Thrombolysis for Elderly Patients—Which Way from Here?

During the last decade the emphasis in management of patients with acute myocardial infarction has changed from treatment of the consequences of infarction to restoration of coronary artery patency and limitation of infarct size by the early administration of thrombolytic therapy. Where do our elderly patients stand with regard to thrombolytic therapy? Ninety per cent of patients suffering from an acute transmural infarction have a thrombotic occlusion of a coronary artery [1]. A number of the major trials of thrombolytic therapy have included patients over 65 years and have demonstrated the efficacy of thrombolytic therapy in patients with proven or suspected infarctions. Although the entry criteria, the ages of the patients and the thrombolytic agent used were different for each study, certain conclusions concerning the use of thrombolytic agents in the elderly can be made.

The AIMS (APSAC Intervention Mortality Study) trial final report has recently been published [2]; 1258 patients, aged up to 70 years, with definite electrocardiographic evidence of infarction, and within 6 hours of the onset of symptoms, were randomized to receive anistreplase (anisoylated plasminogen streptokinase activator complex, APSAC) or placebo. After 30 days, the odds reduction in mortality was 50.5°, and at 1 year it was still 43°. The authors comment that age and an anterior infarction were the most important predictors of a poor outcome. Patients aged over 65 years constituted 18° of the subjects but contributed 40° of the deaths within 30 days. Thus the authors noted that the short-term absolute benefits in deaths prevented per patient treated may be greater in the elderly [3].

The ASSET (Anglo Scandinavian Study of Early Thrombolysis) study published its results in 1988 [4]; 5011 patients aged 18–75 years with suspected myocardial infarctions who presented within 5 hours of the onset of symptoms were randomized to receive either t-PA (tissue plasminogen activator) or placebo, both with heparin. After 1 month the mortality reduction was 26° in the t-PA group. The elderly subjects (65–75 years of age) constituted one-third of the cases and, although their mortality was higher at 1 month in both treated and placebo groups than that of the young, the percentage difference between treated and placebo groups was greater (66–75 years—tPA 10.8° mortality, placebo 16.4°; < 55 years—tPA 3.8° mortality, placebo 4.4°; 56–65 years—6.5° mortality, placebo 7.9°). The first Italian GISSI study randomized 11806 patients who presented within 12 hours of onset of symptoms and who had defined ECG changes compatible with an acute myocardial infarction to receive streptokinase (SK), in addition to the usual treatment of the admitting hospital [5]. There was no upper age limit to this study. At 21 days, overall hospital mortality was 18°, less in the SK group, although the beneficial effect was noted to be a function of treatment time from onset of pain. Thirty-five per cent of the patients were over 65 years and 10.7° over 75 years and, although the major benefit was seen in the under-65s, a statistically nonsignificant beneficial effect of SK in the elderly was seen. This elderly group showed no specific adverse reactions or negative clinical events, and led to the authors’ conclusion that SK could not be contra-indicated in elderly infarct patients.
ISIS-2 (the Second International Study of Infarct Survival) randomized 17187 cases of suspected myocardial infarction, of any age, within 24 hours from onset of symptoms, to receive SK alone, aspirin alone, both or neither [6]. This study, published in 1988, demonstrated that reductions in vascular mortality occurred in both the SK and aspirin groups at all ages. These benefits were clearly independent of each other as the drug combination produced a far greater reduction in odds of death at 5 weeks than either agent alone. The conclusion was that the benefits of fibrinolytic therapy are substantial and some benefit is seen even amongst patients treated up to 24 hours after the onset of pain.

Where do all these results leave us with regard to elderly patients? We know that many present atypically, and often some hours after the onset of symptoms. In absolute terms, the number of lives saved per thousand patients treated in controlled trials of thrombolytic therapy appears to be higher in the elderly. In 1988 Julian et al. commented that thrombolytic therapy should be routine in patients with acute myocardial infarction who had none of the standard contra-indications to thrombolysis [7]. Two years on, Petch has stated that ‘we should continue to administer thrombolytic treatment to all patients’ [8]. Grimley Evans suggests that curing is caring [9], and that as geriatricians we should ensure that our patients have access to the ‘best that modern medicine can offer’. More data are required regarding current practice, long-term outcome and the real cost, both clinical and financial, of thrombolysis in elderly patients with myocardial infarction. This would enable us to establish optimal management policies for the elderly. The results of GISSI-2, which showed no significant difference in mortality between t-PA and streptokinase in 12000 patients, have recently been released. Streptokinase is widely available, relatively safe and cheap, and—unless the results of ISIS-3 suggest strongly to the contrary—when combined with aspirin, is, we suggest, currently the thrombolytic agent of choice. Are elderly patients receiving it?

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References