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Title **Early High-Dose Lipid-Lowering Therapy to Avoid Cardiac Events: A Systematic Review and Economic Evaluation**

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Aim

To evaluate the cost effectiveness of high-dose statins (atorvastatin 80 mg/day, rosuvastatin 40 mg/day and simvastatin 80 mg/day) versus simvastatin 40 mg/day in individuals with acute coronary syndrome (ACS).

Conclusions and results

We screened 3345 titles and abstracts for the review of clinical effectiveness, and retrieved and assessed 125 full papers. Of these, 30 papers describing 28 trials met the inclusion criteria. The Bayesian mixed treatment meta-analysis demonstrated a clear dose-response relationship in terms of reductions in low-density lipoprotein cholesterol (LDL-c), with rosuvastatin 40 mg/day achieving the greatest percentage reduction (56%) from baseline, followed by atorvastatin 80 mg/day (52%), simvastatin 80 mg/day (45%), and simvastatin 40 mg/day (37%). Although serious adverse events with statins are rare, their incidence is likely to be greater at higher doses. We used several clinical scenarios to explore the effect of adherence on the cost effectiveness of treatment regimens. Using a threshold of 20 000 pounds sterling (GBP) per quality-adjusted life-year (QALY) and assuming that the benefits and adherence rates observed in the clinical trials are generalizable to a clinical setting, and that individuals who do not tolerate the higher-dose statins are prescribed simvastatin 40 mg/day, then atorvastatin 80 mg/day and rosuvastatin 40 mg/day would be considered cost effective compared to simvastatin 40 mg/day in individuals with ACS. Simvastatin 80 mg/day is not well tolerated because of the high incidence of less severe adverse events, eg, myopathy, which are likely to affect adherence levels in clinical practice. Simvastatin 80 mg/day cannot be recommended due to the high incidence of adverse events. If the cost of atorvastatin decreases in line with that observed for simvastatin when the patent ends in 2011, atorvastatin 80 mg/day will be the most cost-effective treatment for all thresholds. If the cost reduces to 25% of the current value, atorvastatin 80 mg/day will be the most cost-effective treatment for thresholds between GBP 5000 and GBP 30 000 per QALY.

The reference case shows that at a threshold of GBP 20 000 per QALY, rosuvastatin is optimal treatment in patients with a recent history of ACS. This assumes that the additional incremental reductions in LDL-c observed in patients treated with rosuvastatin 40 mg/day compared with atorvastatin will transfer into corresponding changes in relative risks of cardiovascular events.

Recommendations

See Executive Summary link www.hta.ac.uk/project/1700.asp.

Methods

See Executive Summary link www.hta.ac.uk/project/1700.asp.

Further research/reviews required

Large, long-term RCTs reporting effects in terms of clinical events are needed to determine optimum statin use in subgroups. These include head-to-head studies comparing higher-dose statins with lower-dose statins, studies of rosuvastatin, and studies comparing high-dose statin monotherapy with combination therapies. Studies recruiting high-risk groups should be considered. Long-term registry data are needed to determine adherence rates and adverse events for individual statins and doses when used in general practice. Studies exploring the effects of interventions designed to increase adherence to statin therapy in general clinical practice and in subgroups are also required.

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