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JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 2

Targeted temperature management following third trimester cardiac arrest

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Received: Apr 29, 2021
Accepted: Jun 02, 2021
Published: Jun 07, 2021
Archived: www.jcimcr.org

Abstract

Background: According to the American Heart Association (AHA), post-cardiac arrest use of targeted temperature management (TTM) can be considered for pregnant patients; however, data is lacking, particularly following fetal viability.

Case: A 31 year old, female presented at 36 weeks gestation after an out-of-hospital cardiac arrest. Resuscitation resulted in return of spontaneous circulation (ROSC); however, the patient was unresponsive upon hospital arrival. She underwent TTM, was cooled and rewarmed without incident. She underwent cesarean delivery 36 hours after cardiac arrest. By time of discharge, she had full neurological recovery, with only amnesia surrounding the acute cardiac event. The neonate was discharged after a brief stay in the neonatal intensive care unit, having met discharge criteria.

Conclusion: TTM should be considered post cardiac arrest, even in the third trimester.

Keywords: Targeted temperature management; Cardiac arrest; Pregnancy.

Abbreviations: AHA: American Heart Association; TTM: Targeted Temperature Management; ROSC: Return Of Spontaneous Circulation; EMS: Emergency Medical Services; ARCTIC: Advanced Resuscitation Cooling Therapeutics Intensive Care; NICU: Neonatal Intensive Care Unit; OHCA: Out of Hospital Cardiac Arrest.

Introduction

Cardiac arrest occurs in approximately 1:20,000 pregnancies [1]. Current AHA guidelines recommend resuscitative hysterotomy, also known as perimortem cesarean delivery, if there is no Return Of Spontaneous Circulation (ROSC) within four minutes of arrest. However, when ROSC is achieved prior to delivery, especially in out-of-hospital cardiac arrest, little evidence exists to guide post resuscitation care and delivery planning [1,2].

Targeted Temperature Management (TTM) improves neurological outcomes and overall survival in individuals who have experienced cardiac arrest. TTM is recommended in the case of ROSC if the patient remains comatose or unable to follow verbal commands [3]. Pregnancy does not preclude TTM and can be considered post cardiac arrest with ROSC; however ,outcome data is lacking, and prior case reports included pregnancies prior to fetal viability. This case report joins a select group of favorable maternal and fetal/neonatal health outcomes using TTM in the setting of pregnancy [1,4-6].

Case presentation

A 31 year old gravida 3 para 2 at 36 week's gestation presented for routine prenatal visit at a free-standing clinic. Her pregnancy was complicated by only depression, treated with citalopram and subjective intermittent palpitations. Her obstetrical history included 2 prior uncomplicated term vaginal deliveries. At her visit, she reported decreased fetal movement; therefore, the provider left the room briefly to obtain cardiotocography for a non-stress test. Upon her return, the provider found the patient unresponsive and pulseless.

Basic life support was initiated and Emergency Medical Services (EMS) summoned. An automatic external defibrillator was applied and patient received a total of 3 biphasic defibrillation shocks. Seven minutes into resuscitation, EMS arrived and cardiac monitor showed ventricular fibrillation. En route to the emergency department she received 1mg epinephrine and two additional biphasic 200J shocks with ROSC at 12 minutes from initial event.

On arrival to the emergency department, ger blood pressure was 123/79, respiratory rate 23, and pulse rate 115. She however, had a Glasgow coma score of 3 and was rapidly intubated. The obstetric team was present on arrival, and a limited obstetric ultrasound revealed fetal heart rate in 130s, positive breathing, gross movement and normal amniotic fluid index. Continuous cardiotocography was initiated and was Category 1. Following ascertainment of maternal and fetal stability, she was transferred to the Cardiac Intensive Care Unit.

A 12-lead electrocardiogram showed sinus tachycardia, prolonged QT (388), QTc (496), ST and T wave inversion in inferior leads with occasional premature ventricular contractions (PVCs). Serial troponins were negative. Metabolic profile was significant for hypokalemia (2.9), and lactic acidosis (10.6). Arterial blood gas results showed pH 7.19, pCO_2 45, PO_2 129, and HCO_3 17.2. Liver enzymes were slightly elevated with an AST of 87, ALT of 61 and alkaline phosphatase of 165. Urine drug screen was negative. A formal transthoracic echocardiogram was significant for a concentrically dilatated and hypertrophied left ventricle with normal systolic function. The left atrium was mildly dilated (4.3 cm). She had mild mitral valve prolapse of the posterior leaflet with moderate mitral regurgitation.

Following a multidisciplinary care meeting including maternal fetal medicine, neonatal intensive care, neurology, cardiology and anesthesia, the decision was made with consent from her next of kin to proceed with therapeutic cooling for both maternal and potential fetal benefit. The therapeutic endovascular cooling protocol, ARCTIC (Advanced Resuscitation Cooling Therapeutics Intensive Care) was initiated approximately 60 minutes after cardiac arrest (Table 1).

External cooling was achieved with ice packs and cooling blankets. An intravascular heat exchange catheter was placed and connected to a thermal regulation system. An initial target of 33°C was achieved within 1 hour of initiating TTM. Over the next two hours she was warmed to 35°C, rather than maintaining at 33°C in order to decrease fetal bradycardia. She was rewarmed after 24 hours of sustained cooling at 35°C. Over 8 hours she was rewarmed to 37°C. Seven hours after being rewarmed to 37°C, and with assurance of hemodynamic stability, she underwent cesarean delivery under general anesthesia. The surgery was uncomplicated, she received prophylactic antibiotics and had an estimated blood loss of 800 ml.

Neonatal Apgars scores were 3, 4, 7 at 1, 5 and 10 minutes of life respectively. Cord pH was 7.13, with pCO_2 90, HCO_3 30.2, and base excess of 6.6. The neonate was transferred to the Neonatal Intensive Care Unit (NICU) for continued respiratory support with non-invasive positive pressure ventilation at 21% FIO_2 and transitioned to unsupported spontaneous respirations with room air on day of life two. The neonate initially displayed agitation and hypertonicity. However, imaging was negative for evidence of ischemic brain injury and exam findings normalized. The neonate was discharged home on day of life 10 meeting all milestones and, at the time of this report, has met all developmental milestones without neurologic residua.

Post operatively, the patient returned to the CICU intubated and sedated. Per protocol, her temperature was maintained at 37° via endovascular catheter for an additional 24 hours during which time, her sedation was weaned. Her GCS off sedation was 15, and she was extubated to nasal canula on post-operative day 0. Apart from amnesia surrounding the events of arrest, the patient has obtained full neurological recovery. During her hospital course, she was treated for aspiration pneumonia based on fever and imaging. She received vancomycin and piperacillin/ tazobactam. She was evaluated with a left heart catheterization, cardiac MRI, lower extremity doppler ultrasonography, CT angiography, and electroencephalogram which were all unrevealing. A subcutaneous implantable cardioverter-defibrillator was placed by electrophysiology under sedation. She was discharged home on hospital day 9 on 80 mg of nadolol to reduce mortality from the event.

Outpatient electrophysiology care discovered no pathogenic mutations associated with long QT. However, a high PVC burden was noted with 24 hour holter monitoring. Given finding of mitral valve prolapse on echo, and characteristic appearance of her subsequent EKGs (inverted T-waves in 2, 3, and aVF), she was diagnosed with malignant mitral valve prolapse. She underwent a successful PVC ablation of her anterolateral papillary muscle and is currently asymptomatic with no further adverse cardiac events.

Inclusion criteria

- Return of Spontaneous Circulation (ROSC) after cardiac arrest.
- Comatose or unable to follow verbal commands.

Relative exclusion criteria

- Shock despite escalating pressors.
- ncontrolled bleeding.
- Core temp <34 C or 93.2 F at presentation.
- Significant known pre-arrest co-morbid state limiting life expectancy.
- Advanced directives not wanting aggressive post resuscitation care.

Table 1: Brief overview of the targeted temperature management protocol at our institution.

PHASE 1	PHASE 2	PHASE 3	PHASE 4
Arrival → 33°C	Cooling at 33°C	Rewarming at 0.25°C/ hr	Goal Temp at 37°C
(Reach 33°C in < 4 hours)	(24 hour process)	(16 hour process)	Maintain 24 hours with Alsius

Discussion

In 2015, the American Heart Association (AHA) guidelines established that pregnancy is a relative, but not an absolute contraindication to TTM. They continue to state that the decision of targeted temperature should be made on an individual basis [1]. Still, data on post-cardiac arrest and ROSC use of TTM in pregnancy is limited.

There are four other published reports of the use of TTM in the setting of pregnancy with post-cardiac arrest ROSC (search of PubMed and MEDLINE through April 2020 using search terms "Therapeutic Hypothermia", "Targeted Temperature Management", "Pregnancy" and "Cardiac Arrest").

In a case report by Rittenberger et al., a 35 year old woman who was 13 weeks pregnant had a witnessed ventricular fibrillation arrest with ROSC within 21 minutes. TTM to 33°C for 24 hours was performed, and the patient was discharged home on hospital day 6 with mild neurologic impairment. The neonate was delivered at 39 weeks with Apgars of 8 and 9 and appropriate neurological and development function at birth and 2 months of age [4]. Chauhan et al. reported witnessed cardiac arrest in a 33 year old woman who was 20 weeks pregnant and experienced ROSC within 25 min. That patient was therapeutically cooled for 24 hours. The neonate was delivered via uncomplicated vaginal delivery at 39 weeks. The mother's cardiac and neurological function returned to baseline by 36 months post-arrest. Three year follow-up indicated that the infant met all milestones [6]. Oguayo et al., documented a case of cardiac arrest in a 20 year old woman at 18 weeks gestation, with ROSC within 8 minutes followed by therapeutic cooling for 24 hours. She was discharged with slight short term memory loss with no other neurological deficits. Her fetus was delivered vaginally at 40 weeks with Apgars of 8 and 9, at 1 and 5 minutes respectively [5]. Of note, there is one case report of fetal demise with TTM by Wible EF et al. That patient was a 44-year-old woman at 20 weeks gestation with notable 22 minutes of resuscitation before ROSC [7].

This case represents a case of post cardiac arrest TTM in a third trimester pregnancy, one of the first reports of its kind. Similar to the cases described, the patient experienced an Out of Hospital Cardiac Arrest (OHCA). Upon arrival to the emergency room, the obstetric team was prepared for resuscitative hysterotomy, however ROSC had been achieved. As both the patient and fetus were hemodynamically stable, and the fetal surveillance was reassuring, there was no acute indication for immediate delivery. Our case supports a growing body of literature that affirms that rapid and effective resuscitation with the addition of TTM can result in favorable outcomes.

In this case, a deliberate deviation from the ARTIC protocol referenced below was made with a cooling goal of 35° to reduce the possibility of fetal bradycardia. This decision was supported by a large randomized controlled trial of unconscious patients treated with TTM after out of hospital cardiac arrest with ROSC. Results from the randomization of adult patients to 33°C vs 36°C showed no difference in mortality or neurological function between the two groups [3].

The sedative regimen chosen for TTM must also account for both maternal and fetal implications. In this case, a combination of propofol and fentanyl were used to provide analgesia and amnesia while cooling. Both fentanyl and propofol cross the placenta. Fentanyl is associated with loss of fetal heart rate variability and can also cause depressed respiratory drive after delivery. Prolonged use of fentanyl may also be associated with neonatal abstinence syndrome. Propofol has rapid onset of action, but also a short half-life. When used as an induction agent for general anesthesia during a cesarean section, it has minimal effect on Apgar scores as long as the induction to delivery interval is short. However, little data exists describing delivery after prolonged use of propofol. Furthermore, shivering counters the speed of reduction of body temperature due to increased thermogenesis and accelerated oxygen consumption. A non-depolarizing neuromuscular blocker vecuronium was added to her sedative regiment to preclude this physiologic response. Vecuronium has less placental transfer compared to most anesthetic agents and concentrations in the fetal circulation is generally not sufficient to cause muscle weakness [8]. The NICU team was prepared to provide respiratory support for the neonate at time of delivery. The Apgar scores likely reflect the anesthetics the patient was receiving. However, the infant quickly recovered and, to date, exhibits no neurological or developmental abnormalities.

One factor associated with increasing US maternal mortality rates is progressive increases in age at delivery. Older patients or those with comorbidities that predispose to cardiac complications may lead to an increase in cases of cardiac arrest in pregnancy. Our multidisciplinary approach and use of the ARCTIC protocol supports the use of TTM following maternal cardiac arrest, and prior to delivery in a third trimester pregnancy.

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