Cardiopulmonary Resuscitation in the Pregnant Patient – An Update

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CARDIAC ARREST IN PREGNANCY

Cardiac arrest in pregnancy is a rare encounter, considered to occur in 1:30,000 births [1]. It may lead to perimortem cesarean delivery in order to save the mother and her infant [2].

"Five minutes is just about long enough, depending upon personal preference, to boil an egg and butter some toast. It is also the period of time during which obstetric care givers are expected to identify maternal cardiac arrest, initiate cardiopulmonary resuscitation and, if maternal cardiac output is not immediately restored, deliver the fetus by caesarean section." [3]. This quotation is a quintessence of the complexity involved in providing high-quality medical care quickly and efficiently to the pregnant patient who suffers a cardiac arrest.

Following their analysis of an anonymous questionnaire survey among obstetricians, anesthesiologists and midwives, Einav et al. [4] concluded that specialist clinicians who treat pregnant women in hospital on a daily basis possess a limited knowledge of the recommendations for treating maternal cardiac arrest. This review is therefore intended to update the readers’ knowledge with regard to cardiopulmonary resuscitation in pregnant patients. We start with a brief presentation of a real case and follow with a review of the pathophysiology and etiology of CA in pregnancy, with special emphasis on the anesthetic causes of CA and management strategies. A brief description of CPR in pregnancy is also included, and the importance of emergency delivery (hysterotomy or cesarean delivery) is emphasized.

Case Report

A 35 year old, 38 weeks pregnant, apparently healthy woman was referred by her family physician urgently to our labor and delivery unit due to concern about her lack of appetite over the past week and her altered mood. Her 15 year old son confirmed that she appeared depressed and had not left the house for the past week. Her communication difficulties were attributed to her new immigrant status in Israel. She appeared exhausted with low mood. At this stage there was no specific diagnosis. Upon admission to the hospital her vital signs were stable: blood pressure 120/70 mmHg, heart rate 70 beats/minute and oxygen saturation 98% on room air. Fetal heart rate tracing was also normal. She was not in active labor and did not complain of pain. The on-duty anesthesiologist was asked to consult the patient regarding epidural analgesia once in active labor. The patient appeared confused and uncooperative, and approximately 10 minutes after the history-taking and examination had begun the patient developed witnessed cardiorespiratory arrest (asystole). This was accompanied by severe fetal bradycardia. CPR in the left tilt position was immediately started by the resident anesthesiologist and the obstetrician. The operating room was prepared for an emergency cesarean delivery. The left tilt was achieved with a rolled blanket placed under the patient’s right hip and lumbar area.

The alerted in-house senior obstetrician, anesthesiologist and neonatologist arrived at the scene within 2 minutes. The patient’s trachea was intubated while receiving cardiac massage at a rate of 100/min, 10 breaths/min and two intravenous boluses of 1 mg each of atropine and epinephrine. Spontaneous circulation and normal blood pressure resumed after 2 minutes of CPR, but the patient remained unconscious with both pupils dilated and unreactive to light. Approximately 5 minutes after the diagnosis of CA, an emergency cesarean delivery was performed in the operating room which was situated inside the delivery unit. The patient remained unresponsive (no movement, with unchanged heart rate and blood pressure) to the surgical

Some reasons for cardiac arrest in pregnancy are reversible and should be recognized and managed promptly

CA =cardiac arrest
CPR = cardiopulmonary resuscitation
stimulus. The patient received no anesthesia and only 100 µg IV fentanyl for analgesia, with no muscle relaxants. The baby was delivered with an Apgar score of 4/6 and a pH of 7 and his condition gradually improved during the following hours. Following the cesarean delivery the mother remained unresponsive, with a Glasgow Coma Scale of 3. A brain computed tomography scan revealed severe diffuse brain edema. The patient was treated with mild hyperventilation, mannitol, rest in a semi-recumbent position and oxygen to keep her oxygen saturation above 98%. Following resolution of some brain edema, a huge frontal herniated brain tumor was revealed. The tumor was considered inoperable and the patient died 5 days later.

This case emphasizes that CPR skills may be required unexpectedly in the labor ward and that management of cardiac arrest involves prompt initiation of the correct treatment, which could include cesarean delivery and treatment of the underlying cause of the CA [3,4].

PATHOPHYSIOLOGY OF CARDIAC ARREST IN PREGNANCY

In pregnant women, CA is complicated by the pathophysiological changes that occur during pregnancy, especially aortocaval compression. During CPR with closed chest massage in non-pregnant patients the maximal cardiac output approximates 30% of normal [5]. In patients ≥ 20 weeks pregnant lying in the supine position, the cardiac output is further decreased. This implies that if these patients suffer CA when placed in the supine position, there will be practically no cardiac output at all despite a correctly performed CPR.

Patients in advanced pregnancy also have a tendency for rapid development of hypoxemia and acidosis, a higher risk of pulmonary aspiration, and an increased incidence of difficult intubation as compared to the non-pregnant population. These changes are exaggerated by multiple pregnancy and obesity, all of which make the resuscitation more difficult.

ETIOLOGY AND DIFFERENTIAL DIAGNOSIS OF CARDIAC ARREST IN PREGNANCY

It is imperative to identify reversible causes of CA. The age of pregnancy should be quickly established in order to decide on fetal viability. Abdominal ultrasound examination is used for this purpose but it should not delay resuscitation procedures.

The etiology of CA in pregnancy can be classified into anesthesia-related causes and/or non-anesthesia-related causes [Tables 1 and 2]. Occasionally, the etiology is multifactorial, making the diagnosis and management more challenging.

ANESTHESIA-RELATED MATERNAL MORTALITY

The 1990-2003 USA closed claims data in obstetric anesthesia reported 69 cases of anesthesia-related death or severe brain injury; 18% (vs. 6.7% in the non-pregnant surgical population) were linked to airway problems. Airway catastrophes were also related to some poor fetal outcomes [8].

It is noteworthy that through the decades, a change in anesthesia-related maternal mortality trends has been observed. Around 40 years ago, the aspiration of gastric contents was the leading cause of anesthesia-related maternal death, but in the following 20 years the culprit was failed intubation. More recently, attention to airway loss during induction of anesthesia has led to a decrease in airway mortality during induction. However, mortality related to airway problems during extubation of the trachea has increased, as has spinal anesthesia-related mortality [9,10].

The last Confidential Enquiries into Maternal and Child Health (CEMACH) in the United Kingdom 2003–05 reported that in six cases maternal death was directly related to anesthesia, a similar figure to that reported in 2000–02. There were three cases of postoperative airway loss: all occurred in morbidly obese parturients [11]. Twenty-seven percent of all maternal deaths (directly or indirectly related to anesthesia) occurred among obese women (body mass index > 30 kg/m²), whereas 24% occurred among overweight women (BMI > 25 kg/m²).

Table 1. Etiology, mechanism, characteristics and management of anesthesia-related CA in pregnancy

<table>
<thead>
<tr>
<th>Category</th>
<th>Mechanism</th>
<th>Characteristics</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anoxic/hypoxic</td>
<td>Failure to oxygenate due to failed intubation/ventilation and/or aspiration of gastric contents</td>
<td>• Obese patients</td>
<td>Rescue airway procedures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Other reasons for difficult airway</td>
<td></td>
</tr>
<tr>
<td>Hemodynamic/</td>
<td>High/total spinal (see below: specific mechanisms)</td>
<td>• Local anesthetic overdose</td>
<td>Hemodynamic &amp; respiratory support</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td>• “Barbotage” of the CSF</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Unrelieved aortocaval compression</td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>Local anesthetic toxicity (overdose or IV injection)</td>
<td>• Specific symptoms</td>
<td>Hemodynamic &amp; respiratory support, Intralipid® (Pharmacia &amp; Upjohn)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Neurologic signs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Hemodynamic signs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Respiratory arrest</td>
<td></td>
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BMI = body mass index

Cardiopulmonary resuscitation follows general ACLS guidelines with several modifications for pregnant women, taking into account the lives of both mother and fetus.
or if necessary endotracheal intubation can be performed with cricoid pressure.

**CARDIAC ARREST IN PREGNANCY – ADVANCED CARDIAC LIFE SUPPORT GUIDELINES**

The following are updated guidelines [5,12] for which there are several modifications for pregnant women, taking into account the lives of both mother and fetus since fetal survival depends on maternal survival.

**Key interventions for managing cardiac arrest in pregnant women:**

- First responder or single rescuer will start CPR with chest compression (CAB instead of ABC)
- Place the woman in left lateral position
- Ventilate the patient with 100% oxygen
- Establish IV access and administer fluids using upper extremity veins
- Oxygen 100% should be administered by mask, or if necessary endotracheal intubation can be performed with cricoid pressure.

**Table 2. Etiology, mechanism, characteristics and management of non-anesthesia-related CA in pregnancy**

<table>
<thead>
<tr>
<th>Category</th>
<th>Mechanism</th>
<th>Characteristics</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic</td>
<td>Hemorrhagic</td>
<td>• Placenta accreta, increta, percreta, previa, abruptio&lt;br&gt;• Uterine rupture</td>
<td>Balloons into the hypogastric arteries&lt;br&gt;Surgery&lt;br&gt;Fluid &amp; blood resuscitation&lt;br&gt;Management of coagulopathies</td>
</tr>
<tr>
<td>Hemodynamic</td>
<td>Acute coronary syndromes</td>
<td>• Smokers and older aged-pregnant women are at higher risk</td>
<td>Percutaneous coronary reperfusion is the strategy of choice for ST-elevation myocardial infarction</td>
</tr>
<tr>
<td>Hemodynamic</td>
<td>Rupture of aortic aneurysm</td>
<td>Marfan syndrome &amp; hypertensive patients [ref. 6]</td>
<td>Surgery if indicated</td>
</tr>
<tr>
<td>Hemodynamic /neurologic</td>
<td>Stroke</td>
<td>• Rupture of brain aneurysm&lt;br&gt;• Embolic event&lt;br&gt;• Uncontrolled hypertension</td>
<td>Surgery if indicated&lt;br&gt;Successful use of fibrinolytics in massive, life-threatening ischemic stroke</td>
</tr>
<tr>
<td>Hemodynamic</td>
<td>Air embolism</td>
<td>Uterus above the level of right atrium and hypovolemia</td>
<td>Level the table&lt;br&gt;Fluid resuscitation</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Magnesium</td>
<td>Overdose, particularly in oliguric patients</td>
<td>Calcium gluconate IV (30 ml in 10% solution)</td>
</tr>
<tr>
<td>Complex</td>
<td>Amniotic fluid embolism [ref. 7]</td>
<td>Dramatic evolution with high morbidity/mortality</td>
<td>Life support measures&lt;br&gt;Activated factor VII&lt;br&gt;Inhalation of prostacyclin or nitric oxide&lt;br&gt;Extracorporeal membrane oxygenation&lt;br&gt;Cardiopulmonary bypass</td>
</tr>
<tr>
<td>Complex</td>
<td>Pulmonary embolism</td>
<td>• Usually postoperative&lt;br&gt;• Antiphospholipid antibody syndrome at high risk</td>
<td>Anticoagulants in at-risk patients – problematic regional anesthesia&lt;br&gt;Successful use of fibrinolytics for massive, life-threatening pulmonary embolism</td>
</tr>
<tr>
<td>Complex</td>
<td>Trauma</td>
<td>Important cause of maternal &amp; fetal mortality</td>
<td>Aortocaval decompression&lt;br&gt;Early CS/hysterotomy may be life-saving</td>
</tr>
<tr>
<td>Complex</td>
<td>Preeclampsia/eclampsia</td>
<td>• Diffuse organ impairment/ failure affecting maternal &amp; fetal mortality&lt;br&gt;• Possible airway problems</td>
<td>Magnesium&lt;br&gt;Antihypertensive medication&lt;br&gt;Early epidural placement</td>
</tr>
<tr>
<td>Complex</td>
<td>Sepsis</td>
<td>• Chorioamnionitis&lt;br&gt;• Pneumonia&lt;br&gt;• Epidural abscess</td>
<td>Antibiotics&lt;br&gt;Fluid resuscitation&lt;br&gt;Vasopressors</td>
</tr>
<tr>
<td>Complex</td>
<td>Status asthmaticus [ref 2]</td>
<td>• Airway obstruction</td>
<td>Cardiopulmonary resuscitative measures&lt;br&gt;Specific management of status asthmaticus</td>
</tr>
</tbody>
</table>

Two obese patients died in early pregnancy due to failure in managing their airway adequately. One death was caused by bupivacaine toxicity due to accidental IV infusion of bupivacaine. Thirty-one fatal cases of indirect anesthetic deaths were attributed to poor recognition and management of critical situations (bleeding, sepsis, etc).

**CA AND CARDIOVASCULAR COLLAPSE AFTER SPINAL/EPIDURAL ANALGESIA/ANESTHESIA**

This scenario could occur following spinal analgesia in multiple gestation, obesity, “barbotage” of the cerebrospinal fluid, subdural block, spinal overdose, repeated spinal/epidural blocks, spinal injection following “failed” epidural, epidural overdose, toxic reaction to local anesthetic overdose, or intravascular injection.

High spinal block in pregnancy can be successfully managed by early recognition and aggressive treatment. Management includes left uterine displacement. Fluids are rapidly infused while bradycardia is aggressively treated with atropine or epinephrine and hypotension should be treated with phenylephrine or epinephrine. Oxygen 100% should be administered by mask,
Consider the possible cause of cardiac arrest to ease targeted management.

1. Left lateral position
Place the patient on a hard surface in 15°-30° left lateral tilt position or pull the uterus to the side. The left tilt can be achieved manually or with a rolled blanket under the right hip and lumbar area.

2. Airway and breathing
Apply continuous cricoid pressure during ventilation and intubation due to the risk of regurgitation. Consider the possibility of airway edema especially in parturients with gestational hypertension which can make endotracheal intubation difficult. Start with two rescue breaths of one second each. Bag-mask ventilate at a rate of 8-10 breaths/min and a tidal volume large enough to raise the chest, during pauses of compressions (synchronization). Synchronization between chest compressions and ventilation is not necessary with an advanced airway (endotracheal tube) in place. It must be noted that hyperventilation is harmful and should be avoided.

3. Circulation
Chest compressions are performed higher than in non-pregnant patients, slightly above the center of the sternum due to the elevated diaphragm and abdominal contents. Chest compressions should be performed with the patient lying on a hard surface. “Push fast and hard”! Place the heel of one hand on the center of the chest. Place the other hand on top. Interlock the fingers and compress the chest at a rate of 100/min, a depth of 4-5 cm and equal compression:relaxation times. It is recommended that the CPR operator be changed every 2 minutes. Although vasopressors (epinephrine, vasopressin) reduce blood flow to the uterus, current recommendations advise using standard drugs in standard adult ACLS doses. A single dose of vasopressin 40 units is an alternative to repeated epinephrine injection. Amiodarone 300 mg IV has replaced lidocaine for treatment of ventricular arrhythmias.

4. Compression-ventilation (C-V) ratio
A C-V ratio of 30:2 is recommended. With two or more rescuers switch the compressor every 2 minutes or every five cycles of C-V. In the newborn give two ventilations after 15 compressions (C-V ratio of 15:2) if the etiology of CA is cardiac or a ratio of C-V 3:1 if the etiology is respiratory.

5. Defibrillation
Standard ACLS defibrillation doses should be used. Survival rates are highest with immediate CPR and defibrillation within 3 to 5 minutes of a witnessed pulseless ventricular tachycardia or fibrillation. Defibrillation is administered at the following doses:

- Monophasic – 360 joules (J)
- Biphasic – truncated exponential waveform 150-200 J
- Biphasic – rectilinear waveform: 120 J
- Newborn – 2 J/kg for the first attempt and 4 J/kg for subsequent attempts

The ACLS guidelines emphasize the importance of availability of automated external defibrillators.

Electric cardioversion during pregnancy has been described in the literature and appears to be safe for the fetus [13]. In pregnant women a secondary reassessment of the airway and breathing is critical to consider early intubation owing to the risk of aspiration. The endotracheal tube size should be smaller and the correct position should be confirmed with capnography.

Incorrectly applied cardiac compressions in pregnant patients with CA may be complicated with liver laceration, uterine rupture, hemothorax and hemopericardium.

Successful cardiopulmonary resuscitation (CPR) implies early recognition of cardiac arrest, aortocaval decompression, early hysterotomy/cesarean delivery and acquiring CPR skills by the managing teams.

Emergency delivery
If cardiac arrest is not immediately (4-5 minutes) reversed by basic and advanced life support, emergency hysterotomy (or cesarean delivery) should be performed at > 20 pregnancy weeks. The best survival rate for an infant is at age > 24 or 25 weeks if delivered < 5 minutes after CA [14]. Gestational age may not always be known and ultrasonography can be used if time permits. It is important to recognize that a promptly performed cesarean delivery may save the mother and her infant.

Timely hysterotomy delivers the fetus, empties the uterus, restores venous return and aortic flow and, in addition, allows newborn resuscitation. Cesarean section might be necessary to accomplish a successful resuscitation even if the fetus has died.

Immediately following the diagnosis of CA, a well-trained team comprising a gynecologist, anesthesiologist, neonatologist and midwives should activate the departmental hysterotomy protocol, in parallel with the CPR efforts. This requires preparation of the operating room for an emergency hysterotomy which ideally should be performed no longer than 4-5 minutes after initiation of CPR.

CONCLUSIONS
Cardiac arrest is a rare, unexpected and devastating event for pregnant patients and those treating them. Early anticipation
and treatment may prevent CA, for example following high spinal block. Multidisciplinary teams should be familiar with the ACLS guidelines and their special modifications for pregnant women. In addition, there should be a well-conceived hysterotomy protocol in delivery rooms, which should be fully equipped for both resuscitation and emergency hysterotomy within 4-5 minutes.

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References

The helminth product ES-62 protects against septic shock via Toll-like receptor 4-dependent autophagosomal degradation of the adaptor MyD88

Sepsis is one of the most challenging health problems worldwide. Puneet et al. found that phagocytes from patients with sepsis had considerable up-regulation of Toll-like receptor 4 (TLR4) and TLR2; however, shock-inducing inflammatory responses mediated by these TLRs were inhibited by ES-62, an immunomodulator secreted by the filarial nematode Acanthocheilonema viteae. ES-62 subverted TLR4 signaling to block TLR2- and TLR4-driven inflammatory responses via autophagosome-mediated down-regulation of the TLR adaptor-transducer MyD88. In vivo, ES-62 protected mice against endotoxic and polymicrobial septic shock by TLR4-mediated induction of autophagy and was protective even when administered after the induction of sepsis. Given that the treatments for septic shock at present are inadequate, the autophagy-dependent mechanism of action by ES-62 might form the basis for urgently needed therapeutic intervention against this life-threatening condition.

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SIK2 degradation after ischemia is beneficial to neurons

The transcription factor CAMP responsive element-binding protein (CREB) mediates neuroprotection after stroke. Sasaki et al. identified a cell-signaling pathway that modulates CREB activation after ischemia. CREB activity can be controlled by recruitment of stimulatory cofactors such as transducer of regulated CREB activity-1 (TORC1). In cell culture experiments, the researchers showed that TORC1 translocation to the nucleus was increased after ischemia and was required for activation of CREB. TORC1 over-expression could reduce neuron death in response to ischemia. TORC1 is phosphorylated by salt-inducible kinase-2 (SIK2), which was degraded in cultured neurons after ischemia, and SIK2 phosphorylation by Ca2+/calmodulin-dependent protein kinases seemed to be responsible for this process. Increasing SIK2 expression prevented TORC1 from entering the nucleus and from activating CREB, and this enhanced cell death after ischemia. The researchers found that a SIK2 inhibitor could enhance CREB activity and prevent neuron death in response to ischemia, and SIK2-deficient mice were protected from stroke. These findings suggest that SIK2 degradation after ischemia is beneficial to neurons.

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