Thrombolysis-associated ventricular fibrillation: is it reperfusion, the drug or what?

See page 213 for the article to which this Editorial refers

Primary ventricular fibrillation occurs frequently in the setting of acute myocardial infarction and takes the lives of about 30% of patients in the first hour of symptoms. The mechanisms by which these fatal arrhythmias are initiated are, however, still not completely elucidated. A certain anatomical substrate, a prerequisite for primary ventricular fibrillation, cannot be identified. Prevention of primary ventricular fibrillation in acute myocardial infarction would be a major step forward in the reduction of mortality, but so far only lidocain has shown some efficacy, although the side effects of this prophylaxis hampers its general use.

Reperfusion therapy is a major leap forward in the treatment of acute myocardial infarction and has been shown to reduce mortality by at least 25%[1]. The mechanism of benefit is very clear: reperfusion leads to a smaller infarct size, to preservation of residual left ventricular function and, therefore, to improved survival. Reperfusion of ischaemic myocardium might also result in so-called reperfusion damage, but in humans this has not been substantiated. Another feared complication of rapid restoration of blood flow in ischaemic myocardium is the occurrence of ventricular arrhythmia. Accelerated idioventricular rhythm is a well known complication of reperfusion, but this arrhythmia is generally well tolerated and not associated with any morbidity. Primary ventricular fibrillation, however, is seen less with intravenous thrombolytic therapy than without[2]. These observations have also been made in smaller controlled trials of thrombolysis for acute myocardial infarction. Finally, the occurrence of primary ventricular fibrillation is associated with higher in-hospital mortality, but not with worsened survival after hospital discharge[3]. The clinical findings suggest that primary ventricular fibrillation is associated with larger infarcts and possibly with a lack of successful reperfusion.

In the well known EMIP study, pre-hospital administration of anistreplase was compared to in-hospital anistreplase treatment[4]. It was clearly shown that the time gain of about 60 min resulted in a reduction in mortality of about 15%. The two treatment periods in the study design revealed very interesting findings on the occurrence of primary ventricular fibrillation in very early (pre-hospital) and early (in-hospital) thrombolysis for acute myocardial infarction. The EMIP study group clearly shows that the incidence of primary ventricular fibrillation peaks after treatment with anistreplase, but not with placebo in each of the two treatment periods[5]. The blinded nature of the treatment allocation makes the results convincing. So far, no study has been presented that performed close monitoring of early arrhythmia in patients undergoing thrombolytic therapy.

The authors speculate about the mechanism of this increased incidence of primary ventricular fibrillation. There is little doubt that the observations by Boissel et al. are correct and one wonders why the peaked incidence directly after therapy was not reported in the much larger controlled trials of thrombolysis in acute myocardial infarction, such as GISSI-1 and ISIS-2. Maybe in the latter two studies close monitoring of patients in the first hour after initiation of therapy was not performed sufficiently well for the incidence of primary ventricular fibrillation to be studied specifically and to be reported in the patient record forms. This might explain the discrepancy between the EMIP experience and that in GISSI-1 and ISIS-2.

A more scientific discrepancy is the relationship between the occurrence of ventricular fibrillation in the early hours of myocardial infarction and the worsened in-hospital prognosis, as reported by others[6]. If primary ventricular fibrillation is caused by reperfusion, the prognosis of patients with primary ventricular fibrillation should be better than patients who do not reperfuse. It is also possible that more than one mechanism induces excess primary ventricular fibrillation following thrombolysis. Unfortunately, no angiography was performed in these patients. Angiographic substrates in patients with and without primary ventricular fibrillation after thrombolytic therapy are not very well studied. Small reports do not show any specific coronary angiographic characteristic in patients with primary ventricular fibrillation compared to those without[7]. A definite answer on the mechanism of the observed excess incidence of ventricular fibrillation following anistreplase may never be confirmed. It is also possible that the drug itself initiates the arrhythmia, whether the patient develops reperfusion or not.
However, it is less likely that the drug itself causes this, since this was not observed in the single large randomized clinical trial with anistreplase for acute myocardial infarction [8]. In direct comparative trials with other thrombolytics, a higher incidence of ventricular fibrillation with anistreplase is not reported either, but it is possible that the incidence is under-reported for the above reasons.

In conclusion, primary ventricular fibrillation peaks after initiation of early anistreplase therapy for acute myocardial infarction both pre-hospital and in-hospital. However, this complication can easily be minimized and is not by itself a mechanism of early mortality. However, as reported by other study groups, the occurrence of ventricular fibrillation in the early hours of acute myocardial infarction is an unfavourable prognostic sign for which there is no plausible explanation.

F. W. A. VERHEUGT
University Hospital, Nijmegan, The Netherlands

References


