Early thrombolysis for the treatment of acute myocardial infarction. Who will provide this treatment in the UK? Part 1

This article looks at the published evidence for general practitioners and ambulance paramedics providing thrombolysis. It is based on a submission made by the Primary Care Cardiovascular Society to the National Institute for Clinical Excellence on early hospital thrombolysis. The second part will be published next month.

Abstract

This article looks at the results of four studies which examined the delivery of early thrombolysis by general practitioners and ambulance paramedics to patients suffering an acute myocardial infarction. The studies found that they could provide early thrombolysis safely.

One study in an isolated rural area in Scotland found general practitioners would have very limited experience of thrombolysis – one case per general practitioner per year – and that use of thrombolysis by local general practitioners fell off sharply after the study. A second study carried out in 15 European countries and Canada, found that there was no significant improvement in mortality and morbidity in the pre-hospital group given thrombolysis at home. This was also found by a Dutch study. An American study using computer-assisted diagnostic ECGs relayed to a physician at the base hospital, found little difference in the pre-hospital and hospital treatment arms but a dramatic improvement in the speed of treatment of both groups. Pre-hospital thrombolysis was also reduced. Two studies found ambulances became 'tied up' when thrombolysis was delivered at home.

These studies were used as part of a submission on behalf of the Primary Care Cardiovascular Society to the National Institute for Clinical Excellence. The rest of the submission is discussed in part two of this article next month.

'Thrombolysis should have the same priority as a cardiac arrest'

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Key words: acute myocardial infarction, pre-hospital thrombolysis, early thrombolysis, NICE.

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Introduction

This is the first of two articles adapted from a submission to the National Institute for Clinical Excellence (NICE) on behalf of the Primary Care Cardiovascular Society (PCCS). NICE invited submissions on the subject of 'early hospital thrombolysis' in September 2001 and intend to publish their guidance later this year. This technical appraisal was motivated by the arrival of new, expensive, bolus thrombolytics but it raises more questions than just which drug should be used. NICE used the term 'early thrombolysis' rather than 'pre-hospital thrombolysis' as they wished to examine the use of thrombolysis in accident and emergency departments, minor injury units and community hospitals as well as outside hospitals. This first article concentrates on the published evidence for general practitioners and ambulance paramedics providing thrombolysis.

Rapid delivery of thrombolysis

It is accepted that thrombolysis within two hours of acute myocardial infarction (AMI) is likely to result in little or no myocardial damage, but after six hours it is unlikely to be of benefit. The greatest delay is usually due to the failure of the victim to call for help. Door-to-needle time is minimised by direct admission to the coronary care unit (CCU). Patients diagnosed in the accident and emergency department should undergo thrombolysis before transfer. Thrombolysis should have the same priority as a cardiac arrest.

The Grampian Region Early Anistreplase Trial

The Grampian Region Early Anistreplase Trial (GREAT)[1] was a major pre-hospital thrombolysis trial that ran from December 1988 to December 1991. It successfully achieved its primary objec-

tive to prove that general practitioners could provide this treatment safely. Claims that this trial proved efficacy of pre-hospital treatment are weak because the hospital treatment patients had a placebo ECG and infusion at home and further assessment at hospital, which delayed their treatment. This was not a 'scoop and run' policy. The door-to-needle time was 87 minutes, which by present standards is a very significant delay.

There was approximately one case per general practitioner per year. The trial showed that the ambulance was 'tied up' for longer than usual and therefore had an impact on ambulance availability. One patient died of a dissecting thoracic aneurysm. Such events are difficult for general practitioners to accept and even more so for paramedics because this is a departure from their normal level of responsibility.

After GREAT the use of thrombolysis by local general practitioners fell off sharply. By 1993 half of the practices had given up and only 29% of general practitioners had given thrombolysis in the previous year. The follow-up audit concluded that additional incentives would be required if general practitioners are to give thrombolysis treatment.[2]

This trial represented the needs of one of the most isolated areas in the United Kingdom (UK) and its results cannot necessarily be extrapolated to other areas. Only one case a year is limited on-going experience and no doubt this was a factor in the decision of many general practitioners to give up. The same problem would arise for paramedics unless the work was concentrated in the hands of a few crews. However specialist crews would not be practical in such a large area and it is likely that all crews would have to take part. Although general practitioners could and did exercise the option not to be involved, this would not necessarily be an option for paramedics.

The European Myocardial Infarction Project

A major trial carried out in 15 European countries and Canada was the European Myocardial Infarction Project (EMIP).[3] The service differed in each country but included a physician in all cases. In Northern Ireland, which accounted for 15% of the 5,469 cases, the service comprised hospital outreach teams working in urban areas close to the hospital. Again the study was designed to examine feasibility and safety with all patients receiving an ECG and needle at home, whether they were randomised to home or hospital treatment. Significantly more adverse events (particularly ventricular fibrillation) occurred in the pre-hospital group. This was expected and is not a negative finding.

Feasibility and safety were proved, but as with Grampian there was no significant improvement in mortality or morbidity among the pre-hospital treatment group. A further analysis of EMIP published in 1997 showed that delays in calling for an ambulance were most significant amongst females, the elderly and pulmonary oedema sufferers. Delays were shorter in those with a past history of AMI and for those in shock.

> ***'Additional incentives would be required if general practitioners are to give thrombolysis treatment'***

The authors of the report concluded that: "These results cannot be generalised to geographic areas without staff and equipment similar to those in the EMIP centres". In a later report they stated: "Our findings apply only to situations in which patients with suspected AMI are cared for by mobile emergency units, which, in the EMIP trial, all had a physician on board. In addition, EMIP patients were selected according to prespecified criteria, as is the case with any targeted clinical trial population".

The Myocardial Infarction Triage and Intervention Trial

Based in the Seattle Metropolitan Area, Washington State, USA, the Myocardial Infarction Triage and Intervention Trial (MITI)[4] is the most important paramedic study. The selection criteria were strict. Computer-assisted diagnostic ECGs were used to indicate normal cases and a physician at the base hospital verified abnormal ECGs, giving the go ahead for an alteplase infusion. There were 360 patients, but they only represented 4% of those screened (8,863) and only 21% of all AMIs (1,745) requiring ambulances in the trial period.

The most important finding was that the pre-hospital ECG telemetry carried out on all patients alerted the hospital to know that a definite MI would arrive and there was a significant reduction in door-to-needle time from 60 minutes to 20 minutes. The comparators performance was improved sufficiently to nullify the pre-hospital outcomes. Because the paramedics worked to strict protocols, the overall percentage of AMIs receiving pre-hospital thrombolysis was reduced. It is probable that 'barn door' AMIs benefit while the more subtle AMIs undergo further delay in treatment due to the need for two assessments. It is, however, the 'barn door' AMIs that are most likely to benefit from thrombolysis overall.

The study conclusion refers to the lack of difference between the pre-hospital and hospital treatment arms but with a dramatic improvement in speed of treatment in both groups. Those treated earliest did best, often with no myocardial damage (40%). "The average time saving was modest (33 minutes), and similar to observations of others...It was evident that the trial itself had a marked effect on decreasing hospital treatment times, therefore causing an unanticipated Hawthorne effect, and thus, decreasing the chance of detecting differences in outcomes between the two strategies. The most important need is for public education to not delay calling for an ambulance. In hospital, delay was due to unnecessary examinations by physicians, complacent nurses, lack of formal triage and strategy."

There were an above average 10 fatal strokes, which is a reality of the

Key messages

- General practitioners can safely carry out pre-hospital thrombolysis, even in very isolated areas
- Pre-hospital thrombolysis can 'tie up' ambulances at home
- Ambulance telemetry can significantly speed up door-to-needle time; as can direct admission to the coronary care unit
- The biggest delay is usually in the patient calling for help

risks of thrombolysis and a risk worth taking, but should this be a compulsory task for all paramedics?

The Reperfusion in Acute Infarction Rotterdam

The Dutch Reperfusion in Acute Infarction Rotterdam (REPAIR)[5] study ran between 1988 and 1993. A general practitioner or ambulance nurse provided treatment. The ambulance nurse had six years basic training and then further cardiac training. Some 529 patients were given alteplase or streptokinase. The selection criteria were more restricted than in hospital. It included patients from a previous alteplase study as comparisons, so the study is not very reliable statistically. It recorded an 11% failure rate to achieve intravenous access.

There was a median delay to call for help of 55 minutes and evaluation required a median time of 18 minutes. The median time from ambulance arrival to thrombolysis administration was 68 minutes, which is in marked contrast to MITI and does indicate that the ambulance became 'tied up'. Outcome differences were not statistically significant but the time gain was 50 minutes.

The investigators concluded that: "Both the additional costs and the effectiveness of systems for pre-hospital thrombolytic therapy will depend on the setting in which such a system is introduced. The benefits will be greater if patients can be reached very early and in settings where transportation time is long".

Editors' note

The second part of this article looks at unpublished experiences with pre-hospital thrombolysis, the results of a poll among PCCS members on their attitude to being involved in thrombolysis, and which thrombolytic agents general practitioners and paramedics should use. It also discusses the points made in both articles.

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