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Management of myocardial infarction in the community: a new RCGP study

MYOCARDIAL infarction is the greatest single cause of premature death in the United Kingdom. In England and Wales alone it was the certified cause of death of 181 420 people in 1987, accounting for approximately 35% of all deaths in men and 30% among women.[1] With such large numbers of affected individuals, even small changes in mortality risk can result in substantial changes in the number of deaths occurring in the population.

About one half of all deaths that occur after a myocardial infarction take place within two hours of the start of symptoms, usually because of the onset of ventriculation fibrillation. Many patients die before they can be seen by a doctor, but for those who are alive when their general practitioner arrives the mortality rate in the next month is some 25%.

Clearly, to obtain the maximum benefit, any intervention must be applied early in the course of the attack. In some circumstances immediate admission to hospital will permit the most speedy initiation of treatment, but the interval between arrival at the hospital and the start of therapy needs to be closely monitored in order to minimize delay. There is no doubt that since early treatment is so important and most attacks start outside hospital, it is logical to start treatment in the community. Such treatment, however, must be shown to be quickly available, effective and safe.

Can general practitioners provide such a service? In order to investigate this issue the Royal College of General Practitioner's Manchester research unit, which has been responsible for the highly successful oral contraception study, is now embarking on a major new prospective survey which calls for the collaboration of nearly 6000 general practitioners.

Although the term 'coronary thrombosis' (the putative cause) has been taken to be almost synonymous with 'myocardial infarction' (the assumed effect) it was not until 1980 that De Wood and colleagues[2] demonstrated that thrombus formation in a coronary artery was indeed the usual preliminary to the development of myocardial necrosis. It follows that treatment which can disperse or dissolve the clot or prevent its extension, given early, should be able to limit irreversible damage to the heart muscle.

It is remarkable that the homely remedy of aspirin may, by itself, reduce mortality by 25%.[3] Unless specifically contra-indicated, a crushed or dispersable tablet of 150 mg should be given at the time of the attack and administration is frequently continued daily for at least a month. It diminishes the aggregation of platelets and its benefits are in addition to those derived from agents which can dissolve or disperse the thrombus.

Streptokinase is a naturally occurring thrombolytic agent which was first administered by intra-coronary perfusion. It remains the agent most likely to be used in hospital, but is now given by intravenous infusion over a period of one hour. When supplemented with aspirin, mortality can be reduced by about 50% over the first month.[3] Newer agents include tissue plasminogen activator, now known as alteplase (rt-PA), and anisoylated plasminogen streptokinase activator complex (anistreplase).

Strict clinical trials of each of these agents show reductions in mortality which vary between 25% and 50%.[4-9] The studies were not strictly comparable with one another and the confidence intervals around the estimated benefits overlap. There is thus far no clear evidence that one product is more effective than the others. The advantage of anistreplase, however, is that is has a longer half life than alteplase and can, therefore, be administered as a single bolus intravenous injection over a period of three to five minutes. There is no reason why such a procedure should not be undertaken outside hospital.

The evaluation of the use of anistreplase by general practitioners is one of the objectives of the RCGP study. It is already licensed for use in the community, but the RCGP believes that the introduction of such a powerful new agent should be undertaken under conditions which can be carefully monitored. Because it dissolves clots it can cause bleeding in patients who are prone to this (for example those with a history of peptic ulceration) and such patients should not receive the drug. Since it is derived from tissues it can cause an anaphylactic reaction, but this is rare. Its effect is to reduce myocardial damage and therefore it does not increase the risk of cardiac arrest. In fact it may decrease the incidence of ventricular fibrillation, but this is unproven.

There is a thinly veiled implication in pronouncements by cardiologists[8] that general practitioners are likely to be less accurate in their diagnosis of myocardial infarction than hospital doctors (an accusation that any experienced family doctor would vigorously deny) and that, as a result, anistreplase might be administered inappropriately more frequently at home. There is no doubt that at home or in hospital, with or without an electrocardiogram, total accuracy of diagnosis cannot be achieved.

Two recent articles allegedly assessed the case for and against home treatment.[9,10] However, neither addressed the key issue — what is the risk of giving thrombolytics to patients who have not had a myocardial infarction compared with the risk of not giving them in patients who have?

The hospital-based AIMS study, which treated patients up to six hours after onset of symptoms, showed that 11.1% of the anistreplase treated patients died within one year of their infarction, as opposed to 17.8% of the patients who were given placebo.[7] Thus, failure to provide thrombolysis might deny seven in 100 patients who have had a heart attack the opportunity to live for at least another year. The major mortality risk of inappropriate use would be in someone with a dissecting aortic aneurysm. The entry criteria for the ASSET study[4,5] did not require demonstration of the electrocardiographic changes of myocardial infarction. Eleven of the 2514 patients treated with alteplase were subsequently shown to have a dissecting aortic aneurysm.[5] Five died within one month, giving a mortality rate of 1.99 per 1000 alteplase treated patients. There were nine cases of aortic aneurysm among the placebo treated patients; two died, giving a one month mortality rate of 0.8 per 1000 placebo treated patients. Thus, the excess fatality rate associated with the use of thrombolytics was 1.19 per 1000. Other conditions which might contribute to the mortality risk would be anaphylactic shock and severe haemorrhage. In the ASSET study major haemorrhagic events were infrequent (1.4% of alteplase treated patients, compared with 0.4% of placebo treated subjects). Unfortunately, the authors do not state how many of the patients died from their haemorrhage, but evidence from other studies suggests that very few do so.[3-5,7,11] Anaphylactic shock was similarly rare.

Thus, the risk of patients dying if they are given thrombolytics when they have not had a myocardial infarction is 1.19 per 1000, while the excess mortality of withholding thrombolytics when patients have experienced a myocardial infarction is 70 per 1000. Obviously these data are approximate, but they show a substantial advantage from giving rather than withholding thrombolytics when myocardial infarction is suspected.

While this discussion assesses the risks associated with the giving or the withholding of thrombolytics, the real issue is the safety of giving thrombolytics at home compared with their administration in hospital. Since there is likely to be a substantial advantage in giving thrombolytics whenever an experienced clinician is confident that a myocardial infarction has occurred, early treatment at home is likely to be an advantage. This benefit could only be lost if cases at home were frequently misdiagnosed. Clearly we need hard data on the accuracy of home diagnosis, and this is another objective of the RCGP study.

There will be many general practitioners who will wish their patients to benefit from the use of anistreplase as soon as possible. It is hoped that these doctors (whether or not they are RCGP members) will volunteer to record their cases and provide follow-up information for one year after the attack. On average a general practitioner will be called to treat an acute myocardial infarction only twice a year, and no doctor will be asked to enrol more than four cases over a two year period. On the other hand there will undoubtedly be doctors who would rather wait until further evidence is available before they incorporate thrombolytic drug use into their normal practice. These doctors are asked to record data about all their cases in an identical way to those who wish to use thrombolytics. They will be providing invaluable information about current care of patients in the community and this will be available for use as comparison data in the statistical assessment of the occurrence of reported events in the treatment group. As more evidence on the use of thrombolytics becomes available, doctors in either group will have the opportunity of changing groups should they so wish.

The RCGP has gained international recognition for its conduct of major multi-observer studies in the past. Here is an opportunity to contribute to a new study of outstanding worldwide importance.

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