

# Monitoring of brain tissue oxygen tension and use of vasopressin after cardiac arrest in a child with catecholamine-induced cardiac arrhythmia

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Monitoring of brain tissue oxygenation is not common in the clinical setting. We found that this monitoring, combined with use of vasopressin, aided in the management of hypoxic brain injury in a boy with a rare but potentially lethal catecholamine-sensitive cardiac arrhythmia. This case demonstrates the usefulness of brain tissue oxygen tension ( $P_{tO_2}$ ) as an aid to management of hypoxic injury after cardiac arrest. Reporting of this case was approved by the patient's parents and our institutional review board.

## Clinical record

A 14-year-old boy collapsed while playing in his school playground. He was of European ancestry and weighed 40 kg. Bystanders began effective cardiopulmonary resuscitation (CPR), and he was transported to the local medical clinic where he was diagnosed with pulseless ventricular tachycardia. CPR was continued by bag and mask ventilation for 25 minutes; he was given two 10 mL/kg fluid boluses of 0.9% saline but no epinephrine or other drugs. Eight direct-current shocks were delivered during the resuscitation. Spontaneous cardiac output returned, but the patient remained unconscious. He was intubated, stabilised by a paediatric retrieval team (with sedation, analgesia and a  $\beta$ -blocker [esmolol]) and transferred to a paediatric intensive care unit for treatment of hypoxic brain injury.

The patient was under the care of the cardiac service in his local area which was treating him for catecholamine-induced polymorphic ventricular tachycardia with a  $\beta$ -blocker, metoprolol. He had been asymptomatic for 6 months before this presentation. There was a family history of emotionally triggered palpitations reported in both his mother and maternal grandmother.

On admission to the ICU, the boy's vital signs were very stable, with a heart rate of 116 beats/min, systolic blood pressure of 123 mmHg, arterial pH of 7.27 and a serum lactate concentration of 2.3 mmol/L.

The management plan was twofold. The first aim was to minimise secondary cerebral injury by optimising ventilation, hypothermia, sedation and paralysis, maintaining plasma sodium levels greater than 145 mmol/L, and targeting  $P_{tO_2}$  to more than 20 mmHg. The second aim was to maintain normal sinus rhythm with the aid of a titratable  $\beta$ -

## ABSTRACT

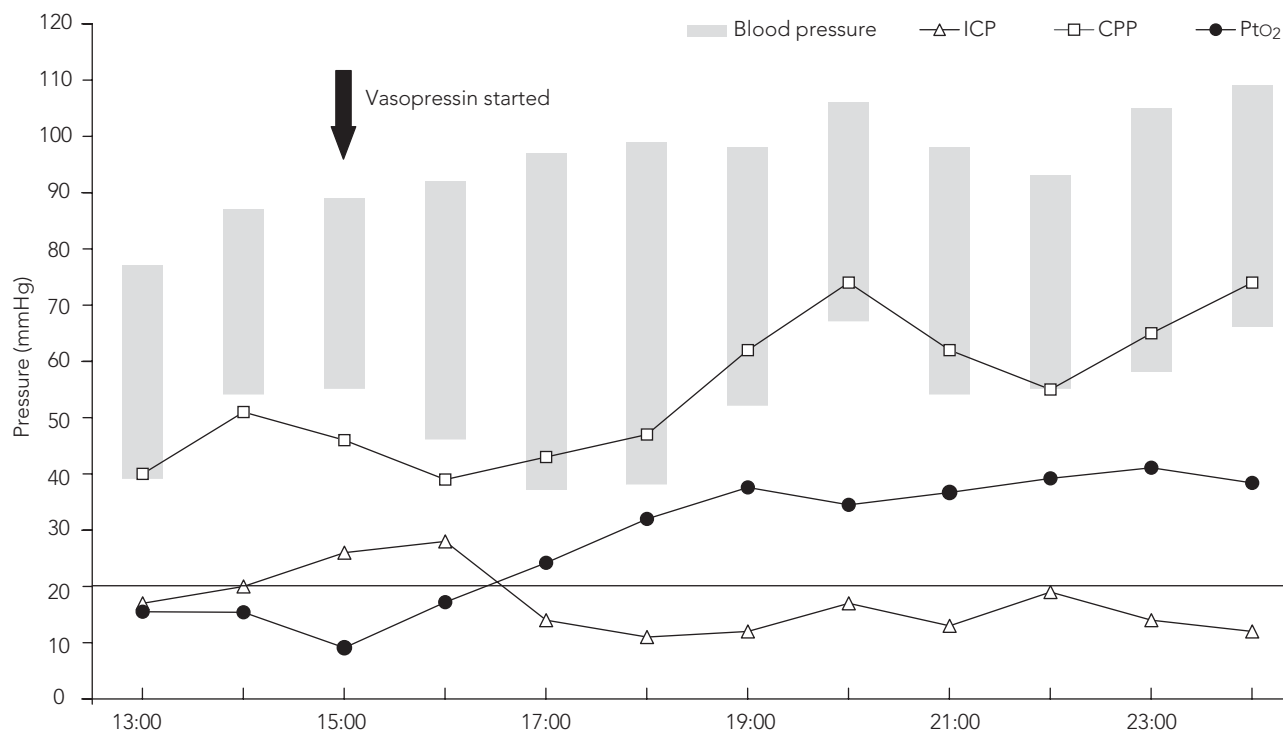
A 14-year-old boy with catecholamine-induced polymorphic ventricular tachycardia was treated for hypoxic brain injury after a 25-minute ventricular tachycardia arrest. He had been treated by the local paediatric cardiology service with  $\beta$ -blockers for syncopal events related to episodes of ventricular tachycardia. As standard inotropic support was contraindicated, he was treated for hypoxic brain injury, with targeting of brain tissue oxygen levels ( $P_{tO_2}$ ) with vasopressin. He was extubated after 7 days and discharged home with an automatic implantable cardioverter defibrillator, with no neurological sequelae.  $P_{tO_2}$  is a reliable and effective clinical assessment tool that can aid in the management of patients with significant cerebral injury. Vasopressin proved a valuable adjunct in treatment of hypoxic brain injury when inotropic agents were contraindicated.

Crit Care Resusc 2008; 10: 316–319

blocker (esmolol), as this agent had proved to control the arrhythmia in transfer. In the event of cardiovascular instability or recurrence of arrhythmias, amiodarone would have been considered as second-line agent. The treatment was delivered in conjunction with the paediatric cardiology team.

The patient's progress over the first 24 hours was uneventful. An invasive arterial line and a central venous line were inserted soon after admission. An intraparenchymal pressure monitor and brain tissue oxygen probe (Ventrix Monitor NL950-100 and LICOX, Integra Neuro Sciences, New Jersey, USA) were placed by the neurosurgical team 18 hours after the arrest.

Thirty hours into treatment, mean blood pressure became unresponsive to fluid boluses (80 mL/kg of 0.9% saline over 8 hours), with values averaging 55–70 mmHg, and cerebral perfusion pressure less than 50 mmHg. A vasopressin infusion (0.06 units/kg/h) was begun. Within an hour,  $P_{tO_2}$  increased, and within 2 hours, cerebral perfusion pressure increased, and intracranial pressure decreased (Figure 1). We continued ventilation, sedation (with a morphine and

**Figure 1. Effect of vasopressin on cardiac and cerebral parameters**

Brain tissue oxygenation (Pto<sub>2</sub>) increased 1 hour after the vasopressin infusion began, but there was a lag of another hour before an effect was seen on intracranial pressure (ICP) and cerebral perfusion pressure (CPP).

midazolam infusion), cooling to 32.5°C, muscle relaxation with regular doses of vecuronium and β-blockade with metoprolol (5 μg/kg/min for 7 days).<sup>1</sup> After active cooling for a total of 72 hours, the patient was gradually rewarmed by 1°C every 4 hours.

Brain magnetic resonance imaging a week after the cerebral insult showed diffuse ischaemic changes (Figure 2). He was extubated and discharged from the ICU to the ward for physical rehabilitation and had an automatic implantable cardioverter defibrillator implanted. Neurologically, he returned to his pre-arrest state with full speech, motor and cognitive functions, and at 6-month follow-up had had no further syncopal events or erroneous discharges from the defibrillator.

## Discussion

Catecholamine-induced polymorphic ventricular tachycardia was first described in children in 1995 by Leenhardt et al.<sup>2</sup> Emotional or physical stress triggers a potentially lethal rhythm in structurally normal hearts, and these children are commonly misdiagnosed with epilepsy.<sup>2,3</sup> This rare condition has generated significant interest among both clinicians and scientists to help understand the

electrophysiology of the myocardium. The coupling of the L-type calcium channel to the type 2 ryanodine receptor causes an influx of calcium into the cytosol that triggers systolic myocardial contraction.<sup>4,5</sup> Gene mutations of the type 2 ryanodine receptor and other regulatory proteins have been identified as the cause of this malignant condition, which is inherited as either an autosomal dominant<sup>6</sup> (type 2 ryanodine receptor mutations) or autosomal recessive<sup>7,8</sup> (mutations affecting the large protein complex involved in calcium regulation). Unfortunately, the genetic profile in our patient is unknown, as testing for these mutations is not yet available in Australia. However, we speculate that it may be an autosomal dominant inheritance, as the condition appears to be present in both the boy's mother and maternal grandmother.

Treatment remains symptomatic, and β-blockers and calcium-channel blockers have been used with moderate success.<sup>4,9</sup> As β-adrenergic stimulation activates cyclic AMP, which in turn phosphorylates many of the calcium-cycling pathways, any inotrope with β-adrenergic actions is highly contraindicated in these patients. It remains unclear whether α-adrenergic catecholamines are safe in these patients, and they were thus not used.

## CASE REPORTS

In children, hypoxic brain injuries are usually secondary to respiratory arrest and rarely due to primary cardiac events. The neurological sequelae of an out-of-hospital cardiac arrest are well documented in the adult population, with increasing evidence that hypothermia can improve neurological outcomes.<sup>10</sup> Several studies have investigated the optimal duration of hypothermia in adults after ventricular tachycardia or ventricular fibrillation arrest,<sup>11,12</sup> with encouraging results and no significant increased rate of side effects such as cardiac arrhythmias or infection.<sup>13</sup> In our patient, the prolonged cardiac arrest time and failure to regain consciousness after return of spontaneous circulation led us to suspect hypoxic brain injury. Hence, hypothermia was used to prevent further cerebral damage while controlling the arrhythmias with  $\beta$ -blockers. The patient was cooled to 32.5°C using boluses of 0.9% saline chilled to 4°C, and then actively kept cool using a cooling blanket for 72 hours. He remained in sinus rhythm throughout this treatment.

The use of hypothermia, including duration and target temperature, was reviewed in our institution when considering participation in a study to assess outcome of active

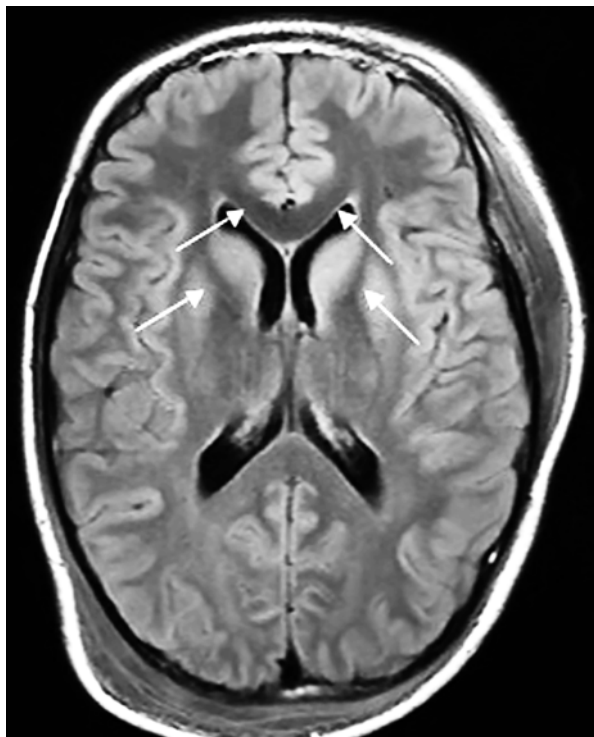
cooling after traumatic brain injury. Guidelines were generated following careful assessment of the paediatric and adult literature. The main studies supporting the use of active cooling for 72 hours are by Shankaran et al<sup>14</sup> and Gluckman et al,<sup>15</sup> with a systematic review on its use in management of traumatic head injury by Henderson et al.<sup>16</sup> The primary concern with cessation of hypothermia at 24–48 hours was the risk of rebound swelling and increased intracerebral pressure at a time when cerebral oedema is believed to be at its greatest.<sup>17</sup>

After hypoxic ischaemic injury, the brain remains susceptible to secondary damage caused by hypotension, hypoxia, hyperthermia and hyperglycaemia.<sup>18</sup> The standard treatment aims to achieve adequate cerebral perfusion pressure — normally estimated in a 14-year old boy to be greater than 60 mmHg — and to minimise cerebral oedema. Vasoconstricting catecholamines such as norepinephrine and dopamine have been shown to improve regional cerebral perfusion in animal models.<sup>19</sup> As discussed above, the use of catecholamine was contraindicated in this patient, and therefore the preferred method to adjust cerebral perfusion pressures was with fluid boluses and optimisation of ventilation. As shown in Figure 1, the effects of vasopressin were noticeable within 2 hours of the infusion beginning, with an increase in cerebral perfusion pressure to more than 60 mmHg.

Adequate reperfusion of brain tissue after hypoxic injury appears critical to preventing the progression of cerebral tissue injury,<sup>20</sup> and several methods have been devised to monitor treatment,<sup>21</sup> the most sensitive being  $P_{\text{tO}_2}$ .<sup>22</sup> Intracranial pressures have been used as a surrogate for cerebral perfusion pressure, yet there is increasing evidence that maintaining  $P_{\text{tO}_2}$  at more than 20 mmHg improves long-term neurological outcome.<sup>23,24</sup> Although  $P_{\text{tO}_2}$  is mainly used in research, it proved very useful for monitoring the response to treatment. In this case,  $P_{\text{tO}_2}$  was less than 15 mmHg before vasopressin therapy, but rose within an hour of the infusion beginning and stabilised above 20 mmHg until monitoring ceased. As shown in Figure 1,  $P_{\text{tO}_2}$  was more sensitive to treatment changes, with changes in cerebral perfusion pressure lagging by an hour. This lag remains unexplained; it may represent improved cellular metabolism, which affects the measured intracerebral pressure, or it may be that an increase in oxygen tension has a direct effect on the vascular network of the injured brain. Targeting  $P_{\text{tO}_2}$  by adjusting vasopressin delivery rate was described in another case,<sup>25</sup> and this vasopressor proved crucial when dealing with a patient with a contraindication to catecholamines.

This case illustrates the treatment of hypoxic brain injury after ventricular tachycardia arrest in a patient with catecholamine-induced polymorphic ventricular tachycardia.

**Figure 2. Magnetic resonance image of the brain 7 days after ischaemic injury**



Axial T1 weighted magnetic resonance imaging showed diffuse ischaemic injury of the frontal regions of the brain (arrows).

The combination of invasive cerebral monitoring and use of a non-catecholamine vasopressor to target Pto<sub>2</sub> achieved optimal results. Surrogates of tissue perfusion and oxygenation, such as intracranial pressures, are used to direct brain protective management.

This case is unique on three counts. Firstly, the patient presented with a ventricular tachycardia arrest, uncommon in the paediatric population, caused by a rare malignant arrhythmia. Secondly, the cerebral hypoxic ischaemic injury generated by the arrest could not be treated using standard head injury protocols. The challenge was to stabilise the cardiac rhythm by minimising the endogenous production of catecholamines and administering a β-blocker, and to optimise perfusion and oxygen delivery to the cerebral tissue. The case describes a management strategy for hypoxic cerebral injury when the underlying condition excludes use of inotropic agents. Finally, recognition and credit are owed to the health care professionals who delivered excellent and effective first aid, ensuring that this challenging patient could be discharged home with no neurological insult.

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### References

- 1 Shann F. Drug doses. 13th ed. Melbourne: Collective, 2005.
- 2 Leenhardt A, Lucet V, Denjoy I, et al. Catecholaminergic polymorphic ventricular tachycardia in children: a 7-year follow-up of 21 patients. *Circulation* 1995; 91: 1512-9.
- 3 Coumel P. Catecholaminergic polymorphic ventricular tachyarrhythmias in children. *Card Electrophysiol Rev* 2002; 6: 93-5.
- 4 Kontula K, Laitinen PJ, Lehtonen A, et al. Catecholaminergic polymorphic ventricular tachycardia: recent mechanistic insights. *Cardiovasc Res* 2005; 67: 379-87.
- 5 Scheinman MM, Lam J. Exercise-induced ventricular arrhythmias in patients with no structural cardiac disease. *Annu Rev Med* 2006; 57: 473-84.
- 6 Priori SG, Napolitano C, Tiso N, et al. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. *Circulation* 2001; 103: 196-200.
- 7 Myriantsefs M, Cariolou M, Eldar M, et al. Exercise-induced ventricular arrhythmias and sudden cardiac death in a family. *Chest* 1997; 111: 1130-4.

- 8 Lahat H, Eldar M, Levy-Nissenbaum E, et al. Autosomal recessive catecholamine- or exercise-induced polymorphic ventricular tachycardia: clinical features and assignment of the disease gene to chromosome 1p13-21. *Circulation* 2001; 103: 2822-7.
- 9 Sumitomo N, Harada K, Nagashima M, et al. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death. *Heart* 2003; 89: 66-70.
- 10 Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest [see comment] [erratum appears in *N Engl J Med* 2002; 346: 1756]. *N Engl J Med* 2002; 346: 549-56.
- 11 Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002; 346: 557-63.
- 12 Broccard A. Therapeutic hypothermia for anoxic brain injury following cardiac arrest: a "cool" transition toward cardiopulmonary cerebral resuscitation[comment]. *Crit Care Med* 2006; 34: 2008-9.
- 13 Oddo M, Schaller MD, Feihl F, et al. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. *Crit Care Med* 2006; 34: 1865-73.
- 14 Shankaran S, Lupton AR, Ehrenkranz RA, et al. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med* 2005; 353: 1574-84.
- 15 Gluckman PD, Wyatt JS, Azzopardi D, et al. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet* 2005; 365: 663-70.
- 16 Henderson WR, Dhingra VK, Chittock DR, et al. Hypothermia in the management of traumatic brain injury. A systematic review and meta-analysis. *Intensive Care Med* 2003; 29: 1637-44.
- 17 Iida K, Kurisu K, Arita K, Ohtani M. Hyperemia before acute brain swelling during rewarming of patients who have been treated with moderate hypothermia for severe head injuries. *J Neurosurg* 2003; 98: 793-9.
- 18 Hickey RW, Painter MJ. Brain injury from cardiac arrest in children. *Neurol Clin* 2006; 24: 147-58.
- 19 Kroppenstedt SN, Sakowitz OW, Thomale U-W, et al. Influence of norepinephrine and dopamine on cortical perfusion, EEG activity, extracellular glutamate, and brain edema in rats after controlled cortical impact injury. *J Neurotrauma* 2002; 19: 1421-32.
- 20 Madl C, Holzer M. Brain function after resuscitation from cardiac arrest. *Curr Opin Crit Care* 2004; 10: 213-7.
- 21 Steiner LA, Andrews PJD. Monitoring the injured brain: ICP and CBF. *Br J Anaesth* 2006; 97: 26-38.
- 22 Narotam PK, Burjonrappa SC, Raynor SC, et al. Cerebral oxygenation in major pediatric trauma: its relevance to trauma severity and outcome. *J Pediatr Surg* 2006; 41: 505-13.
- 23 van den Brink WA, van Santbrink H, Avezaat CJ, et al. Monitoring brain oxygen tension in severe head injury: the Rotterdam experience. *Acta Neurochir Suppl* 1998; 71: 190-4.
- 24 Valadka AB, Gopinath SP, Contant CF, et al. Relationship of brain tissue PO<sub>2</sub> to outcome after severe head injury. *Crit Care Med* 1998; 26: 1576-81.
- 25 Yeh CC, Wu CT, Lu CH, et al. Early use of small-dose vasopressin for unstable hemodynamics in an acute brain injury patient refractory to catecholamine treatment: a case report. *Anesth Analg* 2003; 97: 577-9. □