Can we do more to get patients to cholesterol targets?

Professor Richard Hobbs advises on how to ensure that more patients reach recommended cholesterol targets

Abstract

The role of cholesterol lowering in reducing cardiovascular risk is well established but a large proportion of qualifying patients at the highest risk are still not getting treatment with statins. Of those that do, most are not achieving recommended cholesterol targets. The cost of this, in terms of death and work days lost, is enormous. Patients should not be discharged after an acute event until secondary prevention has been initiated. Individual patient response to therapy should be subsequently monitored and adjusted as appropriate; patients should be reassured on statin safety.

Key words: lipid lowering, cholesterol targets, primary prevention, secondary prevention, guidelines.

The evidence

For over a decade, the role of cholesterol lowering in reducing cardiovascular risk has been debated. Having established, with overwhelming evidence from five landmark trials,[1-5] that statins save lives by reducing cholesterol, their use became mandatory for patients with established coronary heart disease (secondary prevention) or high risk factors for CHD (primary prevention).

The debate has now moved on to the specifics of how far cholesterol should be lowered and how aggressively. It also focuses on the relative importance of altering the various lipid fractions in a favourable direction. In the UK, for example, guidelines are less stringent than in the US and elsewhere. The National Service Framework (NSF) for Coronary Heart Disease (CHD) advocates reducing low density lipoprotein (LDL) to 3 mmol/L or by 30% and total cholesterol to 5 mmol/L or by 25%, whichever is the greater.[6] The joint British guidelines recommend a target LDL level of 3 mmol/L for all, whereas in the US the target for LDL is 100 mg/dL (equivalent to 2.6 mmol/L)[7,8] in secondary prevention patients. Lower targets may be determined by the outcomes of trials in progress, such as TNT, IDEAL, SEARCH and PROVE-IT, but already the Heart Protection Study has shown there is no LDL threshold, at least in western populations, below which cholesterol lowering provided no further benefit.[9] One third of the 20,536 patients in the study had LDL levels below current therapy targets (3 mmol/L) when simvastatin 40 mg treatment was initiated; they showed the same reductions in mortality and morbidity as those with higher baseline cholesterols.

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Richard Hobbs

With all the arguments and evidence cited in their favour, it is all too easy to assume that statins are being given to every patient at risk and that LDL is being lowered to targets stipulated in current guidelines. There have been huge improvements in the number of patients getting the treatment they require.[10] Nevertheless, repeated surveys indicate that, for all the guidelines in all countries, a large proportion of qualifying patients at the highest risk are still not getting statins and, of those that do, most are not achieving the targets.[11-14] EUROASPIRE II, for example,

Glossary of clinical trial acronyms

TNT	Treating to New Targets
IDEAL	Incremental Decrease in Endpoints through Aggressive Lipid Lowering
SEARCH	Study of Effectiveness of Additional Reductions in Cholesterol and Homocysteine
PROVE-IT	Pravastatin or Atorvastatin Evaluation and Infection Therapy
4S	Scandinavian Simvastatin Survival Study
REACT	Reassessing European Attitudes about Cardiovascular Treatment
EUROASPIRE	European Action on Secondary and Primary Prevention by Intervention to Reduce Events
WOSCOPS	West of Scotland Coronary Prevention Study

Key messages

- There is overwhelming evidence that statins save lives by reducing cholesterol
- There appears to be no minimum LDL at which cholesterol lowering will provide no additional benefit in secondary prevention
- Many qualifying patients are still not receiving statin therapy
- Most patients on statin therapy are not reaching recommended cholesterol targets
- Monitoring of patients must be tightened up, increasing statin doses to an effective level
- Patients should be reassured that statins are safe

showed one third of hospital records reviewed provided no details of lipid levels. Some 58% of patients interviewed six months after discharge for a coronary event had poor control of their cholesterol and only half had achieved the goals.[10] The REACT survey paints a similar picture.[15]

The practice

How can this be? Firstly, we can only assume too many patients are slipping through the net and are either not being identified as at-risk or discharged from hospital without a statin. According to a small British survey, even the best centres in the country are only managing to send 40% of patients home with a cholesterol-lowering therapy in the first place. Until recently, this situation was influenced by discharge policies that deferred statin treatment for patients until six months after their acute event. The NSF for CHD now recommends that patients are not discharged until secondary prevention is initiated.

Secondly, current organisational systems are failing to ensure patients are taking sufficient medication to reach even current targets. In some cases, patients are not concordant, in others statin doses are ineffective and have not been up-titrated to a level of greater effectiveness. The consequences of this can be profound. One US study estimated that non-adherence to therapy resulted in more than 125,000 deaths and 20 million work days lost through avoidable hospital admissions.[16] In WOSCOPS, those adhering to treatment throughout the study showed clear benefits in mortality and morbidity.[17] Data from 4S show the greater the LDL reduction, the better the outcome.[1]

Recommended strategy

So how can we remedy the situation? The NSF for CHD has now been running for two years and progress reports tell us some £80 million has been spent on increased drug spending for statins. Audits will tell us how well those statins are being used and how successful they are in getting patients to target. They will also show how feasible it is for practices to recall patients at regular intervals for retesting of cholesterol and upward titration of their statin dose if necessary.

The recent withdrawal of cerivastatin, well publicised in the national media, has made some patients and many GPs more wary of starting patients on a high statin dose. The risks of cerivastatin to cause rhabdomyolysis were, in retrospect, much greater than for all other statins. However, problems of myopathy have tended to occur mainly at the top end of a product's dose range so it makes sense from a safety and economic viewpoint to start low and see if that is sufficient to reach the target. The danger is that patients slip through the net for checking up. It is essential to have practices in place to monitor individual patient response to therapy and increase dose where necessary.

The practical solution is to start therapy with a statin of proven effectiveness at its lower dose range. Here, choice is currently limited and there is often a reluctance to switch patients from one statin to another, particularly if this will mean sacrificing a better all-round lipid profile for lower LDL. Newer agents may improve on current therapies; until then we can only focus on improving the care pathway system to tighten up on monitoring, increasing statin dose to a level of effectiveness, and re-assuring most patients that their statin is safe and should be taken as prescribed.

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