

A Report of Fetal Demise During Therapeutic Hypothermia After Cardiac Arrest

Elissa Fory Wible · Joseph S. Kass ·

George A. Lopez

Published online: 18 June 2010
© Springer Science+Business Media, LLC 2010

Abstract

Background Therapeutic hypothermia is becoming the standard-of-care for coma following out-of-hospital cardiac arrest. Pregnancy has been considered a contraindication for therapeutic hypothermia.

Methods Case report.

Results A 44-year-old woman presented after a witnessed out-of-hospital ventricular fibrillation cardiac arrest. She remained comatose upon hospital admission and was treated with induced hypothermia via surface cooling pads. An intrauterine pregnancy of 20 weeks gestation was discovered on admission. One day after admission, a stillborn fetus was spontaneously delivered. The patient made a good neurologic recovery and now lives at home with her family.

Conclusion During pregnancy, beneficence toward the pregnant woman must be the primary ethical guideline in emergent, life-threatening situations. Pregnancy should not be a contraindication to therapeutic hypothermia following cardiac arrest.

Keywords Cardiopulmonary resuscitation · Sudden cardiac death · Hypoxic-ischemic encephalopathy · Induced hypothermia · Pregnancy · Stillbirth · Fetal demise

Introduction

Cardiac arrest or sudden cardiac death occurs in 300,000 to 500,000 people in the United States annually, and accounts for approximately 15% of all deaths in the U.S. [1, 2]. Therapeutic hypothermia is becoming the standard-of-care for patients with coma following out-of-hospital ventricular fibrillation or ventricular tachycardia cardiac arrest [3–5]. Induced hypothermia both decreases mortality and improves neurologic outcomes following cardiac arrest. None of the trials have included pregnant patients [3, 4, 6, 7] as preventive ethics principles guide against fetal exposure to an unproven therapy [8]. However, now that hypothermia is known to be beneficial, the treatment's risks and benefits to the mother and the fetus must be considered.

Case Report

E. F. Wible (✉)
Department of Medicine, Duke University Medical Center,
DUMC Box 2900, Durham NC27710, USA
e-mail: elissa.wible@gmail.com

J. S. Kass
Department of Neurology, Baylor College of Medicine,
Houston, TX, USA

G. A. Lopez
Department of Neurology, University of Texas Health Science
Center at Houston, Houston, TX, USA

A 44-year-old woman was brought to the Emergency Department after an out-of-hospital cardiac arrest. The patient had been complaining of “heartburn” during the previous 24 h. In the late evening, the patient’s husband left the room for a short time and returned to find her unresponsive. He called emergency medical services (EMS) and then performed cardiopulmonary resuscitation (CPR). EMS arrived after approximately 22 min. Ventricular fibrillation was the initial recorded cardiac rhythm. The patient was intubated and received 10 rounds of

cardioversion, 6 mg of epinephrine, and 1 mg of atropine during the resuscitation. The exact time of return of spontaneous circulation was not recorded.

Admission vital signs were temperature 36°C, heart rate 150 beats per minute, and blood pressure 140/80 mmHg. Cardiac auscultation revealed a tachycardic, regular rhythm. Pupils were 3 mm in diameter and minimally reactive to light, and corneal and gag reflexes were present. There were spontaneous respirations above the ventilator rate. Flexor posturing was present spontaneously. The initial Glasgow coma score was five (E1-M3-V1).

On the admission electrocardiogram, there were 3 mm ST-segment elevations in leads V2 through V4; the initial troponin was 0.15 ng/ml. Lactate was 3.5 mmol/l. Urine toxicology was positive for cocaine. Both urine and serum pregnancy tests were positive. A transabdominal ultrasound showed fetal heart tones at 160 beats per minute, and the estimated gestational age by fetal measurements was 20 weeks.

The patient's husband had been previously unaware of the pregnancy. The risks and benefits of therapeutic hypothermia were explained in detail to the husband, including the uncertain effects on the fetus and the possibility of fetal demise. The patient's husband and the cardiology, neurocritical care, and obstetrics teams agreed that life-saving treatment of the mother was the primary objective, and all concurred with therapeutic hypothermia.

Hypothermia was induced with 3 l of 4°C normal saline at 5 h and 40 min after cardiac arrest. A core temperature of 33°C was reached in 150 min. The Arctic Sun® Temperature Management System (Medivance, Inc., Louisville, CO) was used for maintenance. Other measures per our institutional hypothermia protocol included neuromuscular blockade with cisatracurium, sedation with midazolam, and ventilator rate adjustment for normocarbia (goal PCO₂ 35–40 torr). The mean arterial blood pressure was targeted to greater than or equal to 90 mmHg for cerebral perfusion, and therefore a dobutamine drip was required for less than 24 h. Initial blood glucose measurements were 130–150 mg/dl, but increased to greater than 200 mg/dl within 24 h of admission; a continuous insulin infusion was started.

Aspirin, clopidogrel, and beta blockers were given for myocardial ischemia. Due to the pregnancy, angiotensin-converting enzyme inhibitors were withheld. An echocardiogram performed 7 h after the cardiac arrest showed an ejection fraction of less than 10% with global left ventricular hypokinesis and moderate right ventricular hypokinesis.

Approximately 28 h after the cardiac arrest, a stillborn fetus spontaneously delivered. A dilatation and curettage was necessary to complete placental extraction.

The patient was rewarmed at 0.15°C/h to 36.5°C over the subsequent 24 h, and normothermia was maintained with surface cooling for the next 48 h.

The troponin peaked at 34 ng/ml on hospital day 2. A repeat echocardiogram on hospital day 4 was improved, with an ejection fraction of 30%; however, akinesis was present in the mid-anterior, apical, and septal myocardial wall segments. Cardiac catheterization revealed a 100% mid-left anterior descending artery occlusion with good collateral flow; no revascularization was performed. Due to recurrent ventricular tachycardia in the setting of cardiomyopathy, an automatic internal cardiac defibrillator was placed. Further medical complications included acute renal failure requiring temporary hemodialysis, cardiogenic pulmonary edema, an upper extremity deep vein thrombosis, and heparin-induced thrombocytopenia.

Continuous electroencephalography (EEG) was used during the hypothermia protocol to screen for seizures. The initial EEG during hypothermia showed a low voltage 1–1.5 Hertz (Hz) background that was not reactive to stimulation. During the 24 h rewarming period, the EEG contained semi-rhythmic 4–6 Hz waves and remained unreactive. On the 3rd day, the patient remained seizure-free and the EEG tracing had improved to a 6–7 Hz background which was reactive to stimulation.

On examination, the patient also slowly improved. Three days post-arrest and following rewarming, the patient required intravenous sedation due to hypoxia requiring high ventilatory support. On examination, her pupils were 3 mm, equal, and reactive to light. She opened her eyes and withdrew all four extremities to pain. She remained sedated for the next week due to the need for continued mechanical ventilation and ventilator dysynchrony when sedation was held. On hospital day 11, the patient remained intubated but opened her eyes to voice and followed commands. She was extubated on hospital day 13. At that time, she followed commands, demonstrated fluent speech, and was oriented to self and the hospital. The patient was discharged from the intensive care unit 3 days later. That day, she scored a zero on the NIH Stroke Scale (NIHSS). She was oriented to person, place, and time, but when asked the circumstances of her hospitalization, responded, "A problem." She was discharged home on hospital day 42. At a follow-up visit with the neurointensivist more than 1 year later, she did not remember her hospitalization. The NIHSS was zero, and the Barthel Index was 100. She was able to perform her activities of daily living and helped care for her other children.

Discussion

Mild therapeutic hypothermia has both randomized, controlled studies [3, 4] and consensus statements [5, 9, 10]

supporting its use for coma after out-of-hospital cardiac arrest. Hypothermia significantly decreases mortality and increases the likelihood of good neurologic outcome in survivors [3, 4].

The first report of a pregnant patient receiving therapeutic hypothermia after cardiac arrest was published in 2008 [11]. In that case, the fetus was 13 weeks gestational age. Fetal bradycardia accompanied hypothermia treatment. The infant was delivered at term via cesarean section without complication [11]. In our patient, fetal demise occurred approximately 28 h after cardiac arrest, during the hypothermia treatment. Whether the hypothermia treatment contributed to the death of the fetus cannot be known. Many factors—including the cardiac arrest itself, prolonged time to return of spontaneous circulation, possible cocaine-induced vasoconstriction, and global myocardial hypokinesis—may have impaired uterine blood flow and contributed to the fetal demise.

Cardiac arrest during pregnancy is rare, occurring in 3–6 in 100,000 pregnancies [12, 13]. Much of the literature on cardiovascular resuscitation in pregnant women focuses on increasing venous return and arterial forward flow with a left lateral wedge position during chest compressions, and on prompt emergency cesarean section for unsuccessful resuscitation efforts lasting longer than 5 min [14, 15]. The few reports of maternal hypoxic-ischemic or metabolic encephalopathy describe events during the first two trimesters and depict generally good fetal outcomes [11, 13, 16–18]. However, these isolated accounts may not reflect the true natural history of fetal outcomes following cardiac arrest in pregnancy.

In considering the ethical implications of treating a pregnant woman with hypothermia after cardiac arrest, the interests of both the pregnant woman and the fetus must be measured [18, 19]. The question of fetal personhood and autonomy, and therefore the physician's duty toward the fetus, is the source of much theological, ethical, and legal debate and leads to an ethical stalemate. An alternative approach is to focus on a beneficence-based ethical analysis [20]. Beneficence requires a physician to take positive steps to help patients [21]. The physician has an undisputed duty of beneficence toward the pregnant woman throughout the pregnancy. Especially during pre-viability, fetal outcome is invariably tied to maternal outcome. Even after viability, the physician must consider the gravity of the pregnant woman's medical condition when determining an appropriate degree of risk to which to expose the fetal patient. Fetal risk should be minimized whenever possible. However, in an acute life-threatening situation such as cardiac arrest, beneficence toward the pregnant woman allows exposing the fetus to a substantial risk [20].

The effects of therapeutic hypothermia on a fetus are unknown. Even if the fetal risks were substantial,

therapeutic hypothermia should not be withheld from a comatose pregnant patient since treatment substantially reduces mortality and neurologic morbidity. Finally, it is possible that therapeutic hypothermia may actually benefit the fetus by increasing the likelihood of maternal survival.

In non-emergent circumstances with a competent pregnant patient, the pregnant woman expresses her autonomy by weighing her beliefs and values to guide medical decisions for both herself and her unborn fetus. In this case, the husband, using substituted judgment, was able to express the patient's autonomy through the informed consent process [18, 19].

Conclusion

Our patient had a good neurologic outcome after treatment with induced hypothermia but spontaneously delivered a stillborn fetus 28 h after the cardiac arrest. The risks and/or benefits of therapeutic hypothermia to a fetus are unknown. However, the principle of beneficence allows pregnant women and their physicians to expose the fetus to greater than minimal medical risk in emergent or life-threatening situations, such as after cardiac arrest. Thus, pregnancy should not be a contraindication to therapeutic hypothermia following cardiac arrest.

References

1. Heron M. Deaths: leading causes for 2004. *Natl Vital Stat Rep.* 2007;56:1–95.
2. Turakhia M, Tseng ZH. Sudden cardiac death: epidemiology, mechanisms, and therapy. *Curr Probl Cardiol.* 2007;32:501–46.
3. Hypothermia After Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med.* 2002;346:549–56.
4. 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.
5. 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2005;112:IV1–203.
6. Bernard SA, Jones BM, Horne MK. Clinical trial of induced hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Ann Emerg Med.* 1997;30:146–53.
7. Zeiner A, Holzer M, Sterz F, et al. Mild resuscitative hypothermia to improve neurological outcome after cardiac arrest. A clinical feasibility trial. Hypothermia After Cardiac Arrest (HACA) Study Group. *Stroke.* 2000;31:86–94.
8. McCullough LB, Coverdale JH, Chervenak FA. Preventive ethics for including women of childbearing potential in clinical trials. *Am J Obstet Gynecol.* 2006;194:1221–7.
9. Nolan JP, Deakin CD, Soar J, Bottiger BW, Smith G. European Resuscitation Council guidelines for resuscitation 2005. Section 4. Adult advanced life support. *Resuscitation.* 2005;67(Suppl 1):S39–86.
10. Nolan JP, Morley PT, Hoek TL, Hickey RW. Therapeutic hypothermia after cardiac arrest. An advisory statement by the

- Advancement Life support Task Force of the International Liaison committee on Resuscitation. *Resuscitation*. 2003;57:231–5.
11. Rittenberger JC, Kelly E, Jang D, Greer K, Heffner A. Successful outcome utilizing hypothermia after cardiac arrest in pregnancy: a case report. *Crit Care Med*. 2008;36:1354–6.
 12. Li JM, Nguyen C, Joglar JA, Hamdan MH, Page RL. Frequency and outcome of arrhythmias complicating admission during pregnancy: experience from a high-volume and ethnically-diverse obstetric service. *Clin Cardiol*. 2008;31:538–41.
 13. Nelissen EC, de Zwaan C, Marcus MA, Nijhuis JG. Maternal cardiac arrest in early pregnancy. *Int J Obstet Anesth*. 2009; 18:60–3.
 14. Atta E, Gardner M. Cardiopulmonary resuscitation in pregnancy. *Obstet Gynecol Clin N Am*. 2007;34:585–97, xiii.
 15. Mallampalli A, Guy E. Cardiac arrest in pregnancy and somatic support after brain death. *Crit Care Med*. 2005;33:S325–31.
 16. Ayorinde BT, Scudamore I, Buggy DJ. Anaesthetic management of a pregnant patient in a persistent vegetative state. *Br J Anaesth*. 2000;85:479–81.
 17. Hill LM, Parker D, O'Neill BP. Management of maternal vegetative state during pregnancy. *Mayo Clin Proc*. 1985;60:469–72.
 18. Webb GW, Huddleston JF. Management of the pregnant woman who sustains severe brain damage. *Clin Perinatol*. 1996;23: 453–64.
 19. Bush MC, Nagy S, Berkowitz RL, Gaddipati S. Pregnancy in a persistent vegetative state: case report, comparison to brain death, and review of the literature. *Obstet Gynecol Surv*. 2003;58: 738–48.
 20. McCullough LB, Chervenak FA. Ethics in obstetrics and gynecology. New York: Oxford University Press; 1994.
 21. Beauchamp TL, Childress JF. Principles of biomedical ethics. 4th ed. New York: Oxford University Press; 1994.