Thrombolytic treatment for recurrent myocardial infarction

Avoid repeating streptokinase or anistreplase

The widespread adoption of thrombolytic treatment and widening indications for its use have led to an increasing number of patients presenting to coronary care units who have previously received thrombolytic treatment. In the first year after thrombolytic treatment reinfarction occurs in about 9% of patients, and about 20% of patients admitted with myocardial infarction to a coronary care unit will have had a previous infarction. Both streptokinase and anistreplase are antigenic, and after their administration antibody titres rise within a few days, peak one to two months later, and then slowly recede. High titres of antibodies might potentially be associated with major anaphylactic reactions and may result in ineffective thrombolysis. Many of the patients presenting with recurrent infarction will have received streptokinase and some will have received anistreplase. It is therefore an important issue whether these drugs should be given again. Moreover, patients who are circulating antibodies to streptokinase as a result of a previous streptococcal infection, and for effective thrombolysis the dose of streptokinase must overcome neutralisation by antibody binding. Before Verstraete et al advocated a standard dosing regimen streptokinase resistance was tested and the dose modified for each patient. Streptokinase doses greater than 1-25 million units will overcome these antibodies in most patients. The currently recommended dose of 1-5 million units of streptokinase should therefore be effective in all patients except those who have recently received streptokinase or who have had a recent streptococcal infection.

Even though some patients may have high antibody titres, the incidence of allergic reactions is low. In the second international study of infarct survival 8392 patients received streptokinase and none had anaphylactic shock. In 5860 patients treated in the trial by the Gruppo Italiano per lo Studio Della Streptochinasi nell'Infarto Miocardico there were seven cases of anaphylactic shock but no deaths. Several measurements can be made to assess the likelihood of reduced fibrinolytic activity with repeat administration of streptokinase or anistreplase. The total streptokinase resistance test measures the inhibition of fibrinolysis and reflects the contribution of IgG, IgM, and IgE streptokinase antibodies as well as plasmin inhibitors such as α2 antiplasmin. The measurement is also influenced by the amounts of fibrinogen and plasminogen present. Assays have been developed for detecting specific IgG, IgM, and IgE antibodies.

Streptokinase resistance titres increase by the fifth day after administration of either streptokinase or anistreplase and remain raised in most patients for at least one year. In a small group of patients Jalilah and Morris showed that at three months all patients had neutralising titres to 1-5 million units of streptokinase. Massel et al showed that at one year about 70% (95% confidence interval 48% to 92%) of patients who had previously received streptokinase for acute myocardial infarction had neutralising antibodies to 1-5 million units of streptokinase.

The effect of high antibody titres on lytic efficacy when these drugs are given again is uncertain. Moran et al showed a poor correlation between streptokinase specific IgG measured by radioimmunoassay and the functional streptokinase resistance titre. A recent study, in which patients were given streptokinase again within a year, minor allergy was common, but analysis of cardiac enzyme activities and late coronary angiography suggested successful thrombolysis in 70% of this group.

It remains uncertain which thrombolytic drug is best used in acute infarction. Tissue plasminogen activator is more effective than streptokinase at attaining early arterial patency as judged by a 92 minute angiogram. Nevertheless, there may be little difference between the drugs in terms of sustained patency, which is the likely mechanism of benefit. No difference has been detected between the two drugs in their effect on subsequent left ventricular function or on mortality. The results of the third international study of infarct survival comparing streptokinase, recombinant tissue plasminogen activator, and anistreplase are awaited. In the mean time streptokinase is the cheapest drug and should be used unless there are doubts about safety or efficacy.

No comparative trials are available to guide the choice of thrombolytic drug for repeat treatment. The risk of major allergic reactions seems to be low when repeat administration is delayed for more than six months, but there are uncertainties about the efficacy of repeat administration. What then can be recommended in the light of our present state of knowledge?

Although the efficacy of repeat administration of streptokinase or anistreplase has not been studied in detail, the high prevalence of raised neutralisation titres at 12 months will probably be associated with decreased thrombolytic efficacy. Treatment shown to be effective should be given and streptokinase or anistreplase should not be administered again within 12 months if non-allergic thrombolytic drugs are available. Further information is required about antibody titres after 12 months. Meanwhile several strategies could be adopted. Jahil and Morris have recommended measuring neutralisation titres before readministering an individualised dose. But this may take up to an hour as several dilutions have to be made, and this approach is untenable in the light of the substantial evidence of the benefits of early thrombolytic treatment. Moreover, an in vitro test may not reflect the
Random breath testing now

Roadside checkpoints would not be affront to freedom

Alcohol contributes to an estimated one in 10 road traffic accidents in Britain, accounting for 800 deaths and 22,000 casualties each year.1,2 Yet more than a quarter of male drivers admit to having driven at least once in the previous year believing that their blood alcohol concentrations exceeded the legal limit (A Guppy, unpublished communication). And between 10 pm and 3 am 2% of drivers are likely to be over the limit.3 Certainly, inroads have been made in the problem of drink-driving over the past decade, but just as certainly further deterrents are needed. Random breath testing, proposed in an all party amendment to the Road Traffic Bill, would be one. Based on evidence from other countries, it should work.

Introducing the breathalyser in 1968 substantially reduced drink-driving because people were frightened of being caught. Now many are not. In a recent survey 42% of people who admitted to drinking and driving thought that they ran little risk of detection.4 As long as people think that they can get away with it penalties won’t work—and stopping the offence is clearly better than punishing it. The police agree. “A deterrence based enforcement system,” said Mr Peter Joslin, chairman of the traffic committee of the Association of Chief Police Officers, “is far more effective in reducing drink-drive fatalities than the traditional enforcement model.”

At present the police can require a breath test in three circumstances: when the driver is suspected of having alcohol in his or her body, has committed a moving traffic offence, or has been in an accident. They also have a general power to stop any vehicle at any time. According to case law these powers may be combined: a police officer may stop any vehicle to “establish suspicion” that the driver has been drinking, after which a breath test may be required. The police argue that establishing grounds for suspicion before testing should be unnecessary and that they should have unrestricted powers to require a breath test (“unfettered discretion”).

The proposed amendment provides for random breath testing at roadside checkpoints. Regulations would permit roadside checks at which either all vehicles or a sample of vehicles could be stopped by a constable in uniform for the administration of breath tests. Roadside checkpoints would be authorised in writing and clearly signposted. As a deterrent to drinking before driving its great virtues are its high visibility and the fact that roadside testing could be encountered anywhere and at any time (though there is no reason why it should not be “targeted”). The Parliamentary Advisory Council for Transport Safety favours the amendment, as do many other experts and members of the public. Experience from abroad, notably in Scandinavia and most of Australia, supports its introduction. In New South Wales, for example, in the first four years of random breath testing the average number of fatal and serious accidents related to alcohol fell by one third.5 The hospital and social security savings were over 20 times the initial cost of implementing the scheme.6

An argument sometimes used against random breath testing is the low detection rate.7 No one, however, is talking about random testing as a substitute for existing procedures: it would be an additional weapon in the armoury. Only in the completely impartial context of roadside checkpoints would the requirement for establishing suspicion be waived. The impartiality of random breath testing is a crucial asset, and the National Council for Civil Liberties supports it. So did 77% of people interviewed in a government survey last November.8

The BMA, among other bodies, is pressing for the measure and is writing to urge MPs to vote for the amendment, on which there could be a vote in the next week or two. It ought to be a free vote. In the short time that remains doctors and other health workers must make their voices heard.

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5 Lennon R, Quinny A. A survey of drink-driving behaviour, knowledge and attitudes. Crowtherome: Transport and Road Research Laboratory, 1990. (TRRL Contractor Report 147.)