Title **Clopidogrel Used in Combination with Aspirin Compared with Aspirin Alone in the Treatment of Non-ST-segment-elevation Acute Coronary Syndromes: A Systematic Review and Economic Evaluation**

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Aim

To systematically review the clinical and cost effectiveness of clopidogrel in combination with standard aspirin therapy, compared with standard therapy alone for treating non-ST-segment elevation acute coronary syndromes (ACS).

Conclusions and results

One randomized controlled trial (RCT), the CURE trial, was double-blinded, placebo- controlled, and of high quality. It showed that clopidogrel plus aspirin was significantly more effective than placebo plus aspirin in patients with non-ST-segment elevation ACS for the composite outcome of death from cardiovascular causes, non-fatal myocardial infarction, or stroke over the 9-month treatment period. However, clopidogrel was associated with significantly more episodes of bleeding. Five systematic reviews showed aspirin to be associated with a significantly higher incidence of hemorrhagic stroke, extracranial hemorrhage, and gastrointestinal hemorrhage compared to placebo. A model found clopidogrel to be cost effective compared with standard care alone in patients with non-ST-elevation ACS, as long as the NHS is willing to pay £6,078 per quality of life year (QALY). Although 12 months of clopidogrel treatment was cost effective for the overall cohort, provisional findings indicate that shorter treatment may be more cost effective in patients at low risk.

Recommendations

The CURE trial indicates that the benefit of clopidogrel plus aspirin is largely related to a reduction in Q-wave myocardial infarction. There was no statistically significant benefit in relation to mortality. Much of the benefit derived from clopidogrel is achieved by 3 months, with further small benefit over the remaining 9 months of chronic treatment.

Methods

Rigorous criteria were used to select studies. The quality of RCTs was assessed according to criteria based on CRD Report No. 4. The quality of systematic reviews was assessed according to the guidelines for the Database of Reviews of Effects (DARE) criteria. The quality of economic evaluations was assessed according to a specifically tailored checklist. The clinical effectiveness and cost effectiveness of clopidogrel in combination with standard therapy compared with standard therapy alone were synthesized through a narrative review with full tabulation of the results of the included studies. A cost-effectiveness model was constructed for the economic evaluations, using the best available evidence to determine cost effectiveness in a UK setting.

Further research/reviews required

A prospective trial that randomized patients to various durations of therapy would be required to estimate the exact length of time that clopidogrel plus standard therapy should be prescribed for patients with non-ST-segment ACS. This would accurately assess whether a 'rebound' phenomenon occurs in patients if clopidogrel were stopped after 3 months of treatment.

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