High intensity lipid-lowering therapy after acute coronary syndromes: room for improvement

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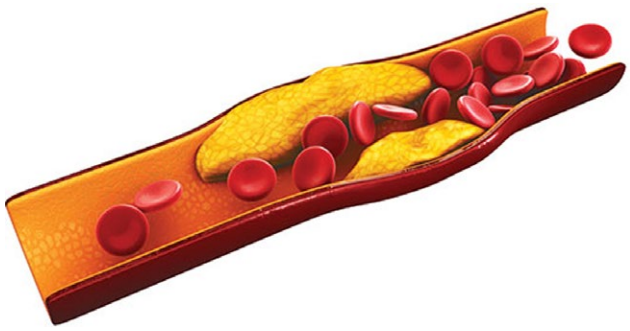
Effective therapies are available, but too few patients are receiving them

There is a significant amount of evidence that intensive statin therapy reduces the likelihood of cardiovascular events in people who have had an acute coronary syndrome (ACS), and such therapy is given the highest grade of recommendation in Australian clinical practice guidelines.[1] Post hoc analyses of randomised trials of treatment with statins, statins and ezetimibe, or, more recently, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors indicate that patients who achieve very low low-density lipoprotein cholesterol (LDL-C) levels are at very low risk of cardiovascular events after an ACS, and that the rates of adverse events related to attaining such levels are not increased.[2,3] In the Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT), the combination of simvastatin and a non-statin LDL-lowering treatment (ezetimibe) reduced LDL-C levels to a median 1.4 mmol/L, and this was associated with reduced numbers of clinical events.[4] In the Odyssey Outcomes trial, a combination of statins and alirocumab (a PCSK9 inhibitor) reduced LDL-C levels to below 1.0 mmol/L and this was associated with reduced numbers of major adverse cardiovascular events.[3] These trials provide further support for the LDL-C hypothesis of cardiovascular risk, which suggests that the risk of a cardiovascular event is reduced by about 22% for each 1.0 mmol/L reduction in LDL-C levels.[2]

Adherence to lipid-lowering therapies is an important determinant of outcomes for patients who have had an ACS, but only 50% are still taking statins one year after discharge from hospital.[5] Adherence to treatment with cholesterol-lowering medications is generally poor, partly because hypercholesterolaemia is symptomless. Patients' beliefs about medicines and possible adverse events are also significant predictors of adherence. For example, reports by patients of statin-associated muscle symptoms are often related to negative media items about statin therapy or to patients misunderstanding its potential effects. The adherence problem is exacerbated by therapeutic inertia; doctors hesitate to properly educate patients and to prescribe high dose statin therapy in a climate of negative media reports, and the effect is compounded by reduced patient compliance resulting from the perceived or real side effects of statin therapy.

In this issue of this Journal, Brieger and colleagues report their analysis of data from CONCORDANCE, an ongoing prospective,



Australian investigator-initiated ACS registry.[6] The authors found that only half the patients hospitalised in Australia for an ACS were receiving intensive lipid-lowering therapy 12 months after their release from hospital. Predictors of not receiving intensive lipid-lowering therapy included not being prescribed it at hospital discharge, being female, being medically managed in hospital, and, interestingly, being referred for cardiac rehabilitation. Limitations to the study included the retrospective observational design, the lack of data on reasons for non-adherence, and the limited data on lipid levels and type of statin prescribed.

These findings nevertheless have important clinical implications, most notably the need for strategies for increasing the prescribing at hospital discharge of high intensity lipid-lowering therapy, particularly of statins. This is especially important because high intensity statin therapy and treatment with ezetimibe are not only clinically effective, but also cost-effective. These therapies should be tried before considering more expensive novel approaches.

The article by Brieger and his colleagues also highlights the fact that a multidisciplinary approach to lowering the barriers between patient, provider, and health system is needed. Strategies for improving medication adherence and ultimately outcomes for patients could include:

- Identifying and developing techniques for reducing specific barriers for individual patients.[7]
- Personalised, patient-focused programs involving frequent contact with health care professionals, or a combination of strategies based on physician or nurse communication and pharmacist involvement.[8]
- Regular counselling about medication adherence, by phone or app, has been found to improve survival.[9]
- Digital interventions, such as the American College of Cardiology Statin Intolerance smartphone app (http://www.acc.org/StatinIntoleranceApp) can assist physicians manage and treat patients who experience statin-associated muscle symptoms. The app can guide their assessment of whether their patient is statin-intolerant and the management of their symptoms according to clinical guidelines, including

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comparison of the characteristics of different statins and potential drug interactions.
- Fixed dose combinations of statins and ezetimibe, readily available in Australia and reimbursed by the Pharmaceutical Benefits Scheme, reduce the burden of compliance for patients.
- Implementing recommended guidelines by governments and specialist societies could also lead to better adherence and reduce therapeutic inertia.

In summary, very effective therapies are available for reducing LDL-C levels to recommended levels after an ACS, but too few patients are receiving these treatments. The challenge for health care providers is to improve this situation with a multifaceted, patient-focused approach.

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