Time delay to thrombolytic therapy – a Sri Lankan perspective

G R Constantine, P N Thenabudu

Summary
Reducing the time delay in initiating thrombolytic therapy in acute myocardial infarction is critical in maximising the functional and survival benefit. We analysed 120 consecutive admissions for thrombolytic therapy to the Coronary Care Unit. The total delay was divided into prehospital, in-hospital and Coronary Care Unit stages, and the median delays were found to be 130, 70, and 15 minutes, respectively. The delay was significantly longer in patients who sought prehospital medical advice, and when the diagnosis was not made at the emergency treatment unit. Educating at-risk groups and modifying the admission system may help to minimise these delays, while the establishment of an emergency ambulance service with well-trained crew would also improve the prognosis after acute myocardial infarction in Sri Lanka.

Keywords: thrombolysis; acute myocardial infarction; Sri Lanka

The use of thrombolytic agents has had a great impact on the management of acute myocardial infarction (AMI). It is clear that early administration of thrombolitics confers both functional and survival benefit. Coronary thrombi are more susceptible to lysis when these agents are given early. Streptokinase has been the main thrombolytic agent used in Sri Lanka for about a decade. Maximising the benefit of streptokinase and antiplatelet agents are important steps in improving the outcome of AMI. In this study we analyse the time delay encountered at various stages before the administration of streptokinase.

Subjects and methods
The study was conducted at the Institute of Cardiology of the National Hospital of Sri Lanka. We included 120 consecutive admissions for streptokinase therapy to the Coronary Care Unit (CCU) for a period of six months from May 1995. All patients were diagnosed to have AMI on clinical, electrocardiographic (ECG) and in many (98 patients) biochemical criteria.

All the patients were interviewed by the investigators regarding the time of onset of pain, prehospital medical advice, and time taken to arrive at the out-patient department. The time of admission at out-patients, ward and/or CCU and time of initiation of streptokinase infusion were obtained from patient records.

ADMISSION POLICY
Patients with suspected AMI are admitted to the emergency treatment unit from the out-patients department. An ECG is done in the emergency treatment unit. If the ECG shows changes characteristic of AMI the patient is sent to the CCU for streptokinase therapy. Some patients are missed at this stage due to lack of specific ECG changes or failure to recognise them. These patients are sent to general medical wards initially and with subsequent ECG changes or recognition of changes they are transferred to the CCU.

STATISTICAL METHODS
The Mann-Whitney U test was used to compare median delay times. All time delays are expressed as medians with interquartile range.

Results
Our study included 108 men (mean age 53 years) and 12 women (mean age 57 years). Anterior AMI was found in 61, inferior AMI in 50 and a combination in nine. The delay to initiation of thrombolyis was analysed in three different stages (figure 1 and table). The median prehospital delay was 130 minutes. Out of our 120 patients, 82 (68%) sought prehospital medical advice. The prehospital delay was significantly longer in this group compared with patients who came directly to the hospital (176 vs 85, Z = 5.2, p<0.001) (figure 2).

The median in-hospital delay was 70 minutes. The length of the in-hospital delay was partly dependent on the mode of admission to the CCU. The 56 patients (47%) who were initially sent to general medical wards had a significantly longer delay than those sent directly to the CCU (129 vs 61, Z = 5.8, p<0.001) (figure 3).

Discussion
The benefits of early thrombolytic therapy are well established. A meta-analysis of the time to thrombolytic therapy showed the absolute reduction in mortality per hour of delay to be 1.6 (SD 0.6) per 1000 patients, and modern guidelines for the management of AMI emphasise the need for early treatment.
In our study, the longest delay was encountered at the prehospital stage. This is mainly due to patient-related factors. Lack of awareness is an important contributory factor. Only 28 (23%) patients recognised the pain as being of cardiac origin, of whom only 12 (10%) thought immediate medical attention was important. The lack of awareness can be improved by public education. In a study in the urban area of Goteborg, Sweden, a significant reduction in time delay was achieved following public education. However, the effects of education programmes are transient, and may also lead to unnecessary admissions and presentations at out-patients departments. In our situation, this will reduce efficacy and accuracy of diagnosis, as facilities for ECG recording during non-working hours are limited. Education of the high-risk group is an effective tool, as is the education of their relatives. In our study, the majority of the patients who decided to see a doctor very early (within 15 minutes) did so due to pressure from family members.

The problem of transportation of patients is another important factor contributing to prehospital delay. All our patients reached the hospital by private transport, which takes time to arrange. In more developed countries, emergency ambulance services, administration of prehospital thrombolytic therapy, and other facilities have been developed to deal with transportation problems. A British study on thrombolytic therapy in six district hospitals revealed that 86% of patients reached the hospital by ambulance and only 11% came by private transportation. The emergency ambulance service has a significant role in reducing the prehospital delay. In Sri Lanka, there is no emergency ambulance service and only a minority of the population has access to telephone facilities. Apart from reducing the transit time, the ambulance crew can provide cardiopulmonary resuscitation (CPR) if required and can also initiate prehospital thrombolytic therapy, which can reduce the prehospital delay by up to 60 minutes. About 50% of deaths due to coronary artery disease occur outside the hospital. Most of these deaths are due to ventricular fibrillation. These deaths can be reduced by CPR alone. Thus, an ambulance service with well-trained staff can greatly improve the prognosis of AMI.

With the initial symptoms, the first step most patients take is to contact their general practitioner. In our study, 68% of patients sought prehospital medical advice. These

**Table**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number</th>
<th>Median (min)</th>
<th>Interquartile range (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehospital</td>
<td>120</td>
<td>130</td>
<td>90–182</td>
</tr>
<tr>
<td>Pain to out-patients (direct)</td>
<td>38</td>
<td>85</td>
<td>30–140</td>
</tr>
<tr>
<td>Pain to out-patients (indirect)</td>
<td>82</td>
<td>176</td>
<td>117–310</td>
</tr>
<tr>
<td>In-hospital</td>
<td>120</td>
<td>70</td>
<td>60–120</td>
</tr>
<tr>
<td>Out-patients to CCU (direct)</td>
<td>64</td>
<td>61</td>
<td>35–70</td>
</tr>
<tr>
<td>Out-patients to CCU (indirect)</td>
<td>56</td>
<td>129</td>
<td>65–190</td>
</tr>
<tr>
<td>CCU to streptokinase</td>
<td>120</td>
<td>15</td>
<td>15–20</td>
</tr>
</tbody>
</table>

**Figure 2** Median prehospital delay to thrombolysis

**Figure 3** Median in-hospital delay to thrombolysis
patients had double the delay to thrombolysis compared to patients who came directly to the hospital. Similar trends have been seen in other countries. Studies have shown that failure to recognise the symptoms as cardiac in nature, delays in contacting and being seen by general practitioners, and prescription of symptomatic medication, are important factors contributing to this extra delay. The office of the average general practitioner is not adequately equipped to initiate thrombolytic treatment for AMI. Aspirin is the most important drug that can be administered by the general practitioner. However, only 22% of patients who sought prehospital medical advice for suspected AMI received aspirin. Hence, patients with history suggestive of AMI should be encouraged to go to the nearest hospital without delay. In general, prehospital delay is longer with older age (>55 years), female sex, low socioeconomic status, history of angina and diabetes mellitus, and prehospital consultation.

In-hospital delay depended on the mode of admission to the CCU. There was significant delay in patients who were sent initially to the general medical wards and then transferred to the CCU. The reason for the delay was failure to diagnose AMI at the time of admission. In addition, patients who were sent to the medical wards had a mean delay of 90 minutes before an ECG was done.

In-hospital delay can be reduced by changing the admission policy. A ‘fast track’ admission policy, whereby the emergency cardiac team evaluates the patient in the emergency unit and initiates thrombolytic therapy, has been shown to reduce the in-hospital delay significantly without requiring additional staff or equipment and without compromising the accuracy of diagnosis.

In conclusion, the median delay from the onset of pain to streptokinase therapy (130 and 70 minutes) in Sri Lanka compares favourably with that of developed countries. However, this study reflects delay encountered in a tertiary care centre; similar studies need to be undertaken in other hospitals.

Further reductions in prehospital and in-hospital delays are important as these are both economically feasible and effective measures to improve the prognosis of AMI. The establishment of an emergency ambulance service with well-trained crew; at least on a small scale, would be a major step in this direction. The use of streptokinase therapy in general medical wards is increasing. This trend needs to be encouraged. ECG facilities should be available in medical and emergency units such that doctors can record ECG independent of technicians. Reduction of time delay to thrombolytic therapy requires collective responsibility from the general public, patient, general practitioner and the hospital staff. Group spirit and proper awareness need to prevail among hospital staff.

Ischaemic heart disease is a growing problem in developing countries. Hence, economically feasible measures to salvage the myocardium should be explored to the maximum.


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doi: 10.1136/pgmj.74.873.405

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