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Authors

Fabian Spöhr, *MD*

BerndW. Böttiger

MD, DEAA

Dept. of Anesthesiology Ruprecht-Karls-University Heidelberg, Germany

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fabian.spoehr@uni-heidelberg.de

Risk of life-threatening bleeding complications has prevented the use of thrombolytic drugs during CPR, although recent cases suggest improved short and long-term outcomes in certain patient groups. The Thrombolysis in Cardiac Arrest (TROICA) trial is assessing the efficacy and safety of a generalized use of thrombolytic drugs during CPR in patients suffering cardiac arrest.

Out-of-hospital cardiac arrest is associated with a very poor prognosis. Only 5-14% of all patients suffering cardiac arrest are expected to be discharged from hospital (Böttiger et al. 1999; Newman et al. 2000). Although several drug therapies during cardiopulmonary resuscitation (CPR) have been proposed, none has proved to improve longterm outcome in these patients (Brain resuscitation clinical trial I study group 1986 & trial II study group 1991; Kudenchuk et al. 1999). The two major underlying diseases leading to sudden cardiac arrest in more than 70% of cases are acute myocardial infarction (MI) or ischemia-related arrhythmia and massive pulmonary embolism (PE) (Silfvast 1991; Spaulding et al. 1997; Zipes andWellens 1998). Systemic thrombolysis is an effective therapy for acute MI or PE with haemodynamic instability (Arcasoy and Kreit 1999). Thrombolytic therapy during CPR causes direct thrombolysis at the site of coronary or pulmonary artery occlusion. In addition, experimental and clinical studies have shown a marked activation of coagulation during CPR which is not counterbalanced by an adequate activation of fibrinolysis (Böttiger et al. 1995; Gando et al. 1997). This generalized hypercoagulable state leads to formation of microcirculatory thrombi which may severely impair organ function even after restoration of spontaneous circulation, especially in the brain (Fischer et al. 1996).

The fear of causing life-threatening bleeding complications which may be increased by mechanical CPR, however, has been a major drawback for using thrombolytic drugs during CPR. Consequently, thrombolytic agents have historically been withheld in the setting of cardiac arrest. However, in patients failing to achieve restoration of spontaneous circulation despite immediate advanced cardiac life support after in-hospital cardiac arrest, thrombolysis during CPR has been used as a last resort therapy. As a result, case reports and small case series of thrombolysis published over the last 30 years have suggested an improved long-term outcome of neurologically intact survivors without causing critical bleeding complications (Padosch et al. 2002).

In addition, several clinical studies on thrombolysis during out-of-hospital cardiac arrest have shown an improved short-term outcome. The Heidelberg thrombolysis trial (Böttiger et al. 2001) was the first prospective, controlled study that compared thrombolytic treatment during CPR with standard treatment in patients who had failed to achieve spontaneous circulation after more than 15 minutes of conventional resuscitation. Patients treated with the thrombolytic drug alteplase were admitted to hospital significantly more frequently as compared to the control group (58% vs. 30%). In addition, there was a trend towards improved survival at hospital discharge in the thrombolysis group (15% vs. 8%). These results were confirmed by a retrospective study with 108 out of hospital patients who received alteplase during CPR (Lederer et al. 2001). Compared to 216 conventionally resuscitated patients both short and long term survival were improved in the thrombolysis group. Significantly more patients who were treated with alteplase survived to discharge (25.0%, as compared to 15.3% in the control group). The recent guidelines for cardiopulmonary resuscitation recommend considering thrombolytic therapy in patients suffering cardiac arrest in whom an acute thrombotic etiology for the arrest is suspected (Nolan et al. 2005).

In order to assess the efficacy and safety of a generalized use of thrombolytic drugs during CPR in patients suffering cardiac arrest of presumed cardiac origin (i.e. acute MI or PE), a large randomised study is currently under way in Europe. The Thrombolysis in Cardiac Arrest (TROICA) trial is a double-blind, placebo-controlled multicentre trial on thrombolysis during CPR after out-of-hospital cardiac arrest, designed to enrol more than 1000 patients in ten European countries. Adult patients who suffer witnessed out-of-hospital cardiac arrest of presumed cardiac origin can be randomised, if basic or advanced life support is started within 10 minutes of onset. Patients presenting with asystole, however, are not included. Patients are randomised to receive a weight-adjusted dose of tenecteplase or placebo. Primary endpoint will be survival at 30 days and at hospital admission; secondary endpoints include neurological performance of surviving patients and survival after 24 hours. Safety endpoints will assess the incidence of symptomatic intracranial haemorrhages and major bleeding complications. Enrolment is expected to be completed by summer of 2006.

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