions using many different chronic medications, most have reported a similar "50% or lower" number for adherence to cardiovascular preventive therapies.[14] For example, only 45% of commercially insured patients are fully adherent with beta-blockers in the 1 year after an acute MI,[15] and only 42% of Medicare patients enrolled in a pharmacy benefit program are adherent with their prescribed statin after 2 years.[16] Less than 40% of patients who had undergone cardiovascular procedures at a large academic hospital reported consistently using the combination of lipid-lowering agents, beta-blockers, and aspirin.[17]

Not surprisingly, poor adherence is associated with poor health outcomes. Patients who adhere to a statin after MI have a relative risk of recurrent MI which is 81% lower than that of non-adherent patients.[18] Post-MI patients who discontinue their prescribed aspirin, statin, and beta-blocker are more than three times more likely to die than patients who remain adherent.[19] Such disparities, which are based on observational studies, are not entirely explained by the "healthy user effect"—the phenomenon that healthier patients are more likely to adhere to therapy.[20]

The economic impact of non-adherence is also enormous. At least a third of all medication-related hospital admissions are caused by poor medication adherence,[21] and these events alone are estimated to cost $100 billion annually in the USA.[22] Health care costs are also lower among adherent patients and may more than offset their greater medication costs.[23] Accordingly, non-adherence not only represents a waste of the billions

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spent developing and evaluating effective cardiovascular therapeutics and educating physicians and patients about which medications they should take after a MI, it is also a wasted opportunity to constrain spiraling health care costs.

It is important to note that the patients in the study of Akincigil et al. all had "good" insurance, were fairly healthy and fairly young, did not have documented contraindications to these medications, had access to disease management programs, and faced only modest co-pays for their medications, yet despite this had high rates of non-adherence. This highlights the multitude of reasons why patients do not take the medications they have been prescribed. Medication cost, complexity of treatment regimens, treatment side effects, cognitive impairment, poor understanding of the benefits of treatment, poor provider–patient relationships, difficulties that patients have accessing physicians or pharmacies, and physician knowledge gaps about insurance formularies have all been identified as relevant factors.[22] Adherence may be particularly challenging for some cardiovascular medications, as patients may not immediately appreciate improvements in symptoms from taking them or worsening of symptoms from discontinuing therapy, and providers may forget to ask about their patients' use of medications that were initially prescribed some time ago.

So what can we do? Interventions to improve medication adherence have been developed and evaluated and may generally be classified as being "informational" (e.g., telephonic coaching, group classes, or the mailing of instructional materials), "behavioral" (e.g., pillboxes, mailed reminders, simplifying treatment regimens, or audit and feedback), "family and social focused" (e.g., support groups and family counseling), or some combination thereof.[24] Less than half of randomized trials have demonstrated a consistent improvement in adherence from the interventions they evaluated; more importantly, less than half of the trials that assessed clinical variables, such as blood pressure or cholesterol lowering, found significant improvements in these outcomes.[24]

Several conclusions can be drawn from these generally disappointing results. First, some interventions, such as those that simplify dosing schedule, provide monitoring and feedback, or that employ more than one tool, have more promise than others.[24] Therefore, existing efforts should focus on these strategies. Second, we need to develop and rigorously evaluate other creative interventions. For example, reducing patient cost-sharing for essential post-MI medications has been proposed as a strategy that will improve adherence and clinical outcomes while simultaneously reducing overall health care costs because of the cost-savings resulting from averted clinical events.[25] Third, and perhaps most importantly, adherence interventions may have been less than completely effective because each patient has his or her own set of reasons for not taking prescribed medications; in other words, there is no "one size fits all" solution to this problem.

While it took 25 years to achieve near universal beta-blocker prescribing after MI, the complex reasons for non-adherence and the modest effects observed from existing interventions will likely mean that at the current rate, it will take much longer for adherence to reach an acceptable level. Given the clinical and economic impact of non-adherence, we should not be satisfied with this rate of change, and, accordingly, the development of better solutions to help patients take their medications as prescribed should be a clear public health priority. Of course, we may not strive for 100% adherence, as some patients are non-adherent because of potentially dangerous side effects and others do not use medications after making carefully considered choices. Nevertheless, the study of Akincigil et al. makes it clear that there is a huge gap between where we are and where we ought to be.

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