

Thrombolysis and cardiopulmonary resuscitation: TROICA — lost war or lost battle?

We would like to thank M. Koziński and J. Kubica for their very interesting and important comments [1]. We are happy that our article prompted the expected discussion [2]. It was our intention to show that thrombolytic therapy during cardiopulmonary resuscitation goes beyond the previous logic of applications in myocardial infarction, pulmonary embolism and stroke. This form of therapy is therefore directed not only to the possible cause of non-traumatic cardiac arrest but first of all to combating its effects.

It should be emphasised again that the idea of the use of thrombolysis during cardiopulmonary resuscitation (CPR) results from theoretical premises, initially verified experimentally, and since then, albeit only recently, clinically [3]. Smaller non randomised studies have shown the benefit of thrombolytic therapy. This is confirmed by the meta-analysis conducted [4]. It is as well to mention that the clash of many projects, conceived on the basis of pathophysiological knowledge and the resulting logic, with the harsh reality of randomised tests, compliant with evidence based medicine (EBM) principles, often results in failure. The problem is that the effect obtained in the specified test, seen through the prism of lack of influence on endpoints, does not necessarily undermine the elements of prior theoretical and clinical knowledge, on the basis of which the research project has been formulated.

The TROICA trial was prematurely halted, after preliminary findings indicated there were no likely benefits of the treatment over placebo [5]. The results of the TROICA tests show that in patients to whom thrombolytic therapy was applied during cardiopulmonary resuscitation differences in the return of spontaneous circulation, hospital admission, 24-hour and 30-day survival, symptomatic intracranial hemorrhage and major bleedings were not statistically significant. This may be evidence that the combating of disseminated thrombosis in small vessels after circulatory arrest by means of the thrombolytic therapy assumed in the protocol did not influence the endpoints described, or that mistakes were made in the planning, methodology or execution of the work or the evaluation of results.

Why has thrombolytic therapy in TROICA testing failed to bring about the anticipated benefits? According to the protocol, patients in whom there was a quick return of spontaneous circulation and patients with asystole were excluded. Moreover, in patients who needed prolonged CPR, blood flow may have been insufficient to bring tenecteplase to the thrombus. Also TNK-tPA interaction with metabolic conditionings such as acidosis, hyperglycemia and the application of vasopressors were not taken into consideration. It would also be advisable to assess the late survivability of patients (after 12 months from ROSC) and their neurological state. It is the increase in the late and not in the early survival rate that is the basis for classification (class I) and the justification for the application of early coronary angioplasty as the optimum method of procedure in acute coronary syndromes complicated by cardiogenic shock [6, 7].

It is also worth emphasising that most of the previous tests of the application of thrombolysis during cardiopulmonary resuscitation were conducted on the basis of streptokinase or alteplase therapy. It emerges from the research of Stadlbauer et al. [8] that there is a higher hospital admission rate, but not a higher discharge rate, after the application of thrombolysis in cardiac arrest in patients with worse baseline characteristics. This points indirectly to the advantageous effects of thrombolysis as a form of improvement of cardiopulmonary resuscitation in susceptible patients.

The TROICA test demonstrates that thrombolytic therapy should not be administered routinely to cardiac arrest patients who need prolonged CPR. On the basis of the literature studied so far we believe that the results of the TROICA test should not put an end to discussion of this kind of therapy but constitute the basis for a broader research perspective on whether interference with the functions of the coagulation system in critically ill patients, including those subject to cardiopulmonary resuscitation, is either necessary or possible.

Like M. Koziński and J. Kubica, we are sure that subanalysis of the TROICA trial could be helpful in identifying patients who would benefit from thrombolysis. To make a conclusive investigation

of the efficacy of thrombolysis during cardiac arrest a much larger study is required on the early use of thrombolytics in patients with a relatively good prognosis.

References

1. Kosiński M, Kubica J. Thrombolysis in cardiac arrest: Initial enthusiasm tempered. *Cardiol J*, 2007; 14: 422–423.
2. Mysiak A, Nowicki P, Kobusiak-Prokopowicz M. Thrombolysis during cardiopulmonary resuscitation. *Cardiol J*, 2007; 14: 24–28.
3. Pedley DK, Morrison WG. Role of thrombolytic agents in cardiac arrest. *Emerg Med J*, 2006; 23: 747–752.
4. Li X, Fu QL, Jing XL et al. A meta-analysis of cardiopulmonary resuscitation with and without the administration of thrombolytic agents. *Resuscitation*, 2006; 70: 34–36.
5. Boettiger BW. The Thrombolysis in Cardiac Arrest (TROICA) Trial. World Congress of Cardiology 2006, 2nd – 6th September, Barcelona, Spain.
6. Dzavik V, Sleeper LA, Cocke JT et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK Trial Registry. *Eur Heart J*, 2003; 24: 828–837.
7. Jeger RV, Harkness SM., Ramanathan K et al. Emergency revascularisation in patients with shock on admission: a report from the SHOCK Trial Registry. *Eur Heart J*, 2006; 27: 664–678.
8. Stadlbauer KH, Krismer AC, Arntz HR et al. Effects of thrombolysis during out-of-hospital cardiopulmonary resuscitation. *Am J Cardiol*, 2006; 97: 305–308.

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