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Domiciliary thrombolytic treatment by general practitioners

EDITOR—The results of the Grampian region early anastreplase trial showed that within the context of the burden of myocardial infarction that is carried by a community, the general practitioners who participated clearly, and effectively, performed a great deal of selection. Recruitment of only patients within the first months means that most patients with myocardial infarction were not entered into the trial. A local estimate for Plymouth Health Authority is that of eight to 10 myocardial infarctions per general practitioner each year. The Grampian study, assuming a 30% death rate if medical help is not called, these general practitioners' patients would have suffered 1537 myocardial infarctions, but only 511 entered the study. Another way of looking at this is to consider the total number of deaths ascribed to myocardial infarction among patients of the doctors in the study. Extrapolation from local data for Plymouth gives 511 deaths per annum for the period of the study. A considerable proportion of these will have been sudden deaths; this still leaves many more deaths than those noted during the study.

Any strategy for implementing a new advance needs to take into account the whole range of presentations of conditions; for thrombolysis this means not only patients with classical myocardial infarction diagnosed by general practitioners but also, for example, people with atypical chest pain and those who do not perceive their symptoms as serious.

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EDITOR—It is surprising that in the Grampian region early anastreplase trial no patients were diagnosed as having unstable angina, which is the most common differential diagnosis and the most difficult to make in the early stages of a myocardial infarction. It is likely that the patients in the diagnostic groups “possible myocardial infarction” and “ischaemic heart disease” in fact had unstable angina. If only definite and probable myocardial infarctions are counted the diagnostic accuracy of the general practitioners was 57% (of the hospital doctors 66%). This may also account for the lower mortality and fewer Q wave infarctions in the domiciliary group.

As there is no evidence that thrombolytic treatment is of benefit in patients who survive that nearly half the patients in the study received thrombolytic treatment inappropriately and were needlessly exposed to the risks of haemorrhage. Colleagues and I found similar figures in a study in Somerset, where the general practitioners could accurately diagnosed myocardial infarction on clinical grounds (without electrocardiography in most cases) in 45% of cases (S Rule et al, unpublished work). Again this was largely because manifestations of unstable angina were thought to be in the early stages of myocardial infarction.

Diaragnosing myocardial infarction at the onset can be difficult, but at a minimum a good history should be obtained, and either an electrocardiogram properly interpreted. In the Grampian study the general practitioner was required to record an electrocardiogram but not to interpret it, which seems pointless. It is the electrocardiogram, however, that causes problems for many general practitioners as individually they will see few cases of myocardial infarction each year. The higher diagnostic accuracy in hospital may relate to this.

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EDITOR—I am sympathetic to P L. Harris's objective of trying to reduce mortality from ruptured abdominal aortic aneurysms. I have recently screened 678 (97.6%) of the 695 patients aged 60-79 in our practice for aneurysms. Twenty six were found to have an aneurysm (range 3.0-8.3 cm external sagittal diameter), and 13 were referred for a surgical opinion. The screening programme has exposed some of the dilemmas in current management of aneurysms.

Patients deserve to know of important risks associated with repair of an aneurysm. Harris's statement that in best centres elective repair carries an “operative risk of under 5%” cannot be generally assumed, and published mortality statistics may not reflect the risk for an average patient. This is illustrated with elective repair of an aneurysm has not been widely published, but in series of mixed elective and emergency repairs it has been considerable. Without reference statistics on mortality and morbidity the balance of whether to operate for a particular size of aneurysm and risk to the patient becomes uncomfortably difficult. For individual patients local results will be most pertinent unless distant referral is considered.

Harris rightly directs attention to aneurysms of 4.0-5.0 cm, for which management is contentious; most aneurysms detected by screening fall into this category. Surgery has been advocated for aneurysms of 4.0 cm or more, but such an aggressive policy is not supported by recent prospective 'and retrospective' studies of the natural course of aneurysm. Rarely, small aneurysms will rupture fatally, but I believe that relatives find unlikely much more tragedy easier to bear than tragedy after well intentioned surgery. A more conservative approach to surgery tips the risk/benefit balance towards benefit, and Scott et al's study exemplifies how such a policy has worked successfully.

With regard to the psychological consequences of detecting aneurysms by screening, will patients with small aneurysms be able to maintain a fair perspective of a low risk of rupture or will their predominant perception be of a time bomb waiting to explode within? The predicament of those with large aneurysms who are considered to be unfit for surgery is particularly unfortunate. The anxiety an aneurysm can generate should not be underestimated or disregarded.

If a low risk aversity is associated with elective surgery, a conservative approach to intervention, and adequate counselling of patients can be combined then I believe that a local screening policy for aneurysms could make good ethical and economical sense. That such criteria apply nationally is doubtful, and currently I do not favour a national screening programme.

Lastly, β blockade has shown promise in the management of athero-sclerotic aneurysms being fairly common, whether physiological β1 adrenergic antagonism can retard their expansion or reduce the rate of rupture is of great importance. An extension of the Medical Research Council's small aneurysm study to address this issue would be expedient.

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1 Harris PL. Reducing the mortality from abdominal aortic aneurysms: need for a national screening programme. BMJ 1992;305:697-8. (19 September.)


study in the absence of electrocardiographic criteria is not necessarily generally applicable. Unless thrombolysis is restricted to those presenting early and with classic symptoms of infarction, the proportion of alternative diagnoses (2.3%) is unlikely to be substantiated. For example, phase 1 of the myocardial infarction triage and intervention project found only one in six confirmed infarctions among those evaluated before admission to hospital. 1

The statement that “even in an urban area there would be a temporal advantage in the general practitioner giving thrombolytic therapy in the home” is untested and cannot be extrapolated from the present study. A 999 cell and shortening of the delays in hospital would have reduced the difference between home and hospital treatment substantially. We have shown that in an urban area the time of administration of thrombolytic treatment after the onset of symptoms was reduced to a median of 150 minutes by the introduction of a “fast track” system. Until these issues are resolved it may be premature to advise widespread implementation of pre-hospital thrombolysis without electrocardiographic confirmation.

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Entron—Much publicity has been, and will be, given to the finding of the Grampian region early anistreplase trial that patients who received thrombolytic treatment (anistreplase) at home had 49% fewer deaths than those who received it in hospital. 1 Unfortunately, the trial was really too small to estimate reliably any reduction in mortality, and so significance could be achieved only if (because of either chance or bias) an impossibly large treatment difference was observed. In clinical trials Bayesian analysis provides a useful interpretation by setting a surprising finding in the context of more cautious prior belief.

First one expresses prior belief about the proportionate reduction in mortality due to thrombolysis at home. Given the known benefits of early thrombolysis 2 and the average two hours saved in time to treatment, it could be argued that a 15-20% reduction in mortality is highly plausible, while the extremes of no benefit and a 40% reduction are both unlikely. The figure (a) shows a distribution of prior belief. This prior is compatible with the results of the European myocardial infarction project, in which the same drug was given to over 5000 patients.

In the Grampian region early anistreplase trial 23 of the 148 patients who received home thrombolysis died within three months compared with 13 of the 163 who received hospital thrombolysis. This is displayed in the figure (b). The observed 49% reduction is the mode of this distribution, and the 2% tail area beyond no effect indicates p<0.02 one sided. The widely spread distribution illustrates the inevitable uncertainty with only 36 deaths in total.

Using Bayes’s theorem, we have combined the prior belief and likelihood to produce a posterior belief distribution (figure (c)). This quantifies how opinion on the efficacy of home thrombolysis should be affected by the limited amount of highly positive data in the Grampian region early anistreplase trial. The peak of the posterior distribution is a 25% reduction in mortality, with a 95% confidence interval from no effect to a 43% reduction. Thus belief is shifted in a positive direction, but not by much, and, specificaly, a halving of mortality remains implausible.

(a) Prior distribution

(b) Likelihood based on 23/148 + 13/163 deaths

(c) Posterior distribution

% Change in risk in using home treatment

Bayesian analysis of data from Grampian region early anistreplase trial

Perhaps the Grampian region early anistreplase trial was just lucky. For instance, based on the figure (a) a difference of 23 versus 13 deaths or more should occur with probability 0.1. We are also concerned, however, about the emphasis on three month mortality (not a predefined end point), the lack of independent monitoring of data, the randomisation method, and the early stopping of the trial.

Overall, such an important therapeutic issue requires larger scale trials which can quantify the treatment effect precisely. Here we seem faced with publication bias. A small positive trial (the Grampian region early anistreplase trial) gets emphasised while another larger trial of the same issue (the European myocardial infarction project) remains unpublished. On a broader note, we would encourage a wider use of bayesian methods in reports of clinical trials, especially when a small trial is claiming a large treatment benefit.

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On site medical services at major incidents

EDITOR,—Matthew W Cooke 1 and D G Nancekivell emphasise the need for better organisation and training for hospital staff in providing on site medical services when a major incident occurs. A hospital coping with a deluge of casualties from a major incident might be overstretched in providing one or more appropriate teams as well as a command senior enough to be the medical incident officer (the Department of Health has abandoned the term site medical officer). Cooke highlights the paucity of training in this role. Wide ranging discussions have taken place in London with representatives of the London accident and emergency consultants’ group, the London Ambulance Service, the British Association for Immediate Care, and health emergency planning officers from each Thames regional health authority with the aim of creating a cadre of 40-50 trained and accredited medical incident officers. This scheme relieves the main receiving hospital of the onerous duty of providing all the resources required at the site. The scheme has been approved by all participants, but, in view of its variation from guidance from the Department of Health, individual units will retain the option of making their own arrangements.

Two established training courses for doctors are available nationally. A one day course is run by the British Association for Immediate Care each year in Cambridge, and a three day course on the medical management of major incidents is run jointly by the Royal Postgraduate Medical School and the British Association for Immediate Care at Hammersmith Hospital. This course is multidisciplinary and combines lectures, seminars, and practical training for NHS staff called on to work with medical incident officers or with mobile medical and nursing teams. In the two years that the course has been run, 102 people have been trained. The participants undertake an assessment at the end of the course, a major function of which is to allow the course organisers to assess the effectiveness of the training offered in key principles.

Though advanced trauma life support courses offer excellent training in clinical aspects, specific training is required for all prehospital care, including elements of safety and working with the emergency services.

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1 Cooke MW. Arrangements for on scene medical care at major incidents. RMJ 1992;305:748. (26 September.)
2 Cooke MW, Rice EJ. On site medical services at major incidents. RMJ 1992;305:736-7. (26 September.)