Rationale of fetal intrauterine resuscitation during labor

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ABSTRACT

Cardiotocography is a non-invasive technique used for monitoring fetal heartbeat and uterine contractile activity. Fetal heart rate tracings are usually classified into a three-tiered system, in which there is a category II intermediate class with low probability of hypoxia and acidosis. Intrauterine resuscitation techniques are a series of promptly accessible interventions to promote fetal well-being. They are useful in case of a category II fetal heart rate tracing and in other selected cases. In case of fetal heart rate alterations, an individualized approach should always be adopted to tailor the intervention to the mother and the fetus. In this review, we analyze the pathophysiology of some frequently used intrauterine resuscitation techniques - tocolysis, maternal repositioning, and the administration of oxygen and intravenous fluids - to clarify their mechanisms of action and the clinical situations in which each one of them should be prioritized or should not be applied. Furthermore, we explore ongoing controversies over some intrauterine resuscitation techniques.

KEYWORDS

Fetal heart rate, fetal monitoring, fluid therapy, obstetric, labor, oxygen inhalation therapy, tocolysis.

Introduction

Cardiotocography is a non-invasive technique used for monitoring fetal heartbeat and uterine contractile activity. Most classifications of intrapartum fetal heart rate (FHR) tracings are based on a three-tiered system of crescent fetal hypoxic risk. They range from a first category - predictive of normal fetal acid-base status - to an abnormal category with high risk of pathological fetal acidemia. Halfway, there is an intermediate category, also called *suspicious* or *indeterminate* (category II FHR tracings, Table 1) [1-3].

Intrauterine resuscitation techniques are a series of promptly accessible interventions to promote fetal oxygenation and well-being, such as tocolysis, maternal repositioning, and the administration of oxygen and intravenous fluids. They might revert a category II FHR tracing to a category I FHR tracing. In selected cases, they might also be helpful in a category III FHR tracing, after the exclusion of acute events that require immediate delivery (i.e., cord prolapse, uterine rupture, placental abruption) [2].

Their pathophysiological bases differ from each other. Knowing the underlying mechanisms of action of each intervention allows clinicians to apply them in the right situation.

Besides, there is still controversy over some frequently used techniques, such as maternal oxygen administration.

In this review we analyze the pathophysiology of some intrauterine resuscitation techniques - tocolysis, maternal repositioning, and the administration of oxygen and intravenous fluids - to clarify when they should or should not be applied.

Article history

Received 25 Mar 2022 - Accepted 12 Jul 2022

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Tocolysis

Excessive uterine contractile activity during term labor can be seen in the case of tachysystole - defined as more than five contractions in ten minutes, averaged over a 30-minute window - and in case of uterine hypertonus - a contraction lasting for at least two minutes [1]. The excessive rate or intensity of contractions causes compression of maternal spiral arteries and reduces placental perfusion, eventually causing FHR pattern variations and fetal acidosis at birth [4,5]. Moreover, tachysystole can act as a risk factor for uterine rupture [4,6,7].

Tocolytic therapy acts on uterine contractile activity and can be helpful in some cases of tachysystole or hypertonus and category II FHR tracings [1].

First intervention in the case of tachysystole or hypertonus is the identification and removal of the cause of excessive uterine activity. If the patient was treated with a prostaglandin vaginal insert that can be removed, its extraction usually reduces uterine contractility and normalizes FHR pattern. Administration of a prostaglandin vaginal gel cannot be removed, thus a tocolytic agent should be used. If excessive uterine activity occurs in case of oxytocin infusion, the dose should be reduced or discontinued until the tachysystole has resolved [8-11].

Table 1 Adapted from the 2015 International Federation of Gynecology and Obstetrics classification criteria for fetal heart rate during labor [2].

	Normal (category I)	Suspicious (category II)	Pathological (category III)
Baseline rate	110-160 bpm	Lacking at least one characteristic of normality, but with no pathological features	< 100 bpm
Baseline fetal heart rate variability	5-25 bpm		Reduced variability, increased variability, or sinusoidal pattern
Decelerations	No repetitive decelerations		With repetitive late or prolonged decelerations during > 30 min or 20 min of reduced variability, or one prolonged deceleration with >5 min
Interpretation	Fetus with no hypoxia/ acidosis	Fetus with a low probability of having hypoxia/acidosis	Fetus with a high probability of having hypoxia/acidosis

bpm, beats per minute

Oxytocin is a natural hormone secreted by the posterior pituitary gland. Synthetic oxytocin infusion mimics the natural hormone and causes a uterine response after 3-5 minutes of infusion. Steady state of uterine response occurs after 30-minutes of oxytocin infusion or longer, while steady state plasmatic level can be reached in 40 minutes [11-14]. With low-dose or high-dose regimens, oxytocin infusion can be used for induction and augmentation of labor in case of a Bishop score of 6 or higher [11,15-19]. Low-dose regimens should be chosen because oxytocin has dose-dependent side effects on uterine activity. Low-dose regimens slowly raise contractile activity, whilst high-dose regimens are more likely to cause excessive uterine activity or impaired placental blood flow and hence fetal distress [20]. Moreover, dose increment intervals shorter than 30 minutes are inappropriate and do not agree with oxytocin pharmacokinetic.

After oxytocin discontinuation, infusion can be restored in the case of tachysystole resolution and the presence of a category I FHR tracing. It has been suggested that after stopping oxytocin infusion for less than 30 minutes it can be resumed in a half-rate infusion, and then gradually increase the rate as appropriate, based on low-dose regimen and maternal-fetal status. If oxytocin is stopped for more than 30-40 minutes, most of the drug has already been metabolized and plasma concentration returns to basal level. Therefore, oxytocin can be resumed at initial dose [1,11,21]. In the case of spontaneous excessive uterine activity and a category II FHR tracing, tocolytic agents are recommended [1]. In clinical practice, frequently used agents are oxytocin receptor antagonists (i.e., atosiban, at 6.75 mg intravenous bolus), beta adrenergic receptor agonist (i.e., ritodrine, 100 mg intravenous infusion, or terbutaline, 250 µg intravenous or subcutaneous administration), and nitric oxide donors (i.e., nitroglycerin, 50-150 µg intravenous infusion or 400 µg sublingual administration) [8,22]. In the literature, there is lack of data on the first line of tocolytic agent to be used at term. The choice depends on maternal comorbidities, pregnancy complications and center availability.

In 2008, a randomized clinical trial compared atosiban and ritodrine for acute tocolysis in term labor [23]. The study found that ritodrine acts on uterine beta2-adrenoreceptors and on heart vessels beta1-adrenoreceptors, causing maternal and FHR rate increase and rapidly crossing placenta; while atosiban acts specifically on the uterus. However, the study found no differences in maternal blood pressure, intrauterine pressure, newborn Apgar scores and umbilical arterial pH [23].

There has been a US Food and Drug Administration warning against the use of injectable terbutaline in prolonged preterm labor, due to maternal cardiac complications [24]. It has been suggested to limit the use of terbutaline to short-term acute tocolysis at term [25]. Moreover, studies suggested fetal beta2 receptor agonists exposure might confer a risk of childhood asthma [26]. In the case of labor at term, nitric oxide donors are not first-choice tocolytic agents, because their sublingual or intravenous administration can cause profound hypotension, thus increasing maternal and fetal risks [22,27,28].

In conclusion, tocolytic treatment should be used in category II FHR tracings associated with tachysystole or hypertonus. When possible, identification and removal of the etiological agent are priority interventions. When there is no exogenous cause or its removal is insufficient, tocolytic agents are recommended. The choice of a specific tocolytic agent depends on maternal comorbidities, pregnancy complications and center availability.

Maternal repositioning

Maternal repositioning is an easy, well-accepted, and cost-free intervention. It should be considered when FHR alterations are probably associated with low placental perfusion resulting from vessel compression.

Placental perfusion is supplied by uterine arteries – collateral branches of the hypogastric arteries – that ramify into spiral arteries. These, in turn, supply the intervillous spaces and guarantee maternal-fetal exchanges in the *chorionic villi*.

The relationship between the uterus and abdominal vessels influence uterine and placental perfusion. The aorta and the vena cava are limited anteriorly by the uterus, posteriorly by the thoracoabdominal vertebral bodies, and laterally by the ureters. Therefore, pregnancy uterine growth, especially in the third trimester, causes compression on the abdominal vessels.

Pelvis flowmetry changes during pregnancy and its repercussions on labor have been studied since the 1960s. As pregnancy progresses, the uterus creates a compression at the level of the vena cava and the inferior aorta, causing a pressure drop in uterine arteries – especially in the third trimester. This pressure change is partially corrected by an increase in the number and extent of anastomoses between the collateral branches of the ovarian arteries and the uterine arteries [29].

During labor, this balance is easily disrupted. During contractile activity, the uterus exerts a greater compression on the abdominal portion of the aorta, as well as on the ovarian arteries, to some degree [30]. The supine position, and even more the lithotomy position, increases the aortic compression by adding gravity to the other forces involved [30].

Many authors have studied the most recommended positions for pregnant women, especially during labor. In the 1990s, some authors studied the relationship between maternal position and fetal oxygenation, showing a marked decrease in fetal oxygenation in the supine position. This decrease spontaneously recovers after maternal left or right lateral positioning [31,32]. Other studies have shown a link between the FHR pattern and maternal positioning, reporting an association between supine position and lower heart rate variability [33]. The supine position causes aortocaval compression, thus reducing placental perfusion [30].

The 2009 American College of Obstetrics and Gynecologist and the 2015 International Federation of Gynecology and Obstetrics guidelines agree on the importance of avoiding a prolonged supine position [1,2]. However, they don't recommend a specific position to ensure correct fetal oxygenation, focusing on the importance of freedom of movement throughout labor. Position changes, in fact, improve pain management and avoid the aorta and umbilical cord compression [34].

A 2018 meta-analysis assessed the most recommendable positions for the first stage of labor. It confirmed that a standing or mobile position shortens labor duration by approximately one hour and 22 minutes, increases the probability of vaginal delivery, and reduces the rate of cesarean section [35]. A 2017 meta-analysis reported that a standing position and lateral decubitus during the second stage of labor not only reduced heart rate variability abnormalities, but also lowered the number of operative deliveries and episiotomies. However, long periods of standing during the second stage of labor could be associated in nulliparous women with an increase in second-degree lacerations and postpartum hemorrhages [36].

In conclusion, it is important to avoid the supine or lithotomy position during labor. The standing position or lateral decubitus are recommendable, especially in case of a category II FHR tracing with the suspicion of low placental perfusion. An exclusive left lateral decubitus is only mandatory in case of hypovolemic or cardio-pulmonary shock [37].

Oxygen administration

Oxygen administration to the mother aims at increasing fetal oxygen diffusion across the placenta. It is still vastly performed, most frequently at 10 L/min via a non-rebreather mask, although benefit and potential risks are controversial. The effect of maternal oxygen administration on fetal acid-base status has been debated for decades. Early studies (1967-1969) showed a plausible beneficial effect on neonatal oxygenation and pH, but they were limited by the small samples of patients and inclusion of hypoxic maternal conditions [38,39].

More recent studies have shown no effect on umbilical cord blood gas values or, paradoxically, a negative impact on acid-base status. This might probably be explained by placental vessels hyperoxia-induced vasoconstriction [40,41]. Oxygen administration causes a transient rise in arterial partial pressure of oxygen, followed by a drop of pH and a rise in arterial partial pressure of carbon dioxide, probably caused by developing placental vasoconstriction [42]. Placental vasoconstriction is probably not immediate but shows a latency time. In fact, to further complicate the issue, some authors have shown that oxygen therapy effects can vary in a time-dependent fashion. Longer duration of oxygen exposure strongly worsens umbilical vein partial pressure of oxygen [41,43].

When applied during labor to correct a category II FHR tracing, oxygen administration does not improve umbilical artery lactate nor FHR alterations [44,45].

Moreover, maternal oxygen administration poses a risk of generation of oxygen free radicals. Fetal neurons are extremely sensitive, because of a lack of antioxidant enzymes [46,47]. Hyperoxic states in maternal and placental blood cause a rapid production of oxygen free radicals and consequent structural cellular damage that can be permanent [47].

Based on literature data, there is no evidence that oxygen administration can give any benefit in case of a category II FHR tracing in a normoxic pregnant woman, while potential collateral effects are possible.

Oxygen administration should only be used in the case of a maternal disease or state likely to condition maternal hypoxia, to restore a normal oxygen delivery to the placenta. In this case, minimum time and dosage usage is suggested to ensure a normal maternal oxygen saturation, given the potentially harmful effects of hyperoxygenation.

Intravenous fluids

Administration of intravenous fluids during labor can easily and effectively increase maternal blood volume, thus improving uterine and placental perfusion.

It can be used when there is the suspicion of low placental perfusion with a category II FHR tracing, for example in the case of low maternal blood pressure. Moreover, it can be used before epidural or spinal anesthesia. Anesthetic drugs can cause maternal sympathetic block, leading to hypotension and eventually to FHR alterations. Hydration can also be used after analgesia [48,49].

There is controversy over the most recommended solution type. Glucose solution might shorten labor and improve its outcome [50]. However, in a situation of low placental perfusion and suspected fetal hypoxia, it could increase the amount of lactate, thus decreasing the pH and increasing neonatal damage.

In clinical practice, Lactated Ringer is frequently used during labor, but there is no evidence that it is more effective than a normal saline solution - they are both isotonic crystalloid fluids.

Regarding the fluid dose, a randomized trial compared the efficacy of 500 cc versus 1000 cc boluses on fetal oxygen saturation. Authors showed that 1000 cc fluid bolus leads to a higher increase in fetal oxygen saturation and is more effective in its maintenance [32].

Table 2 Indications, contraindications, and recommendations of some intrauterine resuscitation techniques for category II FHR tracings.

	Tocolysis	Maternal positioning	Maternal oxygen administration	Intravenous fluids
Indications	In some cases of tachysystole or hypertonus and category II FHR tracings	Low placental perfusion	Maternal hypoxia	Suspicion of low placental perfusion, labor analgesia
Contraindications	Specific tocolytic agents are contraindicated in some maternal comorbidities or pregnancy complications	None	Category II FHR tracings with normal maternal saturation	Preeclampsia, heart failure or other conditions that increase the risk of maternal hemodynamic overload
Other recommendations	In case of an exogenous etiological agent, first intervention should be its identification and removal	Avoid supine and lithotomy position, and guarantee freedom of movement throughout labor	Even in case of maternal hypoxia, use minimum time and dosage	Rapid 1000 cc Lactated Ringer bolus infusion to promptly restore maternal blood volume

Infusion rate is target dependent. In the case of a category II FHR tracing, rapid fluid bolus infusion is recommended to promptly restore maternal blood volume and placental perfusion. However, authors showed that 250 ml/h fluid administration during labor reduces labor duration and cesarean section rates [51].

In conclusion, fluid administration should be considered in the case of a category II FHR tracing when there is the suspicion of low placental perfusion, using rapid 1000 cc Lactated Ringer bolus infusion. However, it should be avoided in laboring women at risk of pulmonary edema - such as patients with preeclampsia or heart failure - because it can precipitate this complication.

Conclusion

Intrauterine resuscitation techniques are a series of multiple interventions that are easily accessible by obstetricians and can be used in the case of a category II FHR tracing or in selected cases of category III FHR tracings, after the exclusion of acute events. When facing FHR alterations, an individualized approach should always be adopted to tailor the intervention of patients - the mother and the fetus - and the clinical context. It is important to choose and adopt a suitable measure from the series of intrauterine resuscitation techniques. Moreover, it is crucial to understand their mechanisms of action and the specific situations in which they might be effective, to avoid a useless, possibly harmful intervention.

Table 2 lists indications, contraindications, and recommendations of some intrauterine resuscitation techniques for category II FHR tracings.

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Conflicts of interest: *None declared.*