

# The thrombolytic therapy in the periphery – towards reduction of 'call to needle time'

R L Satarasinghe\*, D H Jayamaha\*\*, H Padmasiri\*\*\*, I Samarasinghe\*\*\*

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## Abstract

**Objectives** To identify and rectify deficiencies in the current practice, with regard to thrombolytic therapy in the management of acute myocardial infarction in the coronary care unit at Base Hospital Panadura.

**Design and Setting** 90 patients (Male = 71) with an ECG confirmed acute myocardial infarction admitted to the said unit between 08/01/1997 to 21/03/1999 were given a questionnaire with respect to the above matters and thus obtained data were analysed.

**Results** Age range of patients was between 25-85 years with a mean of  $55.4 \pm 12.9$  (SD) years. 38 had presented to the hospital within first hour, 27 within next three hours after the onset of chest pain. 71 had presented to local hospitals and 19 to the GPs. 18 had transfer delays from the local hospitals while in 19 this was due to negligence. 11 presented to the GPs had ECG confirmation while none in the hospital transfers. Aspirin 300mg was offered to 70; not given in 16; unknown in 04. 37 had reached the CCU from OPD within 5 minutes; 85 within 15 minutes. The house officers had seen 85 within 5 minutes of admission to the CCU or wards. Immediate ECGs had been done in 50 who presented during hospital hours. 40, presented during hospital hours. 40, presented outside working hours had delayed ECGs due to lack of an ECG machine in the CCU and unavailability of onsite on-call ECG technicians. In 67, junior medical officers have taken the initial decision to thrombolise, out of which 13 had been wrong; ST elevations had been wrong; ST elevations had been the sole indication.

**Interventional measures** ECG machines were made available in the CCU to perform ECGs outside working hours with training of medical officers.

\* Consultant Physician, Base Hospital, Panadura.

\*\* Senior Registrar, Medicine, NHSL, Colombo.

\*\*\* Intern House Officers, Base Hospital, Panadura.

## Conclusions

- "Call to needle time" needs improvement at various levels.
- Logistics such as ECG machines, access to "fast track" transport facilities should be made available to the local hospitals.
- Regional protocols for management of acute infarctions should be formulated and adapted with adequate training of all grades involved.

## Introduction

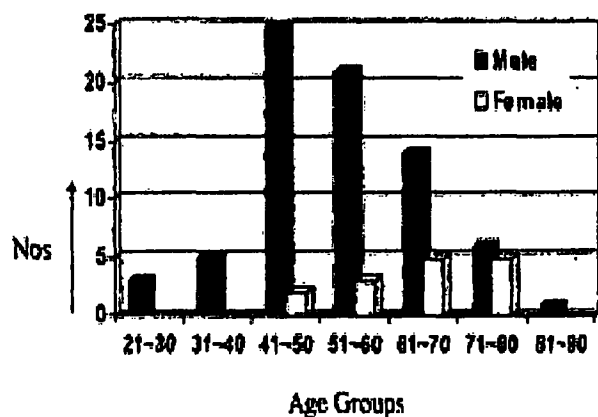
Recent advances in the management of acute myocardial infarction, i.e. thrombolysis, combined with aspirin, beta blockers and ACEI therapy in appropriate cases have revolutionised the outcome of this dreadful acute medical emergency over the last decade. Prompt diagnosis and swift action are two most important aspects of achieving the maximum success in the above. In Sri Lanka the base hospitals serve as the first line referral centres where acute infarctions are managed, with or without ICU facilities. The base hospital Panadura equipped with a seven bedded ICU and a 16 bedded intermediate coronary care unit is one of the largest and busiest units in the country serving large population in both Colombo and Kalutara districts. The following audit was designed to look into various aspects of management of acute myocardial infarctions admitted to the said unit.

## Results

Age distribution of the patients included in the study:

**Table**

Age range (years)	No. of patients	
	Male	Female
20-30	03	-
31-40	05	-
41-50	25	02
51-60	21	03
61-70	14	05
71-80	06	05
81-90	01	-



Figure

### Discussion

Soluble aspirin in a dose of 300mg should be offered at the earliest as the first line therapy to the patients where a diagnosis of an acute myocardial infarction is suspected. Aspirin irreversibly blocks the enzyme cyclo-oxygenase and therefore inhibits prostoglandin biosynthesis. In several animal models aspirin does not accelerate thrombolysis by plasminogen activators, but seems to delay or prevent the occlusion after successful lysis<sup>1,2</sup>. The clinical benefits of oral aspirin in acute infarctions have been impressively documented in the ISIS-2 trial<sup>3</sup> with 23% reduction mortality by giving aspirin alone, whereas in the group assigned to receive intravenous streptokinase alone, there was 28% reduction. The benefit in survival conferred by aspirin was additive to that with streptokinase; the combination of aspirin and streptokinase reduced in hospital mortality by as much as 42%. In addition, non fatal strokes and re-infarctions were reduced in the aspirin treated group in ISIS-2. Since mortality during the early days after randomisation was the same for the aspirin treated and non-aspirin treated groups, prevention of re-infarction, rather than acceleration of lysis also appears to be the mechanism of its benefit in humans. After bypass surgery, shear induced platelet thrombus formation was suppressed by high doses of aspirin (>300 mg daily) but not by low doses (75 mg daily) suggesting a mechanism other than interference with thromboxane formation<sup>4</sup>. In our series aspirin was not offered to 16 and in 4 the details were unknown.

Following aspirin administration next comes the issue of thrombolysis which has been unequivocally shown to improve the survival after an acute myocardial infarction compared with conventional treatment or placebo as demonstrated by the major placebo control trials<sup>3,5-11</sup>. The most striking drug dependant reduction (47% and 56% respectively) was in fact observed in patients treated within 1 hour after the onset of symp-

toms, while approximately half the benefit was shown by patients treated at 2-3 hours and 4-6 hours. The MITI trial<sup>12</sup> showed that when all patients were included in the analysis of effects of very early treatment (<70 min) a substantial reduction in the infarct size and improved survival, 4.9% vs. 11.2% were demonstrated, compared with patients receiving more delayed therapy (>70 min). EMIP<sup>13</sup>, the largest trial of pre hospital thrombolysis enrolling approximately 6000 patients, showed non statistically significant reduction in cardiac mortality (9.7% vs. 11.1%) in the pre hospital group. However in those patients who showed a "time to needle" at least 90 min. shorter than the hospital group, the mortality reduction was definitely significant (6.4% vs. 12.3%,  $p = 0.04$ ). In our series only 38 had presented to the hospital with 1 hour (43% and 72% had presented with 4 hours) in the latter group 18 had transfer delays and in 19 there had been negligence. Once admitted 37 (45%) had reached the CCU within 5 minutes and 85 (94%) within 15 minutes. The house officers have seen 94% of the admissions within 5 minutes, in spite of a very heavy workload. A major drawback seen on performing a confirmatory ECG for those who were admitted after working hours ( $n=40$ ; 44%) due to lack of an ECG machine in the CCU and unavailability of "onsite – on call" ECG technicians. This deficiency was later rectified by providing an ECG machine to the CCU and by training the house officers to operate the same.

In 67 instances (74%), the junior medical officers have taken the decision to thrombolise, out of which 13 had been wrong. In the meta-analysis done by FTT Collaborate Group<sup>14</sup>, pooling the data from 9 open and placebo control trials, the benefits of thrombolysis were clearly seen independently from sex, blood pressure, heart rate on admission, presence of previous myocardial infarction, diabetes mellitus and age. A definitive benefit was clearly seen only among patients with ST segment elevations and bundle branch blocks. The degree of benefit was seen to vary when patients were subdivided according to the presenting ECG. Among the almost 60,000 patients randomised, 68% showed ST elevation, 4% bundle branch block, 7% ST segment depression, 17% other abnormalities (inverted P waves or some other non-specific pattern suggestive of acute ischaemia) and 5% near normal ECGs. No beneficial or harmful effects of lytic treatment was observed among patients with ST segment depression or other ECG abnormalities. These diverging results may probably be explained by the fact that patients with ST segment elevation show a 90% incidence of total occlusion by an intracoronary clot, whereas the correlation of intraluminal thrombus is far weaker in patients with ST depression or T wave changes. Thus the coronary vessel occlusive status in ST segment

elevation patients presenting a larger thrombus rich in fibrin may offer a more favourable milieu for lysis. The same does not seem to apply patients without ST segment elevation, who probably have a significantly smaller amount of thrombus much more rich in platelets. In our series ST elevations have been the sole criterion to institute thrombolysis. "High take-off ST segments" (congenital ST elevations), ST elevations in Prinzmetal's angina, persistent ST elevations in septal leads in old antero-septal infarctions have been the major confusions for the wrong decisions in thrombolysis in our series. This once again emphasises the importance of availability of on-site facilities to perform at least CPK-MB, to resolve such confusions. In the case of a left bundle branch block (LBBB) the initial decision to thrombolise will be difficult due to the unavailability of sophisticated investigations such as CPK-MB or cardiac troponin.

### Conclusions

In our experience, once a patient is suspected of having an acute myocardial infarction, the maximum benefits of the medical therapies available could be conferred by:

- reducing the "Call to needle time" by developing an integrated team approach to treat such patients, involving the referring hospitals or general practitioners in the area.
- providing logistics such as ECG machines, access to "fast track" transport facilities in the peripheral referring hospitals.
- formulating regional protocols for management of acute infarctions with adequate training of all grades involved.
- educating the population at high risk.

### References

1. Fitzgerald DJ, Wright F, Fitzgerald GA. Increased thromboxane biosynthesis during coronary thrombolysis; evidence that platelet activation and thromboxane A module the response to tissue-type plasminogen activator in vivo. *Circulation Research* 1989; **65**: 83-94.
2. Jang I k, Gold HK, Leinbech RC et al. in vivo thrombin inhibition enhances and sustains arterial recanalization with recombinant tissue-type plasminogen activator. *Circulation Research* 1990; **67**: 1552-1561.
3. ISIS 2 (Second International Study of infarct Survival) collaborative group. Randomised trial of intravenous streptokinase, oral aspirin, both or neither among 17,187 cases of suspected acute myocardial infarction; ISIS - 2. *Lancet* 1988; **ii**: 1349-1360.
4. Ratnatunga CP, Edmonson SF, Rees GM, Kovacs IB - High dose aspirin inhibits shear-induced platelet reaction involving thrombin generation. *Circulation* 1992; **85**: 1077-1082.
5. Gruppo Italiano per lo Studio della Streptochinasi nell' Infarto Miocardio (GISSI) Effectiveness of intravenous thrombolysis treatment in acute myocardial infarction. *Lancet* 1986; **i**: 397-402.
6. ISAM Study Group. A prospective trial of intravenous streptokinase in acute myocardial infarction (ISAM). Mortality, morbidity and infarct size in 21 days. *New England Journal of Medicine* 1986; **314**:1465-1471.
7. Wilcox RG, Von der Lippe G, Olsson CG et al. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. *Lancet* 1998; **11**: 525-530.
8. AIMS Trial Study Group. Effect of intravenous APSAC on mortality after acute myocardial infarction: preliminary report of a placebo-controlled clinical trial. *Lancet* 1998; **i**: 842-847.
9. Rossi P, Bolognese L on behalf of Urochinas per via Sistemica nell'Infarto Miocardio Acuto (USIM) Collaborative Group, Comparison of intravenous streptokinase plus heparin versus heparin alone in acute myocardial infarction. *American Journal of Cardiology* 1991; **68**: 585-592.
10. Late study group. Late assessment of thrombolytic efficacy (LATE) study alteplase, 6-24 hours after onset of acute myocardial infarction. *Lancet* 1993; **342**: 759-766.
11. EMARS (Estudio Multicentrico Estreptoquinasa Republicas de America del Sur) Collaborative Group. Randomised trial of late thrombolysis in patients with suspected acute myocardial infarction. *Lancet* 1994; **343**: 311-322.
12. Weaver WD, Cerqueira M, Hallstrom AP et al. Pre hospital initiated vs hospital initiated thrombolytic therapy. The myocardial infarction Triage and Intervention Trial. *Journal of American Medical Association*. 1993; **270**: 1211-1216.
13. EMIP group. Pre hospital thrombolytic therapy in patients with suspected acute myocardial infarction. *New England Journal of Medicine* 1993; **329**: 383-389.
14. Fibrinolytic Therapy Trialists (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 100 patients. *Lancet* 1994; **343**: 311-322.