PREHOSPITAL CARE

Prehospital thrombolysis: lessons from Sweden and their application to the United Kingdom

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Emerg Med J 2002;**19**:578–583

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Accepted for publication 25 March 2002

Objective: To study the successful implementation of paramedic administered prehospital thrombolysis in Sweden, and to consider the implications of this for the UK.

Methods: A series of research visits were undertaken, including visits to Uppsala Hospital and dispatch centre, ambulance stations in several counties of Sweden and Dalarna County, which has one of the longest experiences of telemedicine supported prehospital thrombolysis in Europe. Data relating to prehospital thrombolysis, stages in successful implementation, and potential barriers to change were identified.

Results: Two thirds of the hospitals in Sweden now have some form of prehospital thrombolysis. A nationally agreed and standardised training programme and the fact that many ambulance paramedics are also qualified nurses has facilitated successful introduction, but Sweden's low population density is also an important factor. Data from Dalarna County indicate that the median "pain to needle" time has been reduced by 45 minutes with a concurrent reduction in complications from 50% to 25% (p=0.018). Inhospital mortality has also reduced from 12% to 6%, but with the small numbers involved this improvement does not achieve statistical significance (p=0.36).

Conclusion: If the outcome of acute myocardial infarction in the United Kingdom is to be improved, and National Service Framework targets met, then prehospital thrombolysis is an important development. Several technical solutions already exist, and a single bolus thrombolytic agent is now available, but the main barriers to full implementation are related to the establishment of an effective training programme and the organisational changes that will facilitate this new practice. High quality research is urgently needed to guide the implementation of prehospital thrombolysis in a clinically and cost effective way.

Acute myocardial infarction (AMI) is one of the leading causes of death in the United Kingdom. Three hundred thousand people in the UK suffer an acute heart attack each year, of whom 50% die. Sixteen thousand of these are aged below 65, and chest pain or suspected AMI is the primary reason for a high priority ambulance call (20% of all 999 calls).[1]

Thrombolysis is a treatment that can produce a substantial improvement in mortality and morbidity from AMI, and this improvement is directly related to the delay between symptom onset and administration.[2] It has been demonstrated that for patients presenting two hours after the start of symptoms each hour's delay in receiving thrombolysis leads to the loss of 21 lives per 1000 treated (measured at 30 days).[3]

Any process that can reduce the "pain to needle" time (the time between the patient experiencing symptoms of AMI and the delivery of thrombolysis) will lead to a reduced mortality. As a result of this, the recently published UK National Service Framework for coronary disease established a target "call to needle" time of 60 minutes or less. This sets a new standard of care: "People thought to be suffering from a heart attack should be assessed professionally and . . . thrombolysis should be given within 60 minutes of calling for professional help".[4]

Currently the average "call to door" time (the time between the patient calling for help and arriving at the hospital) is 30–45 minutes in urban areas, and considerably more in rural locations, while very few units are able to achieve a "door to needle" time (the time between the patient arriving at the hospital and delivery of thrombolysis) of 30 minutes or less in 90% of cases.[1] It is therefore apparent that inhospital thrombolysis is unlikely to meet the targets set out in the National Service Framework. Also, as AMI is common and its effects so profound in terms of both mortality and morbidity, even a small decrease in the average "pain to needle" time will have a dramatic effect on the health of the population as a whole.

As "door to needle" times approach a practical minimum of 20 minutes further reductions in the "call to needle" time can only be made by moving thrombolysis into the prehospital environment. A study in the Grampian region of Scotland produced very positive results when general practitioners administered thrombolysis in remote areas,[5] but for the vast majority of patients in the UK the only practical way of ensuring that thrombolysis is given more speedily is for the drug to be administered by paramedics responding to a 999 call. However, at the present time many paramedics are unfamiliar with the principles of electrocardiogram (ECG) interpretation, and therefore cannot determine which patients should receive thrombolysis. Furthermore, very few UK paramedics have practical experience of thrombolytic administration.

The delivery of prehospital thrombolysis depends upon the acquisition and interpretation of a prehospital ECG. Four methods of achieving this have been described:

1 Computerised acquisition and automatic interpretation of the ECG. This approach has been tested with some success,[6] but computer interpretation inevitably errs on the side of caution so that some eligible patients will not receive prehospital thrombolysis. There is also some mistrust of a non-human interpretation in this situation.

2 ECG interpretation by liaison with a local general practitioner. This has proved successful in some rural areas of

Abbreviations: AMI, acute myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; ECG, electrocardiogram

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the UK,[5] but as outlined above is unlikely to achieve effective national coverage, particularly in urban and suburban areas where the first response will usually be from a paramedic ambulance.

3 ECG interpretation by paramedic staff. This is perhaps the ultimate future of prehospital thrombolysis, but at the moment many UK paramedics are not confident in this role, and will require a significant period of training before they are able to provide thrombolysis without real time medical support.

4 Transmission of the ECG to medical staff at the receiving hospital followed by the use of two-way mobile communications to authorise and support the administration of prehospital thrombolysis.[7]

Of these approaches perhaps the most promising is the last: the development of prehospital ECG transmission to facilitate prehospital thrombolysis, with the expectation that this will ultimately lead to autonomous paramedic thrombolysis as described in option three.

A recent meta-analysis has clearly demonstrated that prehospital thrombolysis is capable of significantly decreasing the time to thrombolysis and all cause mortality,[8] and this is facilitated by a series of recent technical advances that permit the reliable transmission of high quality data (including 12 lead ECGs) from a moving ambulance,[9] and the availability of a single bolus injectable thrombolytic agent.[10]

Prehospital acquisition and transmission of an ECG have already been shown to reduce the door to needle time,[11] and are a move in the right direction. The next logical step has been to consider the possibilities that exist for prehospital thrombolysis in the UK.

Previously, some attempts to provide paramedic administered prehospital thrombolysis in the UK proved unsuccessful (PHAROE Study (1998); personal communication with S E McCabe). This has been attributed to human factors, and barriers to change among staff and in the NHS itself.[12] In contrast, prehospital thrombolysis, administered by ambulance staff, has already been successfully described on a number of occasions in mainland Europe.[6 13] Most notably in Sweden, effective communication technologies have been developed and deployed that permit the transmission of high quality patient data (including 12 lead ECGs) and the advent of prehospital thrombolysis.[14]

Sweden is the fourth largest country in Europe, and has a landmass similar in size to the American state of California, yet it is home to only 8.7 million people. Roughly 15% of the country lies within the Arctic Circle.

Sweden is divided into 21 counties, each with its own ambulance service. Initially acting as autonomous organisations, there has recently been much more standardisation across counties, particularly in paramedic training. All paramedics spend three years in training, and start work as "assistant nurses" in a hospital. They then spend at least six months in emergency medicine, with additional training in driving and communications to become qualified as "ambulance health care workers" (paramedics). However, more and more ambulance personnel start out as fully qualified nurses, after which they gain two years experience in anaesthesia, emergency medicine, coronary care, and other relevant acute specialties before joining the ambulance service. Paramedics who are not also qualified as nurses are permitted to administer drugs, but undergo a formal training programme followed by a written and practical assessment and yearly re-evaluation.

The introduction of the UK National Service Framework will act as a spur for the widespread implementation of ECG acquisition and transmission technology, but it is essential that this development be informed by existing expertise. We describe some of the data and observations from Sweden, a country that leads the world in this field, and consider ways in which lessons already learnt could be successfully applied to UK practice.

The objective of this reseach was to study the successful implementation of telemedically supervised, paramedic delivered thrombolysis in Sweden, and to consider the implications of this for the UK.

METHODS

In November 2000 the principal author (JRB) undertook a research visit to Uppsala and Dalarna Counties, Sweden. This included visits to Uppsala City hospital and dispatch centre, ambulance stations in several counties of Sweden and also to Dalarna County, which has one of the longest experiences of prehospital thrombolysis in the world.

Meetings were held with paramedics and doctors involved in prehospital thrombolysis, including the medical directors of two ambulance services and a consultant cardiologist. Results from local audit in Dalarna County were also collected and statistically analysed using χ^2 testing. A p value of less than 0.05 was taken as indicating statistical significance.

Stages in successful implementation, and potential barriers to change, were identified in order to construct a template for application to UK practice.

RESULTS

Background

There are about 75 hospitals in Sweden. Nearly all of these have an established system of prehospital ECG transmission, while approximately 50 have some form of prehospital thrombolysis.

The Swedish Board of Health and Welfare approved paramedic thrombolysis in 1999. This decision was based, in part, on pilot studies undertaken in Dalarna County, which has been researching prehospital thrombolysis by paramedics since 1997. A standardised, and nationally approved, training programme was drawn up consisting of an extra two days in the paramedic training programme plus a one day refresher course every year incorporating a practical rehearsal in which medical students act as "patients".

Many different thrombolytic drugs have been used in Sweden, including streptokinase, tissue plasminogen activator (TPA), and reteplase. Currently reteplase is used almost universally. This is given as two bolus doses of 10 units, 30 minutes apart. Further benefits are anticipated from the introduction of single bolus thrombolytics. At present Swedish paramedics only administer thrombolysis on the authorisation of a doctor after electronic transmission of the ECG. Different regions of the country use different ECG transmission methods, according to local preference. These vary from modified defibrillators/monitors to integrated electronic patient records and dedicated data transmission devices.

General observations from Sweden

Paramedics

- Normal practice is to move the patient into the ambulance to perform and transmit an ECG as the necessary equipment is usually heavy and bulky to carry. This increases the on scene time by around three minutes.
- There was a great deal of trepidation when prehospital thrombolysis was given by each paramedic for the first time, but they quickly became a lot more relaxed once a few patients had been successfully treated.
- In Mora, paramedics are encouraged to give thrombolysis in the ambulance even if they have just arrived at the hospital. This is to avoid the inevitable "door to needle" time that will occur if the patient is unloaded before receiving thrombolysis.

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Table 1 Thrombolysis location for 109 patients with AMI transported by ambulance in Dalarna County during 1998

Region of Dalarna County	Number thrombolysed by a GP	Number thrombolysed in ambulance	Number thrombolysed in hospital	Total
Falun	0	18	22	40
Mora	11	10	31	52
Avesta	0	0	10	10
Ludvika	0	4	3	7
Total	11	32	66	109

Table 3 Breakdown of the median pain to needle time for 32 patients receiving paramedic administered prehospital thrombolysis in Dalarna County during 1998

Median times (min)	Falun (n=18)	Mora (n=10)	Ludvika (n=4)	All patients (n=32)
Pain to call time	69	125	56	90
Response time	8	5	40	8
Arrival to ECG sent	12	42	16	16
ECG sent to thrombolysis	15	23	26	19
Total pain to needle time	104	195	138	133

Doctors

- On the whole Swedish cardiologists are happy with prehospital thrombolysis because heart muscle is being saved.
- There are no concerns regarding prehospital complications: bleeding problems (such a stroke or gastrointestinal haemorrhage) are not encountered in the ambulance, only in hospital afterwards. This view is supported by data collected from Dalarna County (see below).
- Prehospital thrombolysis is found to be more effective when a senior doctor is available to respond to the transmitted ECG: junior staff often lack the confidence to authorise drug administration.

Service delivery

- Initially only very clear cut AMIs were thrombolysed in order to boost confidence in the overall system.
- While it was originally envisaged that prehospital thrombolysis would only be used in rural regions, it is now being administered anywhere, including urban areas. In the city of Uppsala all emergency ambulance calls are reached in five minutes. On scene time averages around 20 minutes, with a five minute journey time to hospital. However, as it requires only two to three minutes to obtain and transmit an ECG, and two to three minutes to give the drug, urban prehospital thrombolysis has been found to be nearly always beneficial.
- In some cases patients are not thrombolysed prehospital, but after ECG transmission are taken, on medical direction, directly to a cardiac catheterisation facility for emergency coronary angioplasty (PTCA). This strategy is most useful in urban areas where the patient is close to a 24 hour catheterisation facility, and where patient characteristics make urgent angioplasty the treatment of choice. If, however, the patient is a long way from a catheterisation facility then thrombolysis may be given first, followed by urgent PTCA if there is evidence of ongoing coronary artery occlusion.
- The most important factor has been to ensure that all parties have continuous education and support. In Uppsala this has led to a general upswing in prehospital thrombolysis, with increasing confidence and activity.
- The adoption of prehospital thrombolysis has increased awareness and led to widespread improvements in the whole chain of thrombolysis, even for those who come to the hospital without calling an ambulance.

Data from Dalarna County

A comprehensive audit of prehospital thrombolysis in Dalarna County has recently been undertaken. During 1998 thrombolysis was administered to 109 patients in the county who called an ambulance as a result of their symptoms. The location of thrombolysis is recorded in table 1. GP thrombolysis (11 patients) was carried out in only one region of Dalarna County, perhaps reflecting a local interest, whereas prehospital and inhospital thrombolysis were more evenly distributed. Only one region, Avesta, did not undertake prehospital thrombolysis in the period studied. Of the 66 patients thrombolysed in hospital, 45 (68%) were male with a mean age of 68 years (range 43 to 88 years). The median duration of each component of the "pain to needle" time for inhospital thrombolysis is recorded in table 2. By comparison, the median time intervals for the 32 patients thrombolysed prehospital by paramedics using reteplase are recorded in table 3. In this group 23 patients (72%) were male, and the mean age was 62 years (range 41 to 79 years). It is clear that prehospital thrombolysis resulted in a considerably reduced "pain to needle" time, even though the average "pain to call" time was longer in the group thrombolysed prehospital. The median response time was the same in both groups, with the on scene time for those patients thrombolysed inhospital being very similar to the time between ambulance arrival and ECG transmission for the patients thrombolysed prehospital. Similarly, the median transport time to the emergency department for patients thrombolysed inhospital was almost identical to the time between ECG transmission and the actual delivery of thrombolysis for patients thrombolysed prehospital.

Table 2 Breakdown of the median pain to needle time for 66 patients receiving inhospital thrombolysis in Dalarna County during 1998

Median time (min)	Falun (n=22)	Mora (n=31)	Ludvika (n=3)	Avesta (n=10)	All patients (n=66)
Pain to call time	75	107	75	77	78
Response time	7	15	6	14	8
On-scene time	17	16	15	10	15
Transport time (to ED)	20	30	10	12	20
ED to CCU time	35	16	20	25	25
CCU to thrombolysis time	29	36	5	53	32
Total pain to needle time	183	220	131	191	178

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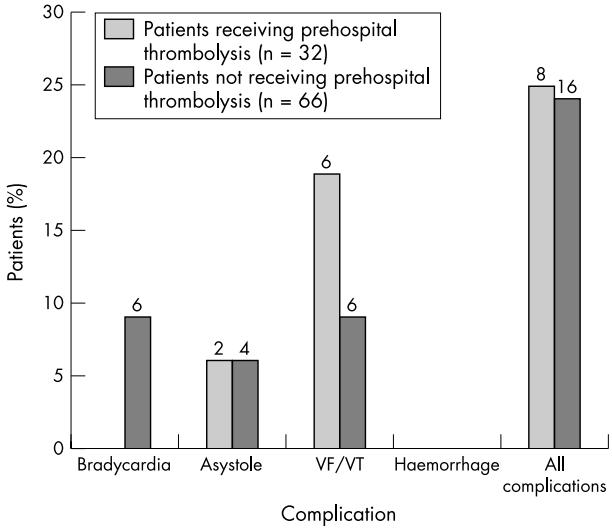

Figure 1 A comparison of prehospital complications for patients with AMI receiving and not receiving prehospital thrombolysis in Dalarna County during 1998. The number shown above each column gives the actual number of patients. VF/VT indicates ventricular fibrillation or ventricular tachycardia.

Interestingly, it was found that the introduction of prehospital thrombolysis reduced the "pain to needle" time for all patients, even those who conveyed themselves to hospital. This was attributed to a heightened awareness of the benefits of early thrombolysis.

Complications were also assessed during the study period. Prehospital complications for those patients receiving prehospital thrombolysis and those simply transported to hospital to receive inpatient thrombolysis are compared in figure 1, while inhospital complications for the two groups are compared in figure 2. Complications in the prehospital phase were found to be identical (25% for the prehospital group versus 24% for the inhospital group) while complications during the inhospital phase of care were doubled (from 25% to 50%) in those patients not receiving thrombolysis until they reached hospital ($p=0.018$ on χ^2 testing). When all prehospital and inhospital complications are combined the benefit of prehospital thrombolysis remains ($p=0.018$). Six per cent of the patients receiving prehospital thrombolysis died while in hospital compared with 12% in the group receiving inhospital thrombolysis, though this difference does not achieve statistical significance ($p=0.36$), perhaps because of the small number of patients involved.

There does seem to be an increased risk of ventricular fibrillation or ventricular tachycardia in those patients thrombolysed prehospital (19% versus 9%), but this also does not reach statistical significance ($p=0.17$) and is a complication that paramedics in both Sweden and the UK are very experienced in dealing with, as evidenced by the fact that there were no prehospital deaths.

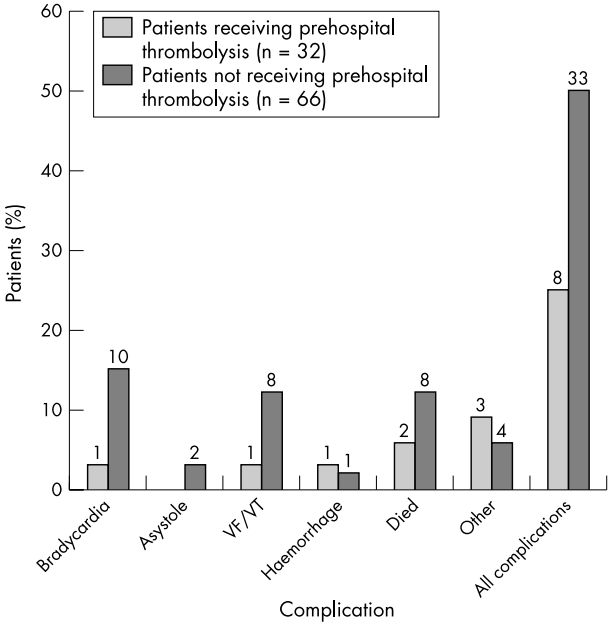

Figure 2 A comparison of inhospital complications for patients with AMI receiving and not receiving prehospital thrombolysis in Dalarna County during 1998. The number shown above each column gives the actual number of patients. VF/VT indicates ventricular fibrillation or ventricular tachycardia.

DISCUSSION

Prehospital thrombolysis has clearly proved successful in Sweden, but there remains a paucity of hard scientific data that can be readily applied to the UK. Sweden is a much larger country with a smaller population, so ambulance journey times are often longer than in the UK. Furthermore, the specialty of emergency medicine is not recognised in Sweden, so that inhospital thrombolysis will usually only be given on a coronary care unit (CCU). This is analogous to the situation in the UK 10 years ago, when patients arriving in the emergency department (ED) were often transferred to the CCU for thrombolysis, causing significant further delays. Improvements in the UK system mean that many patients presenting to an ED with AMI will now be thrombolysed promptly in the ED, with the potential to reduce the "door to needle" time to as little as 20–40 minutes.[15] Nevertheless, patients thrombolysed in hospital will inevitably have a "door to needle" time that is unlikely to be decreased further: this is the primary rationale for carrying thrombolysis into the prehospital environment.

The information that is available from Dalarna County clearly supports prehospital thrombolysis. Median "pain to needle" time was reduced by 45 minutes, with the "call to needle" time falling from 98 to 43 minutes, an improvement of nearly one hour per patient. This time saving is very similar to the "door to needle" time, as a patient receiving inhospital thrombolysis will just be entering the hospital at the point where prehospital thrombolysis could have been administered. If the time between ECG transmission and the delivery of prehospital thrombolysis is used for patient transport then the additional delay in reaching the hospital will be minimal, and the patient will be close to the expertise of the receiving unit when the drug is actually delivered.

There is no evidence that prehospital thrombolysis leads to an increased incidence of complications: quite the reverse in fact. The prehospital complication rate was similar for the two groups, but the inhospital and overall complication rates were much higher for those patients who received inhospital thrombolysis, mainly because of an increased incidence of arrhythmias.

Nevertheless, these results must be viewed with caution as they arise from a process of simple observation and are therefore open to many possible biases. In particular, there is no randomisation, and it may be that the patients thrombolysed prehospital had more straightforward AMIs than those receiving inhospital thrombolysis. The sex distribution was similar between the two groups, but those patients receiving prehospital thrombolysis were, on average, six years younger, and this may have influenced the subsequent outcome. In addition, patients with heart conduction defects such as left bundle branch block are harder to diagnose,[16] and are

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Table 4 Stages and potential barriers in the implementation of prehospital thrombolysis

Stages		Potential barriers
1	Identify and involve all stakeholders, ensuring regular consultation	Scepticism and resistance to change
2	Determine current practice: for example, local "pain to needle" times and the number of patients eligible for prehospital thrombolysis	Lack of reliable information
3	Consider the possible options and their relative costs: for example, measures to improve "pain to call" or "door to needle" times, approaches to prehospital thrombolysis	Lack of reliable financial data
4	Plan implementation, determine goals and set a realistic timetable	
5	Begin paramedic training, regarding the rationale behind thrombolysis and the acquisition/interpretation of the ECG. This should be tailored to local needs	Lack of funding to support initial and ongoing training
6	Purchase equipment and thrombolytic agent	
7	Continue paramedic training, to include those hospital staff who will be providing ECG interpretation and authorising thrombolysis	Fear of technology or unfriendly systems. Resistance to change in current working patterns and responsibilities
8	Begin "practice" ECG transmission to hospital without prehospital thrombolysis. Eligible patients could be given thrombolysis by the paramedic on arrival in hospital to boost confidence	"Teething problems" with equipment and ECG transmission
9	Commence prehospital thrombolysis, starting with the most straightforward cases	Unwillingness to administer thrombolytic drug: concerns regarding safety and side effects
10	Continuing training, audit and formal review by all involved parties	Decline in enthusiasm and interest over time

therefore less likely to receive prehospital thrombolysis, but have a worse prognosis than patients presenting without such conduction defects.[17]

The population of AMI patients and their presentation may be significantly different between Sweden and the UK. For example, in Sweden up to 50% of patients with AMI will transport themselves to hospital, rather than calling an ambulance or their GP. Another major factor may be differences in the "pain to call" time, which is consistently found to be the longest stage in the total "pain to needle" time.[18] In this study the median pain to call time was 12 minutes longer in the group thrombolysed prehospital, but the significance of this is uncertain.

Stages in successful implementation, and potential barriers to change, are summarised in table 4. Aufderheide and colleagues from North America also discuss several of these issues further in a report published in 1996.[19]

While prehospital thrombolysis has proved successful in Sweden this cannot be automatically extrapolated to the UK. The two countries have different demographics and different healthcare systems. In remote regions prehospital thrombolysis will almost certainly be of benefit, as demonstrated in the GREAT study,[5] and successful administration by general practitioners in such locations is an established fact in both countries. However, the vast majority of AMI in the UK occurs in urban and suburban areas where transport times are comparatively short and the potential benefits of prehospital thrombolysis are untested. The Swedish experience in Uppsala suggests that the introduction of prehospital thrombolysis may well prove beneficial even in larger cities, or if the drug is given at or close to hospital arrival, simply because the "door to needle" time is avoided, but research is urgently needed in this area. Patients suitable for emergency PTCA may also be identified and "fast tracked" to an emergency cardiac catheterisation facility, though few hospitals currently provide this service in the UK.

More than anything else there remains a need for robust research into prehospital thrombolysis as applied to the UK. The cost of implementing the sort of nationwide programme described in the recent "NHS Plan" would be considerable,[20] and must be balanced against alternative approaches such as better education of the public to reduce the "pain to call" time. It also seems likely that a transit time beneath which prehospital thrombolysis is no longer beneficial could be accurately identified, but a lack of research evidence significantly hampers the introduction of this important new development. In the meantime, implementation in the UK is likely to be heavily influenced by the recommendations of the European Resuscitation Council. These suggest that prehospital thrombolysis should be undertaken if the combined journey time and inhospital delay is more than 60 minutes, or if the journey time is 30 minutes or more.[21] This is further developed by the National Service Framework for coronary heart disease, which states that prehospital thrombolysis is appropriate if the "call to door" time is likely to exceed 30 minutes.[4]

CONCLUSION

If the outcome of AMI in the UK is to be improved, and National Service Framework targets met, then prehospital thrombolysis is an important and promising development. Successful implementation in Sweden, demonstrating an effective service with considerably reduced "pain to needle" times, a statistically significant decrease in the rate of complications, and a real likelihood of substantial mortality benefit, offers important and valuable lessons for the UK. Several technical solutions already exist, and a single bolus thrombolytic agent is now available, but the main barriers to widespread implementation are related to the establishment of an effective training programme and the organisational changes that will facilitate this new practice. High quality research is urgently needed to guide the implementation of prehospital thrombolysis in a clinically and cost effective way, but ultimately it seems quite possible that a high proportion of the patients suffering AMI in the UK each year will be able to benefit from the mortality and morbidity gains associated with earlier thrombolysis.

ACKNOWLEDGEMENTS

The authors wish to acknowledge Elisabeth Nerpin, cardiology nurse in Falun Dalecarlia, Sweden, who collected the data from Dalarna County, and also thank the Swedish ambulance, nursing and medical staff who generously assisted with their time and comments.

Contributors

Jonathan Benger initiated the project, secured funding, collected data, and drafted the paper. Rolf Karlsten and Bengt Eriksson developed the project, collected data, and edited the paper. Jonathan Benger acts as guarantor.

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Funding: this research was supported by a grant from Ortivus, manufacturers of "Mobimed" equipment.

Conflicts of interest: Jonathan Benger received a grant from Ortivus, manufacturers of "Mobimed" equipment in order to undertake this research, but has no ongoing involvement with, or financial interest in, this company.

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