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CASE REPORT

Therapeutic hypothermia after prolonged cardiopulmonary resuscitation for pulseless electrical activity

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ABSTRACT

We report an 18-year-old female patient with cardiac arrest due to pulseless electrical activity caused by a massive pulmonary embolism. Cardiopulmonary resuscitation was continued for more than one hour. Although the initial clinical signs and symptoms suggested poor outcome, immediate intravenous thrombolysis was instituted. After return of spontaneous circulation (75 minutes) the patient was still comatose and mild therapeutic hypothermia (32.5 °C) was instituted for brain protection during the first 24 hours. She recovered uneventfully without neurological deficit. Therapeutic hypothermia may be effective for neuroprotection in non-VF cardiac arrest.

KEYWORDS

Therapeutic hypothermia, induced hypothermia, cardiopulmonary resuscitation, pulseless electrical activity, pulmonary embolism

INTRODUCTION

Cardiac arrest with global cerebral ischaemia may lead to severe postanoxic encephalopathy and neurological impairment. Several studies have shown that moderate therapeutic hypothermia to a temperature of 32 to 33 °C can reduce brain damage after prehospital cardiac arrest due to ventricular arrhythmia without significant side effects.[1,2] The benefits of therapeutic hypothermia after cardiac arrest due to other causes has not been demonstrated convincingly.[3,4]

We present a young female who underwent cardiopulmonary resuscitation (CPR) for pulseless electrical activity for more than one hour. She presented with extremely unfavourable clinical signs and symptoms for survival and high risk of poor neurological outcome. She was treated with therapeutic hypothermia after return of spontaneous circulation.

CASE REPORT

An 18-year-old female underwent knee surgery three weeks before emergency admission. She had been complaining of dyspnoea and cough for one day before she collapsed at home. Although witnessed by her family, no adequate basic life support was commenced until the ambulance arrived seven minutes later. Extreme bradycardia with no output was noted as a sign of pulseless electrical activity. Immediate basic life support was started by paramedics on arrival. A total of 5 mg of adrenaline (epinephrine) IV was administered during CPR. The patient was endotracheally intubated and transported to the hospital. On arrival to the emergency room, the patient was still in pulseless electrical activity. Initial end-tidal CO_2 was 0.2 kPa. Arterial blood gas analysis showed severe respiratory and metabolic acidosis with severe hypoxaemia: pH 6.60 (7.35-7.45), pCO_2 14.5 kPa (4.5-6.0 kPa), HCO_3- 10.2 mmol/l (22-26 mmol/l), pO_2 4.1 kPa (9.5-13.0 kPa), and SaO_2 16% (92-99%). Arterial lactate was 21.0 mmol/l (0.5-1.7 mmol/l). Prompt thrombolysis with rTPA and subsequent intravenous heparin were instituted for suspected massive pulmonary embolism. On transthoracic echocardiography significant right ventricular distension with collapse of the left ventricle was noted. An electrocardiogram showed supraventricular tachycardia, right-axis deviation, and right bundle branch block. D-dimers were 18.70 μg/ml (0.1-0.5 μg/ml). After thrombolysis, spontaneous circulation returned 75 minutes after arrest and capnographic CO_2 elimination increased to normal. The blood pressure improved with vasopressors (dopamine and noradrenaline). Blood gases and lactate levels normalised within six hours.

On ICU admission, the patient was still comatose (Glasgow coma scale 3). Hypothermia was induced according to our

institutional cooling protocol (*figure 1*), using rapid infusion of two litres of ice-cold saline (4 °C) and two cooling mattresses (Blanketroll II, CSZ, Cincinatti, USA). Temperatures were continuously measured using an oesophageal temperature probe. A target temperature of 32.5 °C was reached within 120 minutes and continued for 24 hours (*figure 2*). Cefotaxime was started for suspected aspiration.

Significant electrolyte disorders (phosphate 0.58 mmol/l (0.8-1.4 mmol/l), Ca^{++} 1.04 mmol/l (1.15-1.29 mmol/l), K^{+} 3.4 mmol/l (3.5-4.7 mmol/l), Mg^{++} 0.69 mmol/l (0.7-1.1 mmol/l) and metabolic derangement (glucose 12.2 mmol/l (4.0-10.0 mmol/l)) as side effects of therapeutic hypothermin were observed. Minor bleeding occurred from mucosal areas and puncture sites due to the combination

Figure 1. *Therapeutic hypothermia protocol*

Selection criteria
Patients with cardiac arrest of any cause and location (IHCA/OHCA)
Return of spontaneous circulation
Comatose (Glasgow Coma Scale < 8)

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Induction phase
Sedation with propofol or midazolam and morphine, in case of severe chills add bolus rocuronium
Rapid infusion of 2 litres of cold (4 °C) NaCl 0.9%
Two cooling mattresses (Blanketroll II, CSZ) underneath and on top of the patient, temperature set at 4 °C until temperature 34 °C is reached, then set at 32.5 °C
Supplementation of 2 g magnesium sulphate iv

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Hypothermia maintenance phase
Maintenance of therapeutic hypothermia with cooling mattresses set at temperature 32.5 °C for 24 hours
Continuation of sedation

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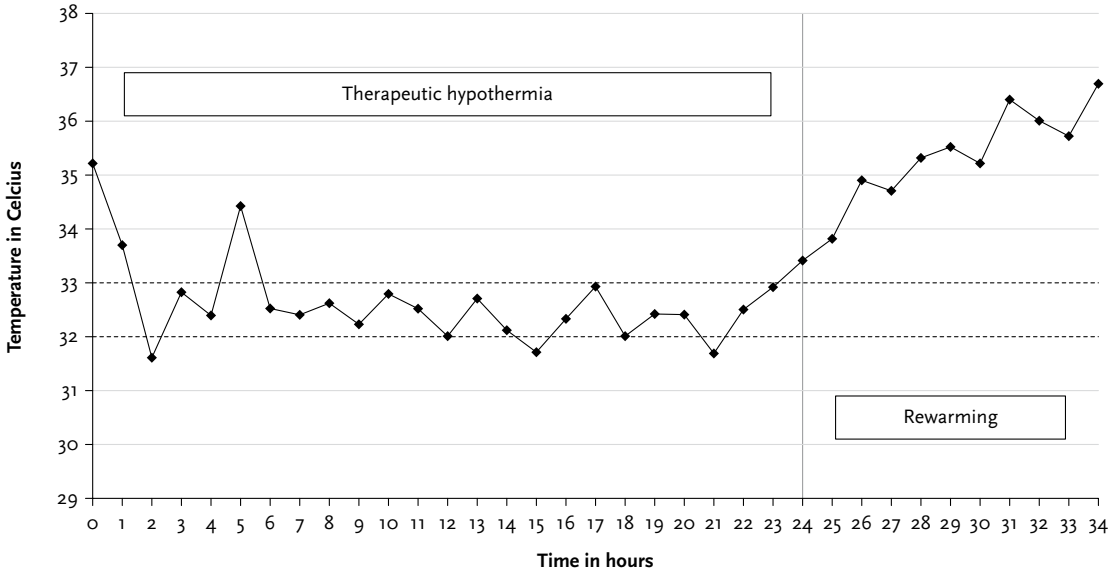
Rewarming phase
Rewarming rate of 0.3 °C per hour to target temperature of 36 °C
Discontinuation of sedation after reaching normal temperature
Preservation of normal temperature during 24 hours, using cooling mattress and/or antipyretics

Laboratory investigation during therapeutic hypothermia
During first 6 hours every 2 hours, thereafter every 4 hours: potassium, calcium, magnesium, phosphate, glucose, arterial blood gas
Once daily: complete blood count, renal functions, amylase, liver enzymes, prothrombin time, activated partial thromboplastin time

Figure 2. *Oesophageal temperatures during induction, maintenance and rewarming phase*



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of thrombolysis, heparinisation and probably additional coagulation disturbances due to therapeutic hypothermia.
After 24 hours of hypothermia, the patient was rewarmed at a rate of 0.3 °C per hour to a temperature of 36 °C. Subsequently, sedation was discontinued to assess the neurological status. She fully recovered without neurological impairments one day after cessation of sedation and could be extubated successfully. She was speaking coherently. Only slight disturbances in short-term memory were noted, although an electroencephalogram showed diffuse excessive slow theta activity as a possible sign of postanoxic disturbances. A computed tomography of the chest was performed to detect possible residues of the pulmonary embolism. Only small peripheral perfusion defects were visible, consistent with the clinical picture of successful thrombolysis.
The patient was transferred to the general ward. Further recovery was uneventful. Fourteen days after admission she was discharged. Her cerebral performance category (CPC) score was 1.[5]

DISCUSSION

Our patient survived pulseless electrical activity due to massive pulmonary embolism after successful thrombolysis. The (neurological) recovery is remarkable since the delay in basic life support, the duration before return of spontaneous circulation, the severity of lactic acidosis and initial coma score suggested a high risk of severe postanoxic encephalopathy. In contrast to this, neurological outcome was beneficial (CPC 1).
Furthermore, prognosis of circulatory arrest due to other causes than ventricular fibrillation is very poor. Reports thus far have not proven convincingly that benefits in outcome of therapeutic hypothermia for arrests other than ventricular arrhythmia are relevant, although animal data suggest similar effects on cerebral protection in both VF and non-VF arrest.[6,7]

Postanoxic encephalopathy is a common complication after cardiac arrest. Only 5% of all out-of-hospital arrests with cardiac aetiology are discharged with a favourable neurological outcome.[8] Several factors in the reperfusion phase contribute to cerebral damage that adds to the ischaemic injury during circulatory arrest.
First, although circulation is restored, there may be a continued and inhomogeneous hypoperfusion of the brain. Second, release of certain amino acids (most notably glutamate) leads to excitotoxicity. Oxygen free radicals trigger chemical cascades causing further damage. This may lead to apoptosis and/or necrosis. Finally, extracerebral causes such as metabolic derangements and organ failure due to circulatory arrest can add to the development of postanoxic encephalopathy.[9]

The exact mechanisms by which hypothermia protects the brain during reperfusion are as yet unknown. The beneficial effects may be mediated through a decrease in metabolism and oxygen demand. Animal studies show that hypothermia attenuates the release of excitatory amino acids and improves cerebral perfusion.[7,10,11]
Several cooling techniques are available.[12] Early induction of hypothermia is important to enhance optimal cerebral protection.[6] In our experience target temperatures can be rapidly reached with cold infusions (time to target temperature 60-120 min) and acceptably maintained using surface cooling devices. Furthermore, rewarming can be controlled using such a cooling device, as passive rewarming may be too rapid and induce reperfusion damage to the vulnerable areas of the brain.
There are no absolute contraindications for therapeutic hypothermia, although several complications have been documented. Most frequently immunodepression, thrombocytopenia and coagulation disorders, arrhythmia, electrolyte abnormalities, lactic acidosis, hyperglycaemia, pancreatitis, and polyuria are reported.[7] In the critical care environment most of these complications may be circumvented by frequent observations and laboratory measurements, and after institution of adequate therapeutic interventions.

CONCLUSION

Therapeutic hypothermia may be beneficial for neuroprotection in cardiac arrest patients due to other causes than ventricular fibrillation. Our observations warrant further research in this area.

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