EMERGENCY CASEBOOK

Bolus thrombolytic infusion during prolonged refractory cardiac arrest of undiagnosed cause

A Sheth, P Cullinan, V Vachharajani, S A Conrad

Emerg Med J 2006;23:e19 (<http://www.emjonline.com/cgi/content/full/23/3/e19>). doi: 10.1136/emj.2005.029132

Acute myocardial infarction (AMI) and pulmonary embolism (PE) account for about 70% of cardiac arrest. Although thrombolytic therapy is an effective therapy for both AMI and PE, it is not routinely recommended during cardiopulmonary resuscitation (CPR) for fear of life threatening bleeding complications. Numerous case reports and retrospective studies have suggested a beneficial effect of thrombolytics in cardiac arrest secondary to AMI and PE; however, we present a case of successful use of bolus thrombolytics during CPR in a patient with undifferentiated cardiac arrest (undiagnosed cause) after prolonged conventional resuscitation without success.

Despite advances in resuscitation research, cardiac arrest still carries a poor prognosis. More than 70% of cases are caused by acute myocardial infarction (AMI) or pulmonary embolism (PE).^{1,2} Although thrombolytic therapy is an effective therapy for both AMI³ and PE,⁴ it is not routinely recommended during cardiopulmonary resuscitation (CPR), owing to fear of life threatening bleeding complications. We present a case of successful use of bolus thrombolytics during CPR in a patient with undifferentiated cardiac arrest (undiagnosed cause) after prolonged conventional resuscitation without response to conventional resuscitative efforts.

CASE REPORT

A 19 year old woman was admitted to the medical intensive care unit for respiratory failure secondary to Guillian-Barré syndrome. She was intubated, and treatment was initiated with daily plasma exchange therapy. On hospital day 7, she was extubated because of marked improvement in clinical status. Post-extubation, she complained of sudden onset chest pain and dyspnoea while resting in a cardiac chair. Within 5 minutes of symptom onset, she suddenly developed asystole. Advanced cardiac life support measures were implemented, including intubation and external chest compression. Ventricular fibrillation set in and she received three attempts at defibrillation, with administration of atropine, epinephrine, sodium bicarbonate, lidocaine, and magnesium sulphate. Her rhythm changed to pulseless electrical activity (PEA) and she remained without return of spontaneous circulation for 18 minutes. In the face of persistent PEA, the patient was given bolus injection of 100 U of recombinant human tissue plasminogen activator (rh-tPA) through a femoral venous catheter. Approximately 3 minutes after the rh-tPA infusion, she had return of spontaneous circulation with wide complex tachycardia, which converted to sinus rhythm following administration of amiodarone. Post-resuscitation, blood pressure was 146/85 mm Hg and heart rate was 151 beats/min. An electrocardiogram 30 minutes post-resuscitation revealed a new right bundle branch pattern

with strain. There was minor bleeding from intravenous sites, which was managed conservatively. Venous Doppler study 2 hours after resuscitation was negative for deep venous thrombosis. A contrast computed tomogram performed approximately 4 hours after resuscitation did not show any evidence of pulmonary embolism or deep venous thrombosis. Two weeks later, she was haemodynamically stable with persistent peripheral weakness but no observable sequelae related to her cardiac arrest.

DISCUSSION

The American College of Cardiology (ACC) and the American Heart Association (AHA), in a joint task force report listed CPR as a "relative minor contraindication" for patient selection for thrombolytic therapy.⁵ Over the past two decades, numerous case reports, case series, and retrospective studies have suggested that thrombolysis during CPR can lead to return of spontaneous circulation (ROSC) with improved neurological outcomes in patients with PE and AMI.⁶⁻⁹

In a retrospective study of 21 patients with cardiac arrest after massive PE who were treated with bolus thrombolytics during CPR, a significantly higher rate of ROSC was observed in the thrombolysis group compared with a control group that did not receive thrombolysis during CPR (81% v 43%; $p = 0.03$).⁸ A pilot randomized trial of thrombolysis in cardiac arrest¹⁰ included 35 patients with out of hospital cardiac arrest, of whom 19 received tenecteplase and 16 placebo. ROSC occurred in eight patients (42%) receiving tenecteplase and one placebo (6%) (36% difference, 95% confidence interval 11% to 61%). A multicentre trial of tenecteplase in out of hospital cardiac arrest¹¹ is underway, with results expected in 2006.

Recent guidelines by ACC/AHA no longer contain the contraindication of thrombolytics during CPR.¹² While most of the clinical evidence suggests beneficial effect of thrombolysis in cardiac arrest secondary to AMI or PE, our case documents a beneficial outcome in undifferentiated cardiac arrest and prolonged unsuccessful conventional resuscitation. The temporal relationship between thrombolytic administration and ROSC after prolonged unsuccessful CPR suggests a beneficial effect in our patient. Although pulmonary embolism was suspected as the aetiology of cardiac arrest in our patient, it could not be confirmed because of the delay between thrombolytic administration and imaging.

The effectiveness of thrombolytics during CPR can be explained by two proposed mechanisms. Firstly, it acts locally at the site of coronary³ or pulmonary vessel^{4,13} thrombosis,

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; AMI, acute myocardial infarction; CPR, cardiopulmonary resuscitation; PE, pulmonary embolism; PEA, pulseless electrical activity; rh-tPA, recombinant human tissue plasminogen activator; ROSC, return of spontaneous circulation

leading to rapid correction of underlying pathology. Secondly, it has a neuroprotective effect secondary to its action on microcirculatory reperfusion.¹⁴ Cardiac arrest and CPR are associated with a striking activation of blood coagulation, without adequate activation of endogenous fibrinolysis, leading to microthromboses throughout the entire microcirculation.^{15–16} Thrombolytic agents thus lead to immediate improvement in cerebral microcirculatory reperfusion and myocardial contractility.^{17–18}

Given the current poor outcome of prolonged unresponsive cardiac arrest, the potential benefits of thrombolysis during CPR may outweigh the risk of major bleeding complications. Single bolus injection of a thrombolytic agent should be considered in this scenario.

CONCLUSION

Bolus thrombolytic administration during refractory CPR may facilitate spontaneous return of circulation even in patients with undiagnosed cause. Current clinical data, although encouraging, is insufficient to recommend routine use of bolus thrombolytic during CPR in all patients. There is a need for randomised prospective studies to investigate the effect of thrombolytic therapy in patients with prolonged unsuccessful cardiopulmonary resuscitation and to identify patients who would benefit from such intervention.

Authors' affiliations

A Sheth, Department of Internal Medicine, Louisiana State University Health Sciences Center, Shreveport, LA, USA

P Cullinan, V Vachharajani, S A Conrad, Critical Care Medicine Service, Louisiana State University Health Sciences Center, Shreveport, LA, USA

Competing interests: none declared

Correspondence to: Dr A Sheth, Department of Medicine, LSU Health Sciences Center, 1501, Kings Hwy, PO Box: 213, Shreveport, LA 71130, USA; drankursheth@yahoo.com

Accepted for publication 20 September 2005

REFERENCES

- 1 **Spaulding CM**, Joly LM, Rosenberg A, *et al*. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. *N Engl J Med* 1997;**336**:1629–33.

- 2 **Silfvast T**. Cause of death in unsuccessful prehospital resuscitation. *J Intern Med* 1991;**229**:331–5.
- 3 **Bode C**, Nordt TK, Runge MS. Thrombolytic therapy in acute myocardial infarction—selected recent developments. *Ann Hematol* 1994;**69**:535–40.
- 4 **Arcasoy SM**, Kreitz JW. Thrombolytic therapy of pulmonary embolism: a comprehensive review of current evidence. *Chest* 1999;**115**:1695–707.
- 5 **Gunnar RM**, Bourdillon PD, Dixon DW, *et al*. ACC/AHA guidelines for the early management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (subcommittee to develop guidelines for the early management of patients with acute myocardial infarction). *Circulation* 1990;**82**:664–707.
- 6 **Tiffany PA**, Schultz M, Stueven H. Bolus thrombolytic infusions during CPR for patients with refractory arrest rhythms: outcome of a case series. *Ann Emerg Med* 1998;**31**:124–6.
- 7 **Scholz KH**, Tebbe U, Herrmann C, *et al*. Frequency of complications of cardiopulmonary resuscitation after thrombolysis during acute myocardial infarction. *Am J Cardiol* 1992;**69**:724–8.
- 8 **Kurkciyan I**, Meron G, Sterz F, *et al*. Pulmonary embolism as a cause of cardiac arrest: presentation and outcome. *Arch Intern Med* 2000;**160**:1529–35.
- 9 **Böttiger BW**, Bohrer H, Bach A, *et al*. Bolus injection of thrombolytic agents during cardiopulmonary resuscitation for massive pulmonary embolism. *Resuscitation* 1994;**28**:45–54.
- 10 **Fatovich DM**, Dobb GJ, Clugston RA. A pilot randomised trial of thrombolysis in cardiac arrest (The TICA trial). *Resuscitation* 2004;**61**:309–13.
- 11 **Spohr F**, Arntz HR, Bluhmki E, *et al*. International multicentre trial protocol to assess the efficacy and safety of tenecteplase during cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest: the Thrombolysis in Cardiac Arrest (TROICA) Study. *Eur J Clin Invest* 2005;**35**:315–23.
- 12 **Antman EM**, Anbe DT, Armstrong PW, *et al*. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004;**44**:671–719.
- 13 **Goldhaber SZ**, Kessler CM, Heit JA, *et al*. Recombinant tissue-type plasminogen activator versus a novel dosing regimen of urokinase in acute pulmonary embolism: a randomized controlled multicenter trial. *J Am Coll Cardiol* 1992;**20**:24–30.
- 14 **Spohr F**, Böttiger BW. Thrombolytics in CPR. Current advantages in cardiopulmonary resuscitation. *Minerva Anesthesiol* 2005;**71**:291–6.
- 15 **Böttiger BW**, Motsch J, Bohrer H, *et al*. Activation of blood coagulation after cardiac arrest is not balanced adequately by activation of endogenous fibrinolysis. *Circulation* 1995;**92**:2572–8.
- 16 **Gando S**, Kameue T, Nanzaki S, *et al*. Massive fibrin formation with consecutive impairment of fibrinolysis in patients with out-of-hospital cardiac arrest. *Thromb Haemost* 1997;**77**:278–82.
- 17 **Lin SR**, O'Connor MJ, Fischer HW, *et al*. The effect of combined dextran and streptokinase on cerebral function and blood flow after cardiac arrest: and experimental study on the dog. *Invest Radiol* 1978;**13**:490–8.
- 18 **Darius H**, Yanagisawa A, Brezinski ME, *et al*. Beneficial effects of tissue-type plasminogen activator in acute myocardial ischemia in cats. *J Am Coll Cardiol* 1986;**8**:125–31.