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Original articles

The effect of reduction of door-to-needle times on the administration of thrombolytic therapy for acute myocardial infarction

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Summary

Optimal management of acute myocardial infarction requires rapid administration of thrombolytic therapy. However, only patients who fulfill the following specific criteria are likely to benefit from this treatment: admission within 12 hours of the onset of symptoms, no contraindications, ST elevation or possible new-onset left bundle branch block on the admission electrocardiogram. We employed an aggressive policy to reduce the delay between admission to hospital and the administration of thrombolysis (the 'door-to-needle time'), and investigated whether this approach affected the accuracy of administration of thrombolysis. Patients admitted to the cardiac care unit with acute myocardial infarction, or who were thrombolysed, were identified retrospectively over two equivalent 4-month periods before and after implementation of our policy. Patients were considered eligible for thrombolysis if they fulfilled the criteria mentioned above. The mean (SD) door-to-needle time for all patients who received thrombolysis on admission decreased from 61(70) to 19(20) minutes (p=0.0004). The proportion of patients eligible for thrombolysis who received treatment increased from 24/38 to 30/30 (p=0.0002). However, the proportion of patients receiving thrombolysis who did not fulfill our criteria also increased, from 3/27 to 11/41 (p=0.1). There were no complications of thrombolysis in the first study period, but two cerebrovascular accidents in the second period; both patients fulfilled our criteria for treatment. We conclude that simple educational measures greatly reduced door-to-needle times and led to a higher proportion of eligible patients receiving thrombolysis. However, greater pressure on medical staff to make rapid management decisions increased the proportion of patients being thrombolysed inappropriately.

Keywords: myocardial infarction; thrombolysis; door-to-needle time

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The introduction of intravenous thrombolytic therapy has revolutionised the acute management of myocardial infarction. Meta-analysis of the large trials has shown a definite reduction in mortality, the benefit decreasing with time from the onset of symptoms in an apparently linear fashion: every hour of delay in thrombolysis is associated with the loss of about 1.6 lives per thousand patients.[1] However, only patients presenting with acute myocardial infarction (AMI) who have ST segment elevation or new left bundle branch block on the electrocardiogram (ECG) benefit from thrombolysis. Those exhibiting other patterns, most notably ST segment depression, may actually have their prognosis worsened. More importantly, patients who have not had an AMI, whose chest pain is in fact due to pericarditis or aortic dissection, may be placed at significant risk of pericardial tamponade or fatal haemorrhage if they receive thrombolysis. It is also well established that thrombolytic therapy delivered within 12 hours of the onset of chest pain in AMI is effective, but there is no conclusive evidence for its use later than this.

Therefore, optimal management of AMI requires administration of thrombolytic therapy as soon as possible after admission to hospital, but the benefit applies only to patients who fulfill specific clinical and ECG criteria. At our institution, we have employed an aggressive policy to reduce so-called door-to-needle times since January 1993. Patients with possible cardiac chest pain, regardless of age, are admitted directly to the Cardiac Care Unit. The nursing staff have been trained to ensure rapid identification of patients likely to require thrombolysis, and they also ensure education of rotating junior doctors. There is regular teaching on the daily cardiologist-led Cardiac Care ward rounds.

We hoped that a generally increased awareness of the importance of thrombolysis would lead to a higher proportion of eligible patients receiving the appropriate treatment. However, we were concerned that any significant reduction in door-to-needle time would lead to a reduction in decision-making time, so that some patients not strictly fulfilling the criteria could potentially receive thrombolysis inappropriately. These patients might have their overall prognosis worsened by thrombolysis, so offsetting at least some of the benefit of a lower mean door-to-needle time.

We therefore compared two time periods, before and after implementation of our policy, to see whether there had been any change in the proportion of eligible patients being

Table 1 Characteristics of patients with myocardial infarction; NS=non-significant

	Oct 91–Jan 92	*Oct 94–Jan 95*	*p*
Number	66	76	
Mean age (SD)	65 (11)	70 (11)	0.02
Sex M:F (%)	42:24 (64:36)	53:23 (70:30)	NS
Site			
Anterior	39 (59%)	45 (59%)	
Inferior	27 (41%)	28 (37%)	NS
Uncertain	0 (0%)	3 (4%)	
Type			
Q-wave	39 (59%)	37 (49%)	
Non-Q	27 (41%)	38 (50%)	NS
Aborted	0 (0%)	1 (1%)	
Pain-to-admission time (hours) (SD)	7.7 (10.5)	10.5 (20.1)	NS
Admission (days) (SD)	6.3 (3.1)	7.3 (4.7)	NS
Peak CK activity (IU/l) (SD)	1292 (1352)	1040 (927)	NS
Survival			
Discharge	55 (83%)	64 (84%)	NS
1 month	52 (79%)	63 (83%)	NS

thrombolysed, or in the proportion of thrombolysed patients being treated in the absence of strict criteria.

Patients and methods

All patients admitted to the Battle Hospital Cardiac Care Unit with a final diagnosis of myocardial infarction, or who had received thrombolytic therapy, were identified from October 1991 to January 1992, and from October 1994 to January 1995. These periods represented times before and after implementation of our policy, during which no recruitment for any trials of thrombolysis was occurring. Equivalent times of year were chosen to ensure equivalent levels of experience amongst junior medical staff.

In total, 287 patients were admitted during the first study period (304 separate admissions) and 410 during the second period (436 separate admissions). Notes were examined for 259 (85%) of the admissions during the first period and 377 (86%) during the second period. The numbers of admissions with a final diagnosis of myocardial infarction were 66 (25%) and 76 (20%), whilst the numbers of admissions receiving thrombolysis at presentation were 27 (10%) and 41 (11%). These differences were not statistically significant.

The timing of events was obtained from the medical and nursing notes, or from the drug chart. Myocardial infarction was diagnosed on the basis of two out of three of the following criteria:

- 20 minutes or more of ischaemic chest pain
- development of Q waves or persistent T wave changes in the ECG
- peak creatine kinase activity at least twice the upper limit of normal for our laboratory (greater than 580 IU/l).

Patients were considered to have been eligible for thrombolysis if they had been admitted within 12 hours of the onset of symptoms, had no contraindications, and the admission ECG showed ST elevation or possible new-onset left bundle branch block. Blinded retrospective review of the admission ECG was performed by two experienced observers. Only patients thrombolysed on the basis of the admission ECG, or who were eligible for thrombolysis on admission, were included in the analysis of door-to-needle times and the accuracy of treatment.

Statistical significance was determined for continuous variables using an unpaired Student's *t*- test, and for categorical variables using a chi-squared test.

Results

The mean (+/-SD) age of patients in the second study period (70+/-11 years) was significantly greater than that of patients in the first study period (65+/-11 years) (p=0.02). Otherwise the two groups were comparable (table 1).

The mean door-to-needle time (SD) for all patients who received thrombolysis on admission decreased from 61 (70) minutes for the first study period to 19 (20) minutes for the second period (p=0.0004) (figure). The proportion of patients with myocardial infarction who were not eligible for thrombolysis increased from 28/66 (42%) to 46/76 (61%) (p=0.03). More importantly, the proportion of patients eligible for thrombolysis who received treatment increased from 24/38 (63%) to 30/30 (100%) (p=0.0002) (figure). In total, 14 patients in the first study period were not thrombolysed despite being eligible: three were not treated because of perceived contraindications which appeared to be unjustified in the notes; five died within a few hours of admission and other aspects of their management (eg, inotropic support, temporary pacing) received precedence over thrombolytic therapy; six were not thrombolysed and no explanation was documented.

The proportion of patients receiving thrombolysis who did not fulfill our criteria also increased from 3/27 (11%) to 11/41 (27%) (p=0.1) (figure). Nevertheless, all patients in both study periods who were thrombolysed inappropriately turned out to have acute coronary syndromes, either myocardial

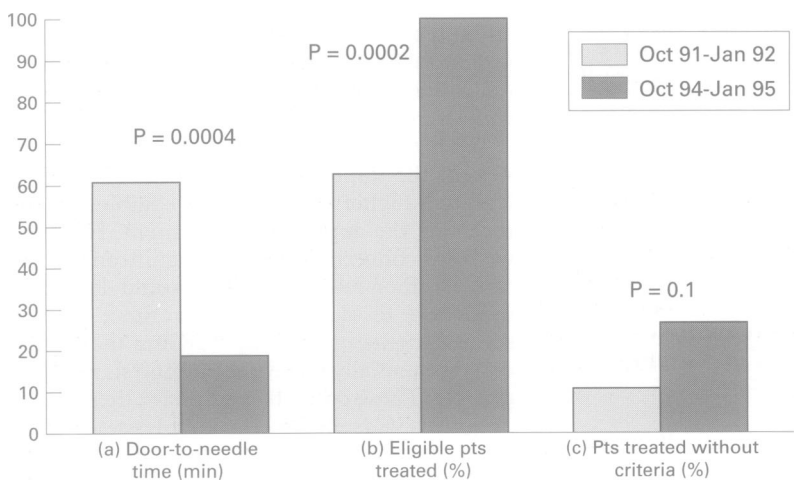

Figure Reduction in mean door-to-needle time and its effect on the accuracy of thrombolysis. (A) Mean door-to-needle time for patients thrombolysed on admission (minutes); (B) patients eligible for thrombolysis on admission who received treatment (%); (C) patients thrombolysed on admission in the absence of strict criteria (%)

infarction not fulfilling our criteria or unstable angina. In particular, none of them was subsequently found to have pericarditis or aortic dissection.

Following thrombolytic therapy, there were two deaths in the first study period and five in the second. All of these were due to progressive cardiogenic shock, and there were no instances of acute electromechanical dissociation (ie, presumed myocardial rupture). There were no obvious complications of thrombolysis in the initial study period, but two cerebrovascular accidents in the later period (men aged 70 and 81 years, both of whom had fulfilled our criteria for treatment). One-month survival was not significantly different between the two groups: 52 (79%) *vs* 63 (83%).

Learning points

- reducing the delay to thrombolysis in AMI is associated with increased clinical benefit
- simple administrative and educational measures can greatly reduce hospital door-to-needle times and increase the proportion of patients receiving appropriate treatment
- education of medical staff must address the potential pitfall of thrombolysing some patients inappropriately

Discussion

For thrombolytic therapy to confer maximal benefit in AMI, it must be administered as soon as possible after the onset of chest pain.[1] Whilst there is an inevitable delay between the onset of symptoms and arrival in hospital, it should be possible to minimise the delay from admission to treatment (the door-to-needle time). We have shown that, with aggressive education and a liberal admission policy to the Cardiac Care Unit, mean door-to-needle time has been reduced by 42 minutes, a highly significant decrease. This implies a reduction in mortality of 1.1 lives per 1000 patients treated.

A number of parameters reflect liberalisation of our admission policy to the Cardiac Care Unit. There was a 43% increase in the number of admissions, as well as a smaller 15% rise in the number of myocardial infarctions. There was also a significant increase in the proportion of patients with AMI who were not eligible for thrombolysis on admission. Previously, such patients were more likely to be managed on the general medical ward to which they were first admitted. Importantly, the increased access to Cardiac Care given to elderly patients with chest pain resulted in a significant increase in the mean age of admissions. This is entirely appropriate because such patients have a higher mortality rate from AMI and derive even greater benefit from thrombolysis than younger patients, albeit with a higher risk of complications.[2]

It is interesting to note that altogether only 48% of patients with a final diagnosis of AMI were eligible for thrombolytic therapy at presentation. This is very similar to the 49.7% found in a recent cohort follow-up study of 3014 patients presenting to four Cardiac Care Units in New Zealand.[3] There is therefore clearly a need for additional reperfusion strategies, as some subgroups of patients ineligible for thrombolysis appear to be at particularly high risk.[4 5]

An important beneficial result of the effort to lower door-to-needle times was a significant increase in the proportion of patients fulfilling strict criteria for thrombolysis who received such treatment. In fact, 100% of eligible patients were thrombolysed in the second study period, extending the benefits of thrombolytic therapy to an additional 37% of eligible patients. The reason for this improvement appears to be a change in attitude of junior medical staff with priority being given to thrombolytic therapy, and improved education about spurious contraindications.

The rate of complications of thrombolytic therapy in our study was low, and there were only two cerebrovascular accidents which occurred in patients who had been treated appropriately. However, the number of patients in our study is relatively small, and overall thrombolytic therapy causes an increase in cerebrovascular accidents of 3.9 per 1000 patients treated.[1]

One disadvantage of our policy was an increase in the proportion of patients who were thrombolysed without fulfilling strict criteria. It is likely that this reflects increased pressure on junior medical staff to make rapid management decisions. It should be emphasised that all of the inappropriately thrombolysed patients from both study periods subsequently turned out to have acute coronary syndromes, and the potentially dangerous administration of such treatment to patients with, for example, aortic dissection or pericarditis was avoided. Nevertheless, thrombolysis of patients without the commonly accepted ECG criteria confers no benefit or even an increase in mortality (table 2).[1] We now emphasise this point in our education of staff, and plan to repeat this study in the future to look for a reduction in the proportion of patients being treated unnecessarily.

One theoretical problem with the concept of strict eligibility for thrombolysis is that patients presenting very early in the development of myocardial infarction may have non-diagnostic ECGs on admission and may not receive treatment. Such patients would be expected to gain great benefit from thrombolytic therapy. We recommend that all patients with possible cardiac chest pain are managed on the Cardiac Care Unit, regardless of the appearance of the ECG on admission. This allows the ECG to be repeated frequently and facilitates rapid and appropriate management.

The simple administrative measures which were used to reduce door-to-needle times were accomplished without any increase in the number of Cardiac Care beds or staffing levels. Patients not felt to require cardiac monitoring on admission were rapidly transferred to the general medical wards. Patients recovering

Table 2 Mortality benefit of thrombolysis according to ECG appearance (from Fibrinolytic Therapy Trialists' Collaborative Group[1])

Entry ECG	*Lives saved per 1000 treated*
Bundle branch block	49
Anterior ST elevation	37
Inferior ST elevation	8
Other ST elevation	27
ST depression	−14
Other abnormality	6
Normal	−7

from myocardial infarction were more likely to complete their in-patient stay on the general wards, thereby freeing Cardiac Care beds for acute admissions. The only direct financial cost of implementing the changes was that of the administration of thrombolysis to an additional 14 patients over 4 months. Assuming an approximate cost of £80 per dose of streptokinase, this equates to a modest increase in expenditure of £3360 per year. This amount would be reduced by nearly one third if inappropriate thrombolysis could be prevented.

Door-to-needle time is only one component of the total delay from the onset of chest pain to administration of thrombolysis in AMI. The majority of the delay occurs between the onset of symptoms and the patient telephoning for medical assistance. This period can only be reduced by improvements in public health education. The delay between a patient's call for help and the delivery of thrombolytic therapy is rather more amenable to reduction. In some areas, significant distances separate patients from the nearest Cardiac Care Unit. In these cases, prehospital administration of the newer bolus thrombolytic agents by general practitioners or paramedics has proven effective.[6] In the area served by our hospital, the journey time to hospital is seldom a significant delaying factor, and we have not adopted this approach. Instead, we have recently introduced a strategy to transport patients from home directly to the Cardiac Care Unit as rapidly as possible by improving the coordination between the general practitioner, the ambulance service, and the hospital.

In conclusion, this study demonstrates that simple measures can reduce door-to-needle times and increase the proportion of eligible patients receiving thrombolysis. However, this improvement was associated with an increase in the number of patients being treated without an absolute indication, potentially diluting the benefit of our policy.

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