CURE: A panacea for all ills?


**SUMMARY**

The CURE study is a randomized, double-blind trial that evaluated the effect of addition of clopidogrel to standard therapy in over 12,000 patients with acute coronary syndromes without ST segment elevation, who were at relatively high risk for adverse events. The primary end-point, a composite of death due to cardiovascular causes, non-fatal myocardial infarction or stroke, occurred significantly less frequently in the clopidogrel group than in the placebo group (9.3% v. 11.4%; p<0.001). Further, the probability of either the primary outcome or refractory angina occurring was also less in the clopidogrel group. However, there were more episodes of major and minor bleeding in the clopidogrel group (major bleeds 3.7% v. 2.7%; p<0.001). The number of episodes of life-threatening bleeding in the two groups was not significantly different.

**COMMENT**

The thienopyridine derivatives are antiplatelet agents that inhibit platelet aggregation induced by adenosine diphosphate. A previous study has shown that in patients with known atherosclerotic vascular disease, long term administration of clopidogrel is more effective than aspirin in reducing the combined risk of ischaemic stroke, myocardial infarction or vascular death.1 Logically, it is to be expected that the two agents used together will act synergistically in inhibiting platelet aggregation. The CURE trial supports such a hypothesis. In this study, 48 patients needed to be treated to prevent either death from cardiovascular causes, non-fatal myocardial infarction or stroke (the primary end-point). A similar number of patients needed to be treated to prevent either the occurrence of refractory angina or any component of the primary end-point. This benefit was accrued at the cost of 10 major bleeds (6 of which required >2 transfusions) for every 1000 patients treated. Although life-threatening bleeds were no more in the clopidogrel group than in the placebo group, this means that for every 2 patients prevented from reaching a primary end-point, one patient had a major bleed.

The incremental benefits derived from newer and more effective treatments tend to become progressively smaller than those of pre-existing therapies. Viewed in this light, the CURE study does demonstrate a significantly greater efficacy of clopidogrel over standard therapy. However, there are two issues that militate against the routine use of clopidogrel in patients with unstable angina who conform to the CURE criteria. The first is the significantly increased risk of major bleeding, often requiring transfusion. The second is the cost of such therapy. Typically, a patient will have to spend Rs 5000 per year, in addition to the cost of usual medications. The reasonable option, therefore, would be to recommend clopidogrel only to those patients who are known to be at the highest risk of adverse events based on established clinical and angiographic criteria.2 The ethics of such an approach are debatable. But this strategy is likely to cause the least damage and will have to be pursued till a mechanism can be worked out to enable all eligible persons to pay for such therapies.

**REFERENCES**


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