Optimizing the management of acute, prolonged decelerations and fetal bradycardia based on the understanding of fetal pathophysiology

Edwin Chandraharan, MBBS, MS, FSLCOG, FRCOG; Tullio Ghi, MD, PhD; Stefania Fieni, PhD; Yan-Ju Jia, PhD

Any acute and profound reduction in fetal oxygenation increases the risk of anaerobic metabolism in the fetal myocardium and, hence, the risk of lactic acidosis. On the contrary, in a gradually evolving hypoxic stress, there is sufficient time to mount a catecholamine-mediated increase in the fetal heart rate to increase the cardiac output and redistribute oxygenated blood to maintain an aerobic metabolism in the fetal central organs. When the hypoxic stress is sudden, profound, and sustained, it is not possible to continue to maintain central organ perfusion by peripheral vasoconstriction and centralization. In case of acute deprivation of oxygen, the immediate chemoreflex response via the vagus nerve helps reduce fetal myocardial workload by a sudden drop of the baseline fetal heart rate. If this drop in the fetal heart rate continues for >2 minutes (American College of Obstetricians and Gynecologists' guideline) or 3 minutes (National Institute for Health and Care Excellence or physiological guideline), it is termed a prolonged deceleration, which occurs because of myocardial hypoxia, after the initial chemoreflex. The revised International Federation of Gynecology and Obstetrics guideline (2015) considers the prolonged deceleration to be a "pathologic" feature after 5 minutes. Acute intrapartum accidents (placental abruption, umbilical cord prolapse, and uterine rupture) should be excluded immediately, and if they are present, an urgent birth should be accomplished. If a reversible cause is found (maternal hypotension, uterine hypertonus or hyperstimulation, and sustained umbilical cord compression), immediate conservative measures (also called intrauterine fetal resuscitation) should be undertaken to reverse the underlying cause. In reversible causes of acute hypoxia, if the fetal heart rate variability is normal before the onset of deceleration, and normal within the first 3 minutes of the prolonged deceleration, then there is an increased likelihood of recovery of the fetal heart rate to its antecedent baseline within 9 minutes with the reversal of the underlying cause of acute and profound reduction in fetal oxygenation. The continuation of the prolonged deceleration for >10 minutes is termed "terminal bradycardia," and this increases the risk of hypoxic-ischemic injury to the deep gray matter of the brain (the thalami and the basal ganglia), predisposing to dyskinetic cerebral palsy. Therefore, any acute fetal hypoxia, which manifests as a prolonged deceleration on the fetal heart rate tracing, should be considered an intrapartum emergency requiring an immediate intervention to optimize perinatal outcome. In uterine hypertonus or hyperstimulation, if the prolonged deceleration persists despite stopping the uterotonic agent, then acute tocolysis is recommended to rapidly restore fetal oxygenation. Regular clinical audit of the management of acute hypoxia, including the "the onset of bradycardia to delivery interval," may help identify organizational and system issues, which may contribute to poor perinatal outcomes.

Key words: basal ganglia, baseline fetal heart rate variability, biomarkers, cardioprotective reflex, cardiotocography, fetal acidemia, fetal bradycardia, hypoperfusion, hypoxic-ischemic encephalopathy, prolonged deceleration

Introduction

A sudden and profound reduction in the fetal oxygen supply causes a prolonged deceleration,[1,2] which refers to a sudden, abrupt decrease in the fetal heart rate (FHR) of at least 15 beats per minute (bpm) (usually the drop is >30 bpm) and persists for longer than 3 minutes (Figure 1). This abrupt and profound drop in the FHR is often the manifestation of an "acute" fetal hypoxia,[1,2] and it should be considered as an obstetrical emergency. This sustained reduction of the baseline FHR is responsible for a decreased cardiac output, which in turn leads to fetal hypotension and reduced tissue oxygenation. This abrupt reduction in organ perfusion may increase the risk of hypoxic-ischemic encephalopathy (HIE), multiorgan failure, and terminal myocardial failure because of the accumulation of lactic acid within the cardiac muscle. Therefore, an immediate intervention is essential to restore the fetal cardiac output to reestablish oxygenation to vital organs. If the

From the Global Academy of Medical Education and Training, London, United Kingdom (Dr Chandraharan); Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, United Kingdom (Dr Chandraharan); Obstetrics and Gynecology Unit, Department of Medicine and Surgery, University of Parma, Parma, Italy (Drs Ghi and Fieni); and Department of Obstetrics, Tianjin Central Hospital of Obstetrics and Gynaecology/Tianjin Key Laboratory of Human Development and Reproductive Regulation/Affiliated Hospital of Obstetrics and Gynaecology of Nankai University, Tianjin, China (Dr Jia).

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Corresponding author: Edwin Chandraharan, MBBS, MS, FSLCOG, FRCOG. edwin.c@sky.com

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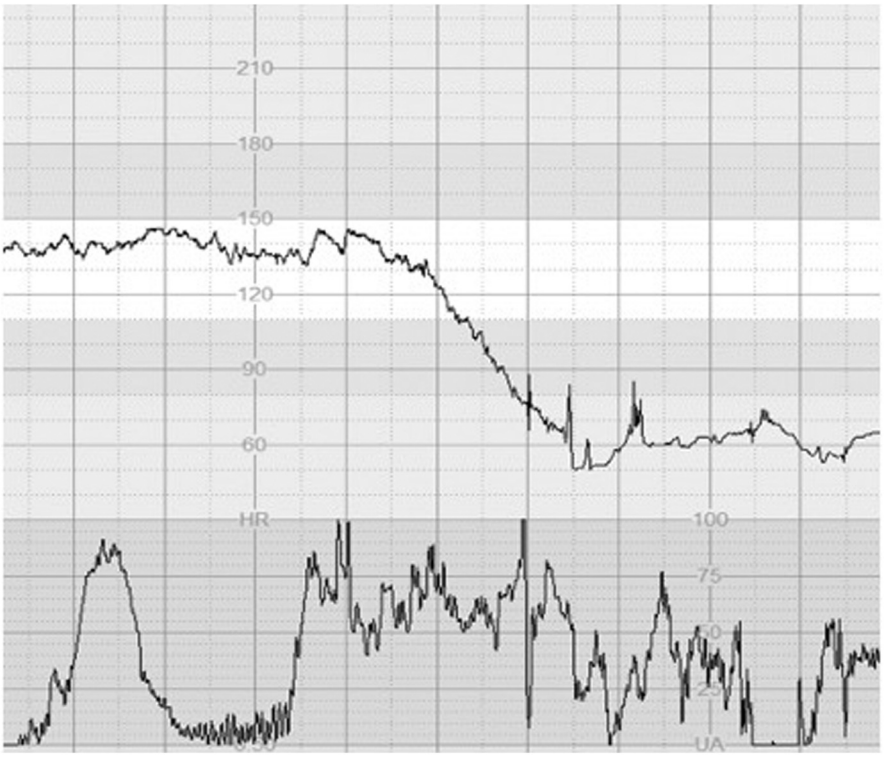
FIGURE 1
Prolonged deceleration



Note the drop in the FHR by >30 bpm lasting for longer than 3 minutes.

FHR, fetal heart rate.

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

underlying cause of acute profound hypoxia is irreversible, then an urgent delivery should be carried out. However, if the sudden reduction of the fetal oxygenation is due to a reversible cause, then immediate action should be taken to restore fetal oxygenation to reverse the underlying condition.[2] This "prolonged deceleration" should be differentiated from "fetal bradycardia," which refers to a reduction in baseline FHR (<110 bpm) lasting longer than 10 minutes.[2] Fetal bradycardia may occur secondary to several nonhypoxic causes, such as congenital heart block.[1,2] The application of knowledge of fetal pathophysiology while interpreting the cardiotocograph (CTG), may help clinicians to avoid unnecessary intrapartum operative interventions to the mother and, at the same time, minimize the risk of HIE to the fetus.

Pathophysiology of acute prolonged deceleration and fetal bradycardia

The fetus attempts to protect the myocardial workload by reducing the heart rate in response to any hypoxic or mechanical stress during labor.[3] These decelerations, which are cardioprotective reflexes, are often intermittent when there is a transient compression of the umbilical cord or reduction in the uteroplacental circulation.[4] The fetal circulation is restored after such intermittent, and repetitive, decelerations. However, if there is an acute and profound reduction in fetoplacental circulation, which is sustained, it may lead to the development of lactic acidosis within the myocardial fibers because of the onset of anaerobic metabolism (Figure 2). Myocardial depression because of the accumulation of lactic acid would lead to a reduced force of contraction and cardiac output, thereby increasing the risk of HIE because of reduced perfusion pressure to the fetal brain. In an experimental study involving the fetal lamb, Westgate et al[4] reported that the initial abrupt drop in the FHR after an acute and total occlusion of the umbilical cord was mediated through the vagus nerve, which has also been shown in other animal experimental studies earlier.[5] In the vagotomized fetal lamb, there was no initial drop in the baseline FHR; however, a progressive reduction in the baseline FHR was recorded approximately 3 minutes after the total umbilical cord occlusion, culminating in terminal bradycardia.[4] Therefore, evidence from experimental animal models suggested that direct myocardial depression may occur if the primary hypoxic insult persists for >3 minutes.

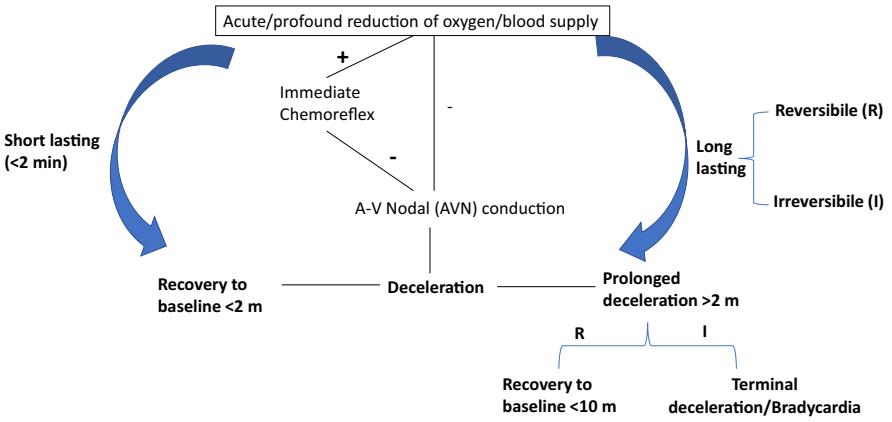
In human labor, such acute and total cessation of fetoplacental circulation is very rare. The presence of the Wharton jelly around the umbilical blood vessels may allow fetal circulation to continue, although at a lower rate. Therefore, in the absence of acute intrapartum accidents (placental abruption, umbilical cord prolapses, and uterine rupture), the likelihood of myocardial depression before 3 minutes of an acute prolonged deceleration is very unlikely. For this reason, the International Consensus Guidelines on CTG interpretation published by the International Federation of Gynecology and Obstetrics has recommended 5 minutes as the cutoff value for the diagnosis of a prolonged deceleration during labor.[6] It is important to appreciate that human fetuses have a much higher hemoglobin concentration (180−220 g/L or 18−22 g/dL), which has a greater affinity for oxygen even at low partial pressures and with a better buffering system (Table 1). Moreover, continuing placental circulation, although at a lower baseline heart rate, enables the gas exchange to continue, with the elimination of carbon dioxide and metabolic acids accumulated through the placenta into the mother's circulation. Therefore, in the absence of an irreversible insult, such as placental

abruption, the likelihood of fetal metabolic acidosis after transient acute reduction of fetal oxygen supply leading to acute prolonged deceleration is very unlikely. Cahill et al[7] reviewed a large cohort of 5388 cases and reported that >98% of fetuses with terminal decelerations (a prolonged deceleration lasting for more than 5 minutes) were born with a normal umbilical cord pH at birth.

Therefore, current scientific evidence suggests that prolonged decelerations that last for more than 3 minutes are not associated with poor perinatal outcomes if the underlying cause is not irreversible. Leung et al[8] reported that the umbilical cord arterial pH did not correlate with the bradycardia-to-delivery interval in reversible cases, whereas the pH dropped at the rate of 0.01 every minute in irreversible cases.[9] During the second stage of labor, a sudden, prolonged deceleration may occur because of dural stimulation or secondary to increased intracranial pressure and resultant reduced cerebral perfusion.[9] However, recent evidence from experimental animal studies suggests that these decelerations occur because of cerebral hypoperfusion during fetal head compression, which stimulate central chemoreceptors, situated within the brain.[10] Loghis et al[11] analyzed 45 cases of fetal bradycardia that occurred during the second stage of labor and concluded that, except in cases of umbilical cord prolapse, these acute prolonged decelerations were not associated with poor neonatal outcomes.

Any sudden and profound change in oxygenation to the fetal myocardium would activate the vagus nerve to reduce the heart rate immediately. Such "hibernation" and resultant reduction in the cardiac workload when there is an insufficient supply of oxygen may deter the onset of anaerobic metabolism. Experimental animal models have suggested that the continuation of the deceleration after the initial vagal response may be due to direct myocardial hypoxia.[4] The reflex reduction in the FHR reduces myocardial oxygen requirement, thereby maintaining the "demand-supply" equilibrium to offset the occurrence of myocardial lactic acidosis. Therefore, the onset of a prolonged deceleration may be considered to be a fetal cardioprotective reflex to avoid myocardial decompensation. However, the persistence of acute hypoxia as in cases of irreversible causes would invariably lead to the onset of

FIGURE 2
Pathophysiology of acute prolonged deceleration and fetal bradycardia



AVN, atrioventricular nodal.

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TABLE 1
Fetal intrauterine adaptive mechanisms

Fetal features	Role of adaption to hypoxia
Ductus venosus Foramen ovale	Shunt oxygenated blood from the umbilical vein preferentially to left atrium, bypassing the right ventricle, and then to left ventricle; supply oxygenated blood to the heart and brain
Ductus arteriosus	Diverts the relatively deoxygenated blood from the pulmonary artery to the descending aorta and placenta, bypassing the lungs
Heart rate of 110–160 bpm	To distribute blood to the vital organs faster
Hemoglobin level of 180–220 g/L	Increased O_2-carrying capacity Increased affinity for O_2 Release of O_2 even in low O_2 tension Effective buffering system during acidosis to avoid fetal damage
Fetal hemoglobin	Ability to withstand reduced arterial O_2 saturation from 70% during late pregnancy to 30% during labor
Decelerations	Cardioprotective reflexes to reduce the myocardial workload when there is decrease or interruption of fetal oxygenation
Catecholamine surge	To increase the fetal heart rate and the cardiac output and redistribute oxygenated blood to continue to maintain aerobic metabolism in fetal central organs. It also causes glycogenolysis to provide additional energy substrate to the myocardium

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TABLE 2
Reversible or irreversible causes of an acute prolonged deceleration

Irreversible causes	Placental abruption
	Umbilical cord prolapse
	Uterine rupture
	Acute fetomaternal hemorrhage
	End stage of chorioamnionitis and fetal systemic inflammatory response
	Rupture of uterine artery pseudoaneurysm
	Rupture of the uterine varices
	Rupture of the vasa previa
Reversible causes	Hyperstimulation because of oxytocin or prostaglandins
	Maternal hypotension secondary to supine hypotension syndrome or epidural analgesia
	Sustained umbilical cord compression secondary to maternal position
	Maternal hypothermia
	Maternal hypoglycemia
	External cephalic version

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

anaerobic metabolism and the subsequent depletion of cardiac glycogen stores. Under such circumstances, myocardial perfusion cannot be restored, thus increasing the risk of fetal metabolic acidosis.

Regardless of the underlying cause of acute hypoxia, the timing of injury would depend on the individual reserve of the fetus, the depletion of buffers before the onset of the prolonged deceleration, the ability of the placenta and the maternal circulation to clear the acidosis rapidly, and the wider clinical picture. This complex interplay of several variables suggests that an arbitrary time limit of 3 minutes or 5 minutes should not be applied blindly in the management of all cases of prolonged decelerations. The features on the FHR trace should be carefully scrutinized to determine the likelihood of recovery while using the proposed "population-based" time limits as a guide. Such an individualized approach would help ensure timely delivery to avoid poor perinatal outcomes while at the same time avoiding unnecessary operative interventions.

Etiology of acute prolonged deceleration and fetal bradycardia

An acute prolonged deceleration culminating in terminal bradycardia may occur because of reversible or irreversible causes (Table 2). Immediate action should be taken to exclude irreversible causes of acute hypoxia, and if these are present, then an urgent delivery either by an emergency cesarean delivery or by an operative vaginal birth (second stage) should be undertaken to optimize perinatal outcomes. Such action is necessary because over time fetal oxygenation becomes progressively worse in acute intrapartum accidents (placental abruption, uterine rupture, and umbilical cord prolapse). In placental abruption, uterine rupture, and acute fetomaternal hemorrhage (FMH), in addition to a reduction of FHR and resultant reduced organ perfusion, there is a concomitant reduction in fetal blood pressure, which may potentiate neurologic injury. Evidence from experimental animal models indicates that fetal hypotension is an important contributory factor to neurologic injury.[12–14] Except in cases of ruptured vasa previa, it is not possible to reliably exclude FMH on clinical examination.

Irreversible causes of fetal bradycardia include sudden maternal hypovolemia and hypotension[15–17] and toxic fetal myocarditis in end-stage chorioamnionitis.[18–20]

Jung et al[21] have suggested that fetal cytokine storm can result in multiorgan dysfunction, and myocarditis is one of the complications of fetal inflammatory response syndrome (FIRS). Experimental infection of pregnant mice with *Listeria monocytogenes* has been shown to cause fetal bradycardia.[18] This finding suggested that inflammatory cytokines, such as interleukins (ILs), especially IL-6 and tumor necrosis factor-alpha (TNF-α), have a depressive effect on the myocardium. Moreover, fetal bradycardia has been reported in human fetuses exposed to group B streptococcus infection[19] and maternal urosepsis,[20] which suggests that fetal bradycardia can occur as a terminal, irreversible event at the end stage of FIRS.

Common reversible causes of acute prolonged decelerations include maternal hypotension secondary to epidural analgesia or supine hypotension syndrome,[22,23] a sudden reduction in placental oxygenation seen in oxytocin or prostaglandin-induced uterine hypertonus, and sustained umbilical cord compression secondary to a maternal position. A systematic review concluded that intrathecal opioids administered during epidural analgesia may almost double the incidence of fetal bradycardia.[24] A higher sensory block with greater sympatholysis was reported to be associated with the increased likelihood of fetal bradycardia.[25] It is likely that sympatholysis and resultant acute reduction in maternal blood pressure causes an acute reduction in placental perfusion, leading to a sudden and prolonged deceleration. The lack of engagement of the fetal head and the presence of variable decelerations before the administration of epidural analgesia have been reported to be associated with 5-fold and 3-fold increases in fetal bradycardia.[26] It is likely that a supine maternal position during epidural analgesia may have resulted in the nonengaged fetus (ie, a hard and bony fetal head is not fixed inside the maternal

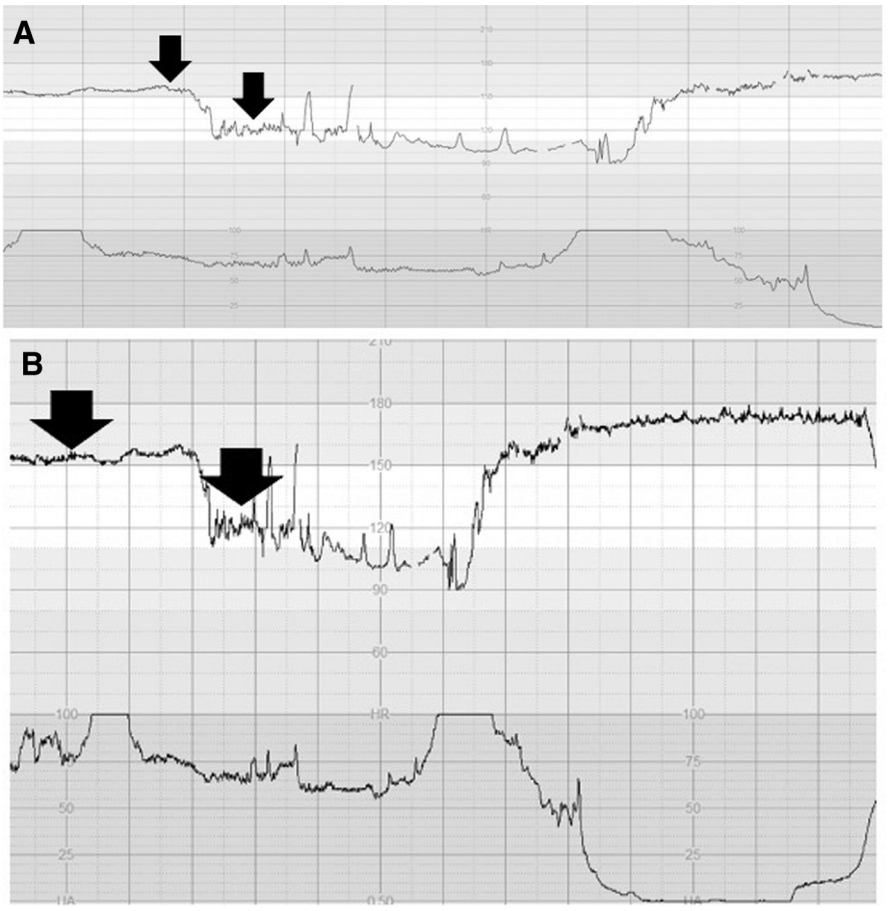
pelvis, and therefore, it is able to shift its position) to compress the inferior vena cava or the umbilical cord, respectively, leading to an acute reduction in fetal oxygenation.

Rare reversible causes of an acute prolonged deceleration include an external cephalic version (ECV),[27–29] and it is postulated that low maternal body mass index, prolonged procedure, and maternal hypotension may contribute to fetal bradycardia during ECV.[23,26] Doubling of the emergency cesarean delivery rate in this group with fetal bradycardia during ECV has been reported.[29] Moreover, maternal hypothermia has been associated with fetal bradycardia,[30,31] and this complication can be precipitated by magnesium sulfate-induced maternal hypothermia.[32] Although the exact mechanism is unknown, maternal hypothermia likely reduces the basal metabolic rate, resulting in the lowering of the heart rate.

Immediate management

Acute prolonged deceleration, which may lead to a baseline fetal bradycardia, should be considered an obstetrical emergency regardless of whether or not the underlying cause is reversible. Relevant maternal history, a thorough assessment of maternal vital signs, and abdominal and vaginal examinations are necessary to exclude an acute intrapartum accident. An urgent birth should be undertaken via the safest, quickest mode if an acute intrapartum accident is identified. Similarly, immediate action should be taken to correct the reversible causes, which may include changing the maternal position (umbilical cord compression or supine hypotension), a rapid infusion of intravenous fluids to restore maternal blood volume and blood pressure (epidural-induced maternal hypotension), and the removal of the uterotonic agent and the administration of a tocolytic, if indicated (prostaglandin or oxytocin-induced uterine hypertonus). Once all irreversible acute intrapartum accidents (ie, placental abruption, umbilical cord prolapse, or uterine rupture) have been excluded and corrective measures have been instituted to correct the reversible causes, the FHR traces should be scrutinized to determine features that indicate the likelihood of recovery of the prolonged deceleration to the normal baseline.

FIGURE 3
Recovery of the prolonged deceleration



A, Note the recovery of the prolonged deceleration with a reassuring baseline FHRV before the onset of prolonged deceleration and normal FHRV within the first 3 minutes of the deceleration (paper speed 3 cm/min [**A**] or 1 cm/min [**B**]).

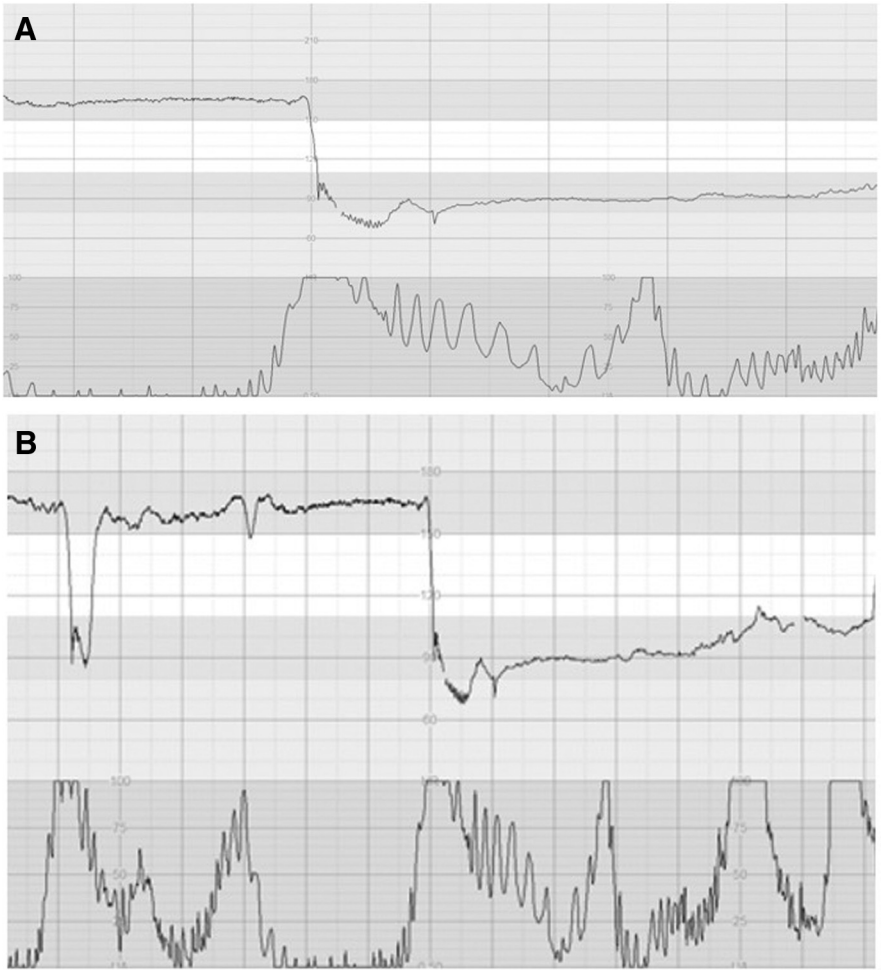
FHRV, fetal heart rate variability.

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

Fetal heart rate patterns and prediction of poor perinatal outcomes

In the absence of any preexisting hypoxic insult and irreversible cause, the FHR should be expected to recover to its original baseline if the underlying reversible condition is corrected. One would not expect to see any hypoxic-ischemic insult if fetal oxygenation is rapidly reestablished by immediate interventions to correct the underlying cause of the hypoxic insult. On the contrary, if the fetus has already experienced decompensation of the central nervous system before the onset of the prolonged deceleration or has lost part of its blood volume (concealed abruption or a concealed uterine rupture) during the prolonged deceleration, then this would result in the rapid onset of hypoxia and ischemia in the brain. Thus, when the fetal baseline heart rate abruptly drops, and if there is reduced fetal blood volume filling the ventricular chambers, the cardiac output and

FIGURE 4
Reduced baseline FHRV before the onset of prolonged deceleration



A, Reduced baseline FHRV before the onset of prolonged deceleration and reduced baseline FHRV within the first 3 minutes of the decelerations are poor prognostic markers for recovery (paper speed 3 cm/min [**A**] or 1 cm/min [**B**]).

FHRV, fetal heart rate variability.

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

resultant perfusion of the brain through the carotid arteries will be considerably impaired. This complication may lead to a rapid onset of hypoxia, ischemia, and acidosis in the fetal brain.

The extent of neuronal damage is likely greater when intrapartum hypoxia leads to fetal hypotension and subsequent cerebral hypoperfusion.[33] Although we are unable to measure the fetal blood pressure during labor, the consistently proven association between the deceleration area and the risk of brain injury seems to confirm the primary role of hypotension in causing cerebral damage.[34,35]

The following FHR features may help clinicians to predict the recovery of a prolonged deceleration, in the absence of irreversible causes: FHR variability (FHRV) before the onset of prolonged deceleration, FHRV within the first 3 minutes of the prolonged deceleration, the depth of prolonged deceleration, and the duration of ongoing prolonged deceleration.

Fetal heart rate variability before the onset of prolonged deceleration

The presence of a stable baseline FHR and a reassuring baseline FHRV before the onset of a prolonged deceleration are important markers of antecedent fetal well-being (Figure 3, A and B). Similarly, the presence of a normal FHRV within the first 3 minutes of the prolonged deceleration (Figure 3, A and B) also suggests that, despite the acute drop in the FHR, there is sufficient, continued perfusion of the fetal brain. Williams and Galerneau[36] analyzed 186 CTG traces with prolonged decelerations and concluded that the most significant feature that predicted the development of neonatal acidosis and urgent operative intervention was a reduced baseline FHRV before the onset of prolonged deceleration[36] (Figure 3). In addition, earlier studies conducted by Gilstrap et al[37] concluded that a reduction of the baseline FHRV before the onset of fetal bradycardia was associated with a 1.5-fold to 3-fold increase in neonatal acidosis.[37] These results were consistent with the findings of Low et al,[38] who reported that the positive predictive value for neonatal acidosis increased from 18% to 26% if the baseline FHRV was reduced before the onset of a prolonged deceleration. Therefore, if the baseline FHRV is normal before the onset of prolonged deceleration, then the risks of nonrecovery and neonatal acidosis are low.

Normal FHRV before the onset of the prolonged deceleration may indicate normal, premorbid fetal well-being (good fetal reserve), whereas a previous abnormal FHRV indicates the presence of abnormal fetal well-being (chronic or preexisting insult) before the acute insult.

Fetal heart rate variability within the first 3 minutes

A normal FHRV reflects a nondepressed fetal autonomic nervous system. Therefore, it is likely that if the acute, profound reduction in the heart rate results in depression of the fetal autonomic nervous system or causes fetal metabolic

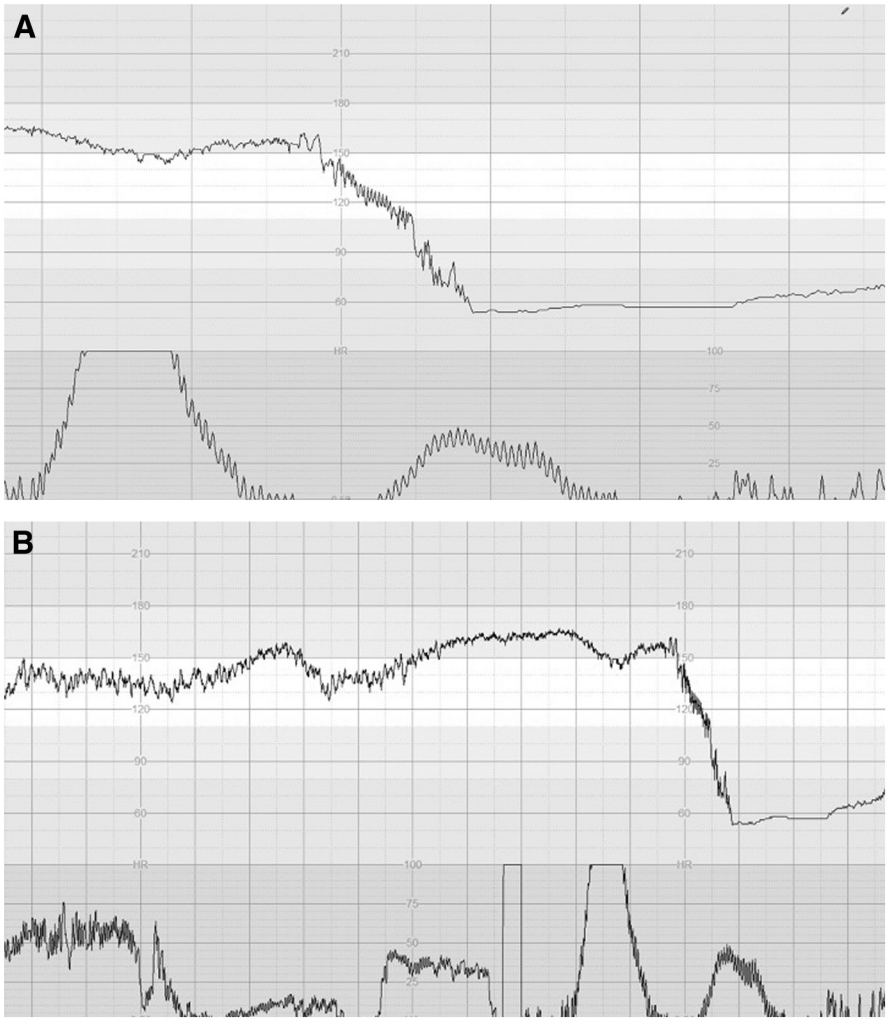
acidosis, then the baseline FHRV will be reduced or absent within the first 3 minutes of the prolonged deceleration (Figure 4, A and B). In such cases, concealed loss of fetal blood volume (eg, concealed placental abruption or uterine rupture) should be suspected, and an urgent birth may be undertaken to avoid HIE, as fetuses have poor tolerance to withstand hypotension that can rapidly cause neuronal damage.[12–14] In a concealed placental abruption, the presence of the retroplacental hematoma can result in the separation of the placenta, reducing the surface area for gas exchange, resulting in an acute reduction in uteroplacental oxygenation. Cardiac output is a product of the FHR multiplied by the stroke volume. Therefore, when the FHR decreases, the fetus has to increase the stroke volume to maintain the cardiac output. However, animal studies suggested that the fetal ventricle operates at the near-maximal ventricular function curve.[39] Therefore, if the findings of the study can be extrapolated to human fetuses, then it may not possible to increase the force of contraction any further to compensate for the loss of cardiac output. Furthermore, in cases of placental abruption and uterine rupture, ongoing fetal hypovolemia and resultant poor filling of the ventricular chambers may adversely affect the Frank-Starling mechanism.

Gull et al[40] concluded that, in end-stage bradycardia, reduced or absent variability within the first 3 minutes of the prolonged deceleration was associated with poor perinatal outcomes.[40] Therefore, a reduced FHRV before the onset of the prolonged deceleration and within the first 3 minutes of the prolonged deceleration should be considered adverse prognostic factors. If there is no reversible cause that can be corrected, then an urgent delivery should be accomplished.

The depth of prolonged decelerations

The greater the decrease in the FHR below the normal baseline, the greater the loss of fetal cardiac output and resultant organ malperfusion. Some consider an abrupt drop of <80 bpm in the baseline FHR as an adverse feature (Figure 5). Sheiner et al[41] reported an association between a decrease below 70 bpm in the FHR, a reduction of <7.20 in the umbilical cord arterial pH, and a base excess of <−12 mmol/L.[41] A recent study concluded that if the baseline FHR drops to a nadir below 60 bpm, then the risk of neonatal acidosis (pH<7.0) is 3-fold.[42] This finding from a fetal pathophysiological point of view was not surprising. Such a precipitous drop in the FHR, if sustained, may cause an acute reduction in the fetal cardiac output and reduced tissue perfusion, resulting in the rapid development of anaerobic metabolism metabolic acidosis. Therefore, even in reversible causes, if there is a drop below 80 bpm in the FHR, immediate measures should be undertaken to facilitate the recovery of the FHR to its original baseline.

FIGURE 5
An abrupt drop in the baseline FHR of <80 bpm



A, An abrupt drop in the baseline FHR of <80 bpm, which is a poor prognostic marker for recovery (paper speed 3 cm/min **[A]** or 1 cm/min **[B]**).

FHR, fetal heart rate.

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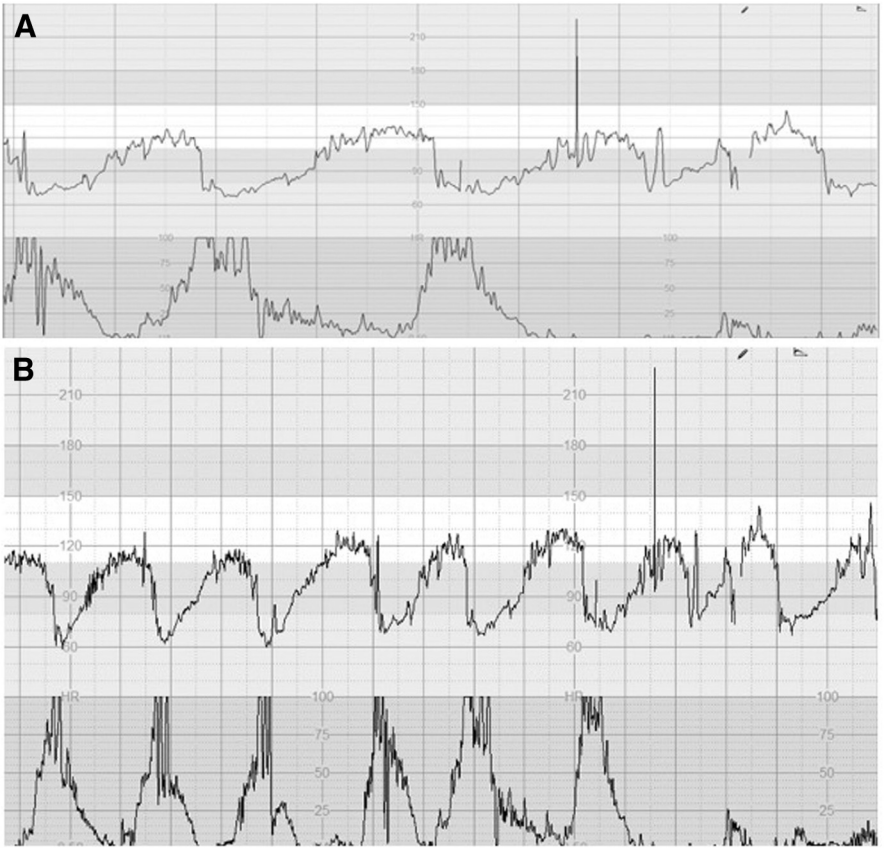
Predictors of uterine rupture

Uterine rupture is often an unpredictable, sudden event characterized by the

FIGURE 6
Repetitive "severe" variable decelerations



Repetitive "severe" variable decelerations that may precede frank uterine rupture (paper speed 3 cm/min [**A**] or 1 cm/min [**B**]).

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

onset of terminal bradycardia on the FHR trace. However, some studies reported repetitive, "severe" variable decelerations or late decelerations as predictors of frank uterine rupture as they preceded the onset of terminal fetal bradycardia.[43,44] It is likely that, during scar dehiscence, a loop of umbilical cord may protrude through the defect, leading to repetitive "severe" variable decelerations (Figure 6, A and B), until there is a complete rupture of the uterus with the separation of the placenta that causes the terminal bradycardia. Similarly, recurrent late decelerations observed before the onset of a terminal bradycardia[43,45] were most likely due to progressive placental separation in scar dehiscence before total rupture. However, these FHR features may not always precede uterine rupture, and conversely, they may occur even in the absence of uterine scar dehiscence. Therefore, these findings cannot be interpreted with confidence to predict rupture. A systematic review concluded that uterine hyperstimulation and cessation of uterine activity may predict uterine rupture.[46] Moreover, excessive uterine contractions may occur if oxytocin augmentation is used in women with a previous uterine scar; therefore, this may not be a reliable sign of impending uterine rupture. However, it is prudent to avoid excessive uterine activity (tachysystole, hypertonus, or hyperstimulation) while using oxytocin regardless of the presence or absence of a uterine scar.

Does the duration of a bradycardia matter?

In cases of uterine rupture, it has been reported that if delivery is accomplished within 18 minutes, adverse perinatal outcomes could be avoided.[47] However, Leung et al[48] reported that if the FHR trace had shown abnormalities before the onset of the terminal bradycardia, then adverse perinatal outcomes may occur in 10 minutes.[48] Similarly, in umbilical cord prolapse, a delay of >20 minutes to accomplish delivery has been associated with poor perinatal outcomes.[49] Therefore, in acute intrapartum accidents, there is no doubt that the earlier the delivery can be accomplished, the better the outcome. As the cause is irreversible, fetal hypoxia, hypotension, and resultant anaerobic metabolism and generation of lactic acid would progressively worsen perinatal outcomes. It is important to differentiate the "decision-to-delivery" interval from the "onset of bradycardia—to—delivery" interval while interpreting the conclusion of scientific studies. From the perspective of the fetus, it is the "onset of bradycardia—to—delivery" interval that is most important because this indicates the duration of oxygen deprivation to fetal central organs. The "decision-to-delivery interval" is dependent on the time the attending clinician makes a decision to accomplish delivery, and therefore, it is influenced by variation in clinical practice and the ability to make a timely decision based on the observed FHR tracing and the clinical context.

However, in the absence of acute intrapartum accidents, there is no significant drop in the umbilical arterial pH even at 30 minutes.[8] Kamoshita et al[50] analyzed the long-term neonatal outcomes after sustained fetal bradycardia and concluded that delivery within 25 minutes of the onset of bradycardia improves outcomes. Therefore, in the absence of an irreversible cause, it seems that the human fetus has a remarkable capacity to withstand acute profound hypoxic stress for a considerable period.

TABLE 3
The "3,6,9,12,15" rule for the management of prolonged deceleration, after excluding irreversible causes

Time (min)	Recommended management
3	Call for help, immediate clinical examination to exclude irreversible causes (placental abruption, umbilical cord prolapse, and uterine rupture), and correct potentially reversible causes (maternal hypotension, sustained umbilical cord compression, uterine hypertonus, or hyperstimulation).
6	Continue intrauterine resuscitation to improve oxygenation, because approximately 90% of prolonged decelerations are expected to return to normal baseline in the absence of irreversible causes.
9	Move to the operating theater, because it is expected that approximately 95% of prolonged decelerations will return to the normal baseline by 9 minutes.
12	Reassess the overall clinical context in the operating theater, including assessment of fetal heart rate to confirm recovery. If an urgent birth was required on the basis of the assessment, then administer anesthesia.
15	Commence emergency operative delivery (by the safest and quickest mode).

Chandraharan. The management of acute, prolonged decelerations and fetal bradycardia using fetal pathophysiology. Am J Obstet Gynecol 2023.

It is important to appreciate that the depth and duration of prolonged decelerations are independent variables that determine poor perinatal outcomes. A combination of a profound drop in the FHR of <80 bpm, persisting for a longer duration, may worsen perinatal outcomes. Moreover, it is important to consider the underlying etiology of the prolonged deceleration (eg, uterine rupture), which may independently worsen perinatal outcomes.

Optimizing the management of intrapartum prolonged decelerations and fetal bradycardia

The "3,6,9,12,15 rule"

Some authors[2,51,52] and national[53] and international consensus guidelines on the physiological interpretation of CTG (FHR tracings)[1] recommended the use of the "3,6,9,12,15" rule for the management of prolonged deceleration (Table 3). This recommendation is based on observational data indicating that in the absence of intrapartum accidents, and in the presence of normal variability before, and within, the first 3 minutes of a prolonged deceleration, approximately 90% and 95% recovered to the normal baseline within 6 minutes and 9 minutes, respectively (Figure 3), with the correction of the underlying cause.[7,8,37] However, this "3,6,9,12,15" rule should be applied only after excluding intrapartum accidents and correcting the reversible

TABLE 4
Recommended drugs for acute tocolysis to abolish excessive uterine contractions

Drug	Dosage	Mode of action	Adverse effects
Terbutaline	250 μg subcutaneously	Beta-sympathomimetic drug, which acts by binding to the beta-2 receptors and by stimulating adenylate cyclase to break down the adenosine triphosphate to cyclic adenosine monophosphate The usual onset of action is 3–5 min, and the myometrial relaxation may last for 15–30 min	Maternal tachycardia (can precipitate arrhythmia if administered in the presence of maternal tachycardia) Hyperglycemia Contraindicated in the presence of maternal hypotension or cardiac conditions
Hexoprenaline	5 μg in 10 mL of normal saline, administered IV within 5 min		
Ritodrine	6 mg in 10 mL of normal saline administered IV within 3 min		
Atosiban	6.75 mg diluted in 5 mL of normal saline, given as slow intravenous bolus within 1 min	Competitive antagonist of the oxytocin receptor The onset of action is approximately 10–12 min	Minimum side effects because of its specific receptor blockage Caution should be exercised in the presence of maternal hypotension
Nitroglycerin	50–100 μg IV as a slow bolus. This can be repeated every 2 min to a maximum dosage of 400 μg	Nitric oxide donor, and activates the enzyme guanylate cyclase, leading to synthesis of cyclic guanosine 3',5'-monophosphate, leading to muscle relaxation It has a rapid onset of action (30 sec), which may last for 1–2 min	Maternal hypotension, tachycardia, palpitations, tremor, and restlessness Contraindicated in placental abruption and uterine rupture (maternal hypovolemia)

IV, intravenously.

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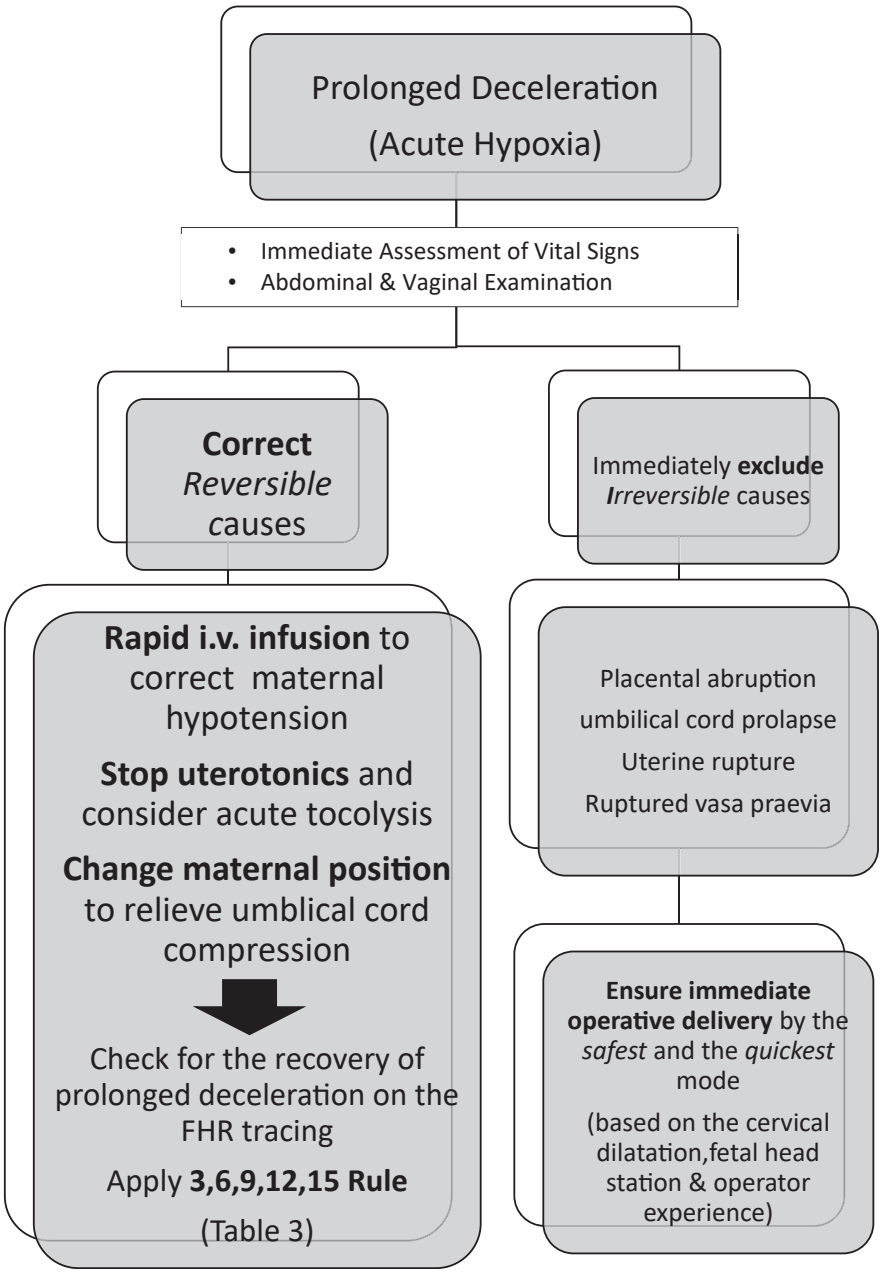
FIGURE 7
Suggested management algorithm for prolonged decelerations



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causes, provided the FHRVs before and within the first 3 minutes of the deceleration are normal. Acute tocolysis, which involves the use of pharmacologic agents to immediately abolish uterine contractions (Table 4), should be considered not only to correct reversible causes, such as uterine hypertonus, but also to improve fetal oxygenation in cases of umbilical cord prolapse.[54,55] Figure 7 illustrates a suggested algorithm for the management of prolonged deceleration. It is important to consider the overall clinical context while making management decisions when irreversible causes of prolonged decelerations are identified. The main objective is to accomplish delivery by the quickest and safest mode of birth to avoid prolongation of hypoxic-ischemic insult. Therefore, during the second stage of labor, an operative vaginal birth is the recommended option. However, this depends on the operator's skill, experience, and familiarity with the chosen instrument (ie, vacuum or forceps). Therefore, continuous training and regular emergency skills and "fire drills" in the management of irreversible causes of acute fetal hypoxia are essential to optimize maternal and perinatal outcomes.

Neurologic injury in acute bradycardia

In healthy fetuses of term gestation, the brain seems to be protected against hypoxic insults by hemodynamic, endocrine, and metabolic compensatory mechanisms.[56,57]

Experimental animal studies have shown that even repetitive late decelerations are not associated with neurologic damage at 3 to 9 months after birth.[58] This is because when a hypoxic insult is moderate and occurs over time, the fetus is able to remodulate the cerebral blood flow, thus preserving some areas of the brain (brainstem and basal ganglia) at the expense of those areas that regulate nonessential activities (cerebral cortex and "watershed areas" of the cerebral hemispheres); on the contrary, in the case of acute hypoxia leading to severe bradycardia and sudden cerebral hypoperfusion, the compensatory mechanisms are not able to protect the deep gray matter, and the brain damage may affect not only the cortex but also the thalami and basal ganglia.[59–61]

This latter pattern has been found to be highly predictive of adverse outcomes and usually corresponds to the brain damage seen in the experimental animal models characterized by total asphyxia.[62,63]

A small pilot study by Yatham et al[64] assessed the correlation between the type of intrapartum hypoxia observed on the FHR traces and the neonatal magnetic resonance imaging (MRI) scan findings. Among 11 neonates with available postnatal MRI scans, 9 showed evidence of intrapartum hypoxia on the FHR, but only 6 demonstrated evidence

of brain damage on the MRI. Those with acute hypoxia showed abnormalities in the basal ganglia and thalami, whereas a gradually evolving hypoxia or subacute hypoxia was associated with lesions in the brain myelination and the cerebral cortex. More recently, Pereira et al[65] demonstrated an association between the type of hypoxia observed on the FHR tracing and the MRI patterns of hypoxic brain injury. Such findings supported the relationship between the type and duration of intrapartum hypoxia and the pattern of brain damage.

Conclusion

Acute and profound hypoxic stresses may occur because of reversible or irreversible causes during human labor. A sudden, prolonged deceleration will be observed on the FHR trace in such cases as the fetus attempts to reduce the myocardial workload to avoid the development of lactic acidosis. The condition of the fetus before the onset of acute prolonged deceleration (ie, the presence of a stable baseline and reassuring FHRV) and the presence of a normal FHRV within the first 3 minutes are good prognostic features for recovery in the absence of any irreversible cause. Immediate action should be taken to correct the reversible causes because sustained, acute, and prolonged hypoxia and hypotension may cause damage to the highly metabolically active deep gray matter (thalami and the basal ganglia). ■

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