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Research Paper

Maternal collapse: Challenging the four-minute rule

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ABSTRACT

Introduction: The current approach to, cardiopulmonary resuscitation of pregnant women in the third trimester has been to adhere to the "four-minute rule": If pulses have not returned within 4 min of the start of resuscitation, perform a cesarean birth so that birth occurs in the next minute. This investigation sought to re-examine the evidence for the four-minute rule.
Methods: A literature review focused on perimortem cesarean birth was performed using the same key words that were used in formulating the "four-minute rule." Maternal and neonatal injury free survival rates as a function of arrest to birth intervals were determined, as well as actual incision to birth intervals.
Results: Both maternal and neonatal injury free survival rates diminished steadily as the time interval from maternal arrest to birth increased. There was no evidence for any specific survival threshold at 4 min. Skin incision to birth intervals of 1 min occurred in only 10% of women.
Conclusion: Once a decision to deliver is made, care providers should proceed directly to Cesarean birth during maternal cardiac arrest in the third trimester rather than waiting for 4 min for restoration of the maternal pulse. Birth within 1 min from the start of the incision is uncommon in these circumstances.

1. Introduction

In 1986, Katz et al. described a case in which a mortally ill woman experienced a cardiopulmonary arrest on the operating table while being prepared for a Cesarean section (Katz et al., 1986). The newborn was promptly delivered and the maternal pulse immediately returned with evacuation of the uterus. Based on this observation coupled with a review of the literature, the authors proposed the "Four-Minute Rule." Citing the fact that adults begin experiencing anoxic brain damage 4 to 6 min into a cardiac arrest, the authors called for initiating a cesarean birth if the maternal pulse has not been restored by 4 min so that the fetus could be delivered in the next minute. The authors reaffirmed this rule in papers published in 2005 and 2012 (Katz, 2012; Katz et al., 2005). Based on a highly original observation about restoration of maternal pulses during a perimortem Cesarean section, the "Four-Minute Rule" has been adopted by the American Heart Association as well as the European Resuscitation Council and the Society for Obstetric Anesthesia and Perinatology (Jeejeebhoy et al., 2015; Soar et al., 2010; Lipman et al., 2014). It is also recommended by the authors of two subsequent review articles (Jeejeebhoy et al., 2011; Drukker et al., 2014). Yet is the "Four-Minute Rule" most consistent with the available evidence?

A cursory examination of its assumptions raises some immediate questions. Pregnant women in the third trimester are not very comparable to "adults" in the physiology of resuscitation: their metabolism is higher and chest compressions are less effective. Hence, the four-minute cut-off for anoxic injury may not apply to this population as it applies to non-pregnant patients. Furthermore, is it reasonable to expect even an obstetrician to perform a Cesarean birth in a minute or less with no notice, and no advance preparation? On the basis of these concerns, the specific case reports used by Katz et al. as well as articles discovered in additional searches using their six key words were analyzed for the relationship between the time of key events and outcomes (Katz et al., 2005). The guideline to begin a Cesarean if pulses had not been restored and to deliver the fetus in the next minute by Cesarean section was reexamined using this combination of new and old case reports.

This study was intended to re-evaluate the Four-Minute Rule and therefore used the same key words and methodology described by Katz and co-authors in their formulation of the rule. Other reviews using different key words have included case reports not used here and included all women with a cardiac arrest but the purpose here was specifically to re-evaluate the evidence for the Four-Minute rule in women who had a perimortem Cesarean birth. Thus the women

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included here were confined to those found by the key-words used by Katz and were necessarily limited to perimortem cesarean sections in keeping with Katz's criteria.

In order to place this data in perspective, it is helpful to review what is known about maternal physiology in the third trimester.

1.1. Maternal physiology—a brief perspective

The changes of maternal physiology would suggest that pregnant women have less than the 4–6 min that non-pregnant adults have before experiencing brain damage during cardiac arrest. During the course of pregnancy, maternal stroke volume, heart rate and cardiac output increase progressively to reach a peak cardiac output in the third trimester that is 45% higher in singleton pregnancies than preconception levels (Hegewald and Crapo, 2011). Oxygen consumption also increases in pregnancy to levels 20–30% higher than preconception in order to meet the needs of the fetus, placenta, and maternal adaption. Arterio-venous oxygen difference is low in early gestation but appears to widen later in pregnancy as oxygen consumption increases (Ouzounian and Elkayam, 2012). Close to 17–20% of cardiac output is directed to the uteroplacental circulation, which includes the growing uterus, the placenta and the fetus (Assali et al., 1960).

Major hemodynamic fluid shifts occur at birth including a significant increase in venous return following the relief of the vena cava compression, and redirection of the circulating blood from the uterine to the systemic circulation. In the setting of normal blood loss, venous return increases at birth. In addition, uterine evacuation may lead to an improvement in chest wall compliance.

The presence of the fetus has a significant impact on the overall metabolic rate of the mother. In mid gestation, lamb fetal oxygen uptake constitutes about 17% of total uterine oxygen consumption and the uteroplacental tissues consume about 80% (Bell et al., 1986). Later in gestation, oxygen consumption is divided equally between the fetus and the uteroplacental tissues. However, oxygen uptake per fetal weight unit appears to decrease as pregnancy progresses. In mid gestation, fetal oxygen uptake per dry weight is about 2–5 times the oxygen uptake in late gestation (Battaglia and Meschia, 1978).

An important consideration in regard to these estimates is the inherent difference between human and animal fetuses. The human fetal brain has a much larger mass when compared to similar weight animals. Furthermore, the human fetus has more adipose tissue, lives at lower body temperature and grows more slowly. However, data comparing similar measures of fetal oxygen consumption in various animal species of different sizes showed these data to be within 20% of the fetal lamb suggesting that it is likely reasonable to extrapolate these data to humans to a certain degree (Bell et al., 1986).

Based on animal fetal estimates, birth around mid gestation will likely improve oxygen consumption by 6% whereas birth in late gestation will improve oxygen consumption and cardiac output by about 17–18% (Hegewald and Crapo, 2011; Meschia, 2011). However, it is noteworthy that under conditions of hypoxia or hypoperfusion, the fetus is likely to use protective mechanisms. For instance, the fetus is capable of reducing its own oxygen consumption and shunting blood to vital organs and has an increased ability to extract oxygen (Peeters et al., 1979; Boyle et al., 1992). Hence it is possible that birth may have a slightly smaller benefit than these estimates.

Beyond altered maternal physiology and fetal oxygen consumption, resuscitation during pregnancy in the third trimester faces another impediment—reduced efficacy of chest compressions. Venous return through the vena cava is completely obstructed in most women in late pregnancy with circulation maintained via collateral flow through the azygos lumbar and paraspinal veins (Kerr, 1965). With the gravid uterus sitting on the maternal great vessels, it has been estimated that chest compressions restore only 10% of cardiac output (Katz et al., 2005). The problem of compression of the great vessels during chest compressions has led to recommendations for using a wedge to create a 15 to 30° left lateral tilt to improve the efficacy of chest compressions (Soar et al., 2010). However, a Cochrane review that evaluated different methods of maternal positioning to improve uterine blood flow during Cesarean sections did not find enough evidence to recommend any specific maternal position on the operating table (Cluver et al., 2013). Whatever method is used, the concern remains that chest compressions in the third trimester will restore a lower percentage of cardiac output than in the non-pregnant adult. Another impediment to successful resuscitation is the reduced oxygen reserve in pregnancy and the tendency for gravidas to develop hypercapnia and hypoxemia in response to apnea significantly faster than non-pregnant controls (Cheun and Choi, 1992).

The key point from what is known about maternal physiology is that one would expect pregnant women to be even more susceptible to oxygen deprivation than the non-pregnant adults who experienced brain injury in as early as 4 min which was the source of the time constraint in the Four-Minute Rule.

2. Methods

The studies included in this review are case reports that were found in the MEDLINE database with the query using the search terms used previously by Katz et al. "(pregnancy OR pregnant) AND (cardiac arrest OR perimortem OR postmortem OR cardiopulmonary arrest OR cardiopulmonary resuscitation OR fatal outcome OR maternal mortality OR death) AND (delivery, birth OR caesarean section OR caesarean birth, cesarean delivery)." (Katz et al., 2005) The search was conducted in English as well as one dozen other languages: Arabic, Chinese, French, German, Italian, Japanese, Korean, Russian, Polish, Norwegian, Spanish, and Portuguese. These searches produced 2918 English language titles and abstracts that were screened to identify relevant studies. Studies were evaluated further if it seemed possible that they contained data that had either maternal or neonatal survival information as well as time interval information on arrest to birth data. Three Spanish, three Portuguese, three French and four German case reports were translated but only German reports were actually incorporated into the analysis. The list of studies used is cited in the on-line supplement "eReferences: Case Citations."

Case reports were included if they provided (1) clinical details regarding the case, (2) key time intervals, and (3) maternal and fetal/neonatal outcomes.

Pregnant women were excluded from this review if they did not report on cesarean deliveries (e.g. spontaneous or assisted vaginal deliveries), if maternal arrest occurred after the birth, or if the full text was not available, or if the paper was not written in one of the thirteen inclusion languages.

There were 29 possible data points collected from the included reports including maternal demographic and pregnancy characteristics, relevant time intervals, maternal and fetal outcomes, and circumstances of arrest.

All women with cardiac arrest were pregnant women in the third trimester of pregnancy. The average maternal age 30.5 (range 17–44) and average number of pregnancies was 2.4 (range 1–4). Fig. 1 shows the etiology of maternal cardiac arrest in 58 women. Among the known causes of arrest, drug toxicity was the leading cause followed by amniotic fluid embolism.

The primary outcomes were maternal and neonatal injury free survival as a function of time interval from arrest to birth, and incision to birth interval. Injury was defined as loss of an organ or function at time of discharge from the health-care facility or as described in specific case reports. A secondary outcome interval was the arrest to birth interval.

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