

No. 347-Obstetric Management at Borderline Viability

This Clinical Practice Guideline was prepared by the Obstetrical Management at Borderline Viability Working Group; reviewed by the Maternal-Fetal Medicine, Clinical Practice-Obstetrics, Diagnostic Imaging and Guideline Management and Oversight committees,* and approved by the Board of The Society of Obstetricians and Gynaecologists of Canada.

Noor Niyar N. Ladhani, MD, Toronto, ON

Radha S. Chari, MD, Edmonton, AB

Michael S. Dunn, MD, Toronto, ON

Griffith Jones, MBBS, Ottawa, ON

Prakesh Shah, MD, Toronto, ON

Jon F.R. Barrett, MD, Toronto, ON

Disclosure statements have been received from all authors.

*Working Group members: Keith Barrington, MB, Montréal, QC; Jennifer Blake, MD, Ottawa, ON; Donna Brown, MN, Toronto, ON; Joan Crane, MD, St. John's, NL; Ann Jefferies, MD, Toronto, ON; Shoo K. Lee, PhD, Toronto, ON; Kellie E. Murphy, MD, Toronto, ON; Renato Natale, MD, London, ON; Eugene Ng, MD, Toronto, ON; Kirsten M. Niles, MD, PhD, Toronto, ON; Nan Okun, MD, Toronto, ON; Kate Robson, MEd, Toronto, ON; Anne Simmonds, RN, PhD, Toronto, ON; Amanda Skoll, MD, Vancouver, BC.

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Corresponding Author: Dr. Noor Niyar N. Ladhani, Sunnybrook Health Sciences Centre, Toronto, ON. noor.ladhani@sunnybrook.ca

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Abstract

Objective: The primary objective of this guideline was to develop consensus statements to guide clinical practice and recommendations for obstetric management of a pregnancy at borderline viability, currently defined as prior to 25+6 weeks.

Intended Users: Clinicians involved in the obstetric management of women whose fetus is at the borderline of viability.

Target Population: Women presenting for possible birth at borderline viability.

Evidence: This document presents a summary of the literature and a general consensus on the management of pregnancies at borderline viability, including maternal transfer and consultation, administration of antenatal corticosteroids and magnesium sulfate, fetal heart rate monitoring, and considerations in mode of delivery. Medline, EMBASE, and Cochrane databases were searched using the following keywords: extreme prematurity, borderline viability, preterm, pregnancy, antenatal corticosteroids, mode of delivery. The results were then studied, and relevant articles were reviewed. The references of the reviewed studies were also searched, as were documents citing pertinent studies. The evidence was then presented at a consensus meeting, and statements were developed.

Validation Methods: The content and recommendations were developed by the consensus group from the fields of Maternal-Fetal Medicine, Neonatology, Perinatal Nursing, Patient Advocacy, and Ethics. The quality of evidence was rated using criteria described in the Grading of Recommendations Assessment, Development and Evaluation methodology framework (reference 1). The Board of the

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Women have the right and responsibility to make informed decisions about their care in partnership with their health care providers. To facilitate informed choice, women should be provided with information and support that are evidence based, culturally appropriate, and tailored to their needs. The values, beliefs, and individual needs of each woman and her family should be sought and the final decision about the care and treatment options chosen by the woman should be respected.

Society of Obstetricians and Gynaecologists of Canada approved the final draft for publication.

Methods: The quality of evidence was rated using the criteria described in the Grading of Recommendations, Assessment, Development, and Evaluation methodology framework. The interpretation of strong and weak recommendations is described later. The Summary of Findings is available upon request.

Benefits, Harms, and Costs: A multidisciplinary approach should be used in counselling women and families at borderline viability. The impact of obstetric interventions in the improvement of neonatal outcomes is suggested in the literature, and if active resuscitation is intended, then active obstetric interventions should be considered.

Guideline Update: Evidence will be reviewed 5 years after publication to decide whether all or part of the guideline should be updated. However, if important new evidence is published prior to the 5-year cycle, the review process may be accelerated for a more rapid update of some recommendations.

Sponsors: This guideline was developed with resources funded by the Society of Obstetricians and Gynaecologists of Canada and the Women and Babies Program at Sunnybrook Health Sciences Centre.

Recommendations

1. Women facing decisions regarding obstetric and neonatal management at extremely preterm gestations should be counselled by an expert multidisciplinary team. Neonatal survival data vary globally, and national and local data are important elements of counselling. The data should be interpreted with the understanding that perinatal management has a role to play in these results (Weak, Moderate).
2. Whenever possible, women at periviable gestations should be offered transfer to a level 3 centre. If a clear, informed decision has been reached not to provide the infant with intensive care if delivered, and if specialized comfort care can be provided at the referring centre, the transfer may not be necessary. Decision to transfer should factor in gestational age, estimated fetal weight, and parental preferences. Practitioners should be educated about the management options for extreme prematurity and should have the option to call specialist practitioners for advice in managing these cases. Care providers should acknowledge the difficulty and disruption associated with transfer and should prepare women and their families for the process and potential outcomes (Strong, Moderate).
3. First trimester ultrasound should be offered in all pregnancies, especially when risk factors for preterm birth are present. The value of ultrasound-measured estimated fetal weight in decision-making around obstetric interventions requires study (Strong, Low).
4. In the periviable periods, antenatal corticosteroids should be administered after careful consideration of the likelihood of delivery and the resuscitation wishes of the family. If delivery is expected within 7 days, and if full resuscitation is planned, a single course of antenatal corticosteroids should be administered to women (Strong, Moderate).
5. A rescue dose of corticosteroid, when the initial course of corticosteroid was given before 25 weeks, should not currently be recommended because benefit or harm of such additional dose is not proven. Further study is required (Strong, Moderate).
6. Magnesium sulfate for neuroprotection should be given after careful consideration of the likelihood of delivery and the benefits of treatment. If delivery is expected imminently, and if full resuscitation is planned, magnesium sulfate should be administered in the extreme preterm population in accordance with local protocols and the existing SOGC guideline (Strong, Moderate).
7. Other than for maternal indications, routine Caesarean delivery in the extreme preterm population should be avoided (Strong, High). In cases of fetal malpresentation or other obstetric indications, the limitations of evidence should be discussed and a multidisciplinary approach should be used to come to a decision that considers both maternal and fetal outcome when active neonatal management is planned (Strong, Moderate).
8. Intrapartum continuous fetal monitoring should be used when active neonatal management is planned. Interpretation parameters should be used cautiously by those experienced in the care of preterm and extremely preterm gestations (Weak, Low).
9. Delayed cord clamping in the extreme preterm population is recommended. When this is not feasible, cord milking should be considered (Strong, Moderate).

ABBREVIATIONS

ACS	antenatal corticosteroids
EFM	electronic fetal monitoring
EFW	estimated fetal weight
IVH	intraventricular hemorrhage
MgSO ₄	magnesium sulfate
RDS	respiratory distress syndrome

INTRODUCTION

As technology and medical interventions have evolved, the lower limits of GA at which newborns are considered viable have shifted. With increased provision of active resuscitative measures to infants born at lower GAs, obstetric interventions remain a key component in ensuring that these very fragile infants have the best chance of intact survival. The borderline of viability is classically defined as the period between 22+0 and 25+6 weeks. Most centres will advocate for active intervention beyond 25+0 weeks, and few will offer active intervention at 22+0 weeks. The period of ambiguity of intervention is greatest prior to and including 24+6 weeks. The lower limit of viability is constantly changing. The role of active obstetric intervention in the outcome of the neonates at borderline viability requires increased discussion and research. This document aims at providing guidance for these difficult cases.

According to Canadian data from level 3 centres, neonates at 23+0 to 24+6 weeks constitute about 2% of admissions to

NICUs. In the 2015 annual report of the Canadian Neonatal Network,¹ 75% and 94% of 23-week and 24-week neonates, respectively, received active management. This was an increase from 2013,² when 46% and 67% of the 23-week and 24-week neonates, respectively, received active management. In 2015, the Canadian Neonatal Network reported that 53% of 23-week neonates and 75% of 24-week neonates survived to discharge from the level 3 NICU. It is unclear from these data what obstetric circumstances and interventions preceded the delivery and what impact these circumstances may have had on neonatal survival.

Because of this lack of differentiation in outcomes based on care provision prior to delivery, and because we know that these interventions may confer a survival benefit, the outcome of database findings should be interpreted with caution. Indeed, as more obstetric interventions are offered, an increase in survival has been seen in database studies examining outcomes in this population.³ At present, there is a paucity of research on outcomes of infants born after mothers received active obstetric management. The impact of administration of ACS for enhanced lung maturity, MgSO₄ for neuroprotection, and mode of delivery on survival on the long-term outcomes of the neonate at borderline viability remains unanswered in the current literature, and although the gaps are being filled by ongoing research, guidelines are necessary to help direct clinical care during this time of rapid change.

The intention of this guideline is to help practitioners in counselling families to make an informed decision about obstetric management relating to the planned resuscitation of their child and to allow clinicians to optimize this management to allow for the best maternal and neonatal outcome when active management is offered and full resuscitation is intended. The present survival of an infant born prior to 23+0 weeks is uncommon but is increasing as more interventions are offered.^{1,2} It should be noted that the lower limit of 23+0 weeks discussed in this guideline may change as technology and interventions evolve. Ultimately, decisions around management in the periviable stage should be made through discussions between families and their care providers.

The guidance provided in this document should be used in conjunction with that of pediatric and neonatal expert groups. A full multidisciplinary team, including maternal-fetal medicine specialists, obstetricians, neonatologists, perinatal nursing, midwifery, and family practice, should be involved in the counselling of women and families making decisions about their potential extremely preterm birth. The development of local guidelines may facilitate this informed consent process.⁴

Table 1. Key to Grading of Recommendations, Assessment, Development, and Evaluation⁷

Strength of the recommendation	Definition
Strong	Highly confident of the balance between desirable and undesirable consequences (ie, desirable consequences outweigh the undesirable consequences or undesirable consequences outweigh the desirable consequences).
Weak ^a	Less confident of the balance between desirable and undesirable consequences.
Quality level of a body of evidence	Definition
High ++++	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate +++0	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low ++00	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very Low +000	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Examples

Strong, Moderate|+++0: Strong recommendation, moderate quality of evidence.

Weak, Low|++00: Weak recommendation, low quality of evidence.

^aWeak recommendations should not be misinterpreted as weak evidence or uncertainty of the recommendation.

Table 2. Judgement and interpretation of strong and conditional recommendations⁷

Judgement/interpretation	Strong recommendation “We recommend...”	Conditional recommendation “We suggest...”
Judgement by guideline panel	It is clear to the panel that the net desirable consequences of a strategy outweighed the consequences of the alternative strategy.	It is less clear to the panel whether the net desirable consequences of a strategy outweighed the alternative strategy.
Implications for patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
Implications for clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Clinicians should recognize that different choices will be appropriate for each individual and that clinicians must help each individual to arrive at a management decision consistent with his or her values and preferences.
Implications for policy makers	The recommendation can be adopted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

METHODS

A group of Canadian perinatal experts from the fields of Maternal-Fetal Medicine, Neonatology, Perinatal Nursing, Patient Advocacy, and Ethics met to discuss the obstetric management of pregnancies at borderline viability. The meeting was funded by Sunnybrook Health Sciences Women and Babies Program and supported by SOGC.

The intention was to develop a consensus statement to help guide clinical management and further investigative research in this important area. Similar documents have been produced by the Society for Maternal-Fetal Medicine⁵ and Royal College of Obstetricians and Gynaecologists.⁶

Medline, EMBASE, and Cochrane databases were searched for the following keywords: “extreme prematurity,” “borderline viability,” “preterm,” “pregnancy,” “antenatal corticosteroids,” “mode of delivery.” Relevant articles were reviewed. The references of reviewed studies were also searched, as were documents citing pertinent studies.

The findings of the literature review were presented at a consensus meeting in June 2014. Fourteen members of the perinatal community were present and all participated in the discussion. The meeting was divided into specific topics as outlined in the following. The relevant data were presented, an open discussion was facilitated, and a consensus statement on the topic was developed with near unanimity. The literature search was repeated until November 2016 as the text of the Committee Opinion was developed and revised.

The quality of evidence was rated using the criteria described in the Grading of Recommendations,

Assessment, Development, and Evaluation methodology framework (Table 1). The interpretation of strong and weak recommendations is described in Table 2. The summary of findings is available upon request.

Disclosures of conflict of interest were collected during the revision process.

TRANSFER TO OBSTETRIC CENTRE WITH A LEVEL 3 NICU

All obstetric providers may encounter women who are unexpectedly faced with a possible delivery before 25 weeks’ GA. A consistent local management protocol and counselling regarding management options should be available to all providers to help support women and families until transfer to a level 3 centre can be facilitated, if appropriate.

The question of maternal transfer has important resource and policy implications.

Beyond the proven benefits of place of birth of the newborn, such as reduction of mortality and severe IVH⁸ and other causes of neonatal morbidity,⁹ it is generally accepted that maternal transfer improves maternal decision-making and may aid in prolonging the pregnancy.^{6,10} A combination of GA, accuracy of dates, EFW, and parental preferences should be considered when contemplating transfer to a level 3 institution. When there is uncertainty and/or a local inability to clarify or interpret this information, maternal tertiary care transfer for the purpose of additional work-up to assist with patient counselling and management may be required and should be offered. The Ontario Provincial Council for Maternal Child Health recommends transfer at borderline viability in

cases in which the family has opted for active management, the family would like to explore options, or if the referring centre is not comfortable with counselling around issues at this stage of gestation.

In cases in which transfer is not possible, telephone or telehealth consultation should be considered. Geographic limitations should not prevent women and families from receiving counselling and the option to proceed with active management of periviable newborns. Sensitivity around displacement from home and family should be employed, and maternal and family wishes are of primary importance when decisions around transfer are made. After counselling has been provided, if there is a clear, informed decision not to provide the infant with intensive care, and if specialized comfort care,¹⁰ including warmth for the newborn and bereavement services for the family, can be provided at the referring centre, the transfer may not be necessary. If the decision to avoid active management and to instead provide comfort care has been made after transfer to a level 3 unit, retro-transfer should be initiated so that women can be in their communities and close to their families.

Care of the woman delivering at borderline viability requires a multidisciplinary team made up of specialist obstetricians, neonatologists, and perinatal nurses, all of whom should understand the impact that the management decisions may have on the future health of the mother and newborn. Specifically, obstetric interventions at this stage are controversial and require consultation with specialists in the area and thorough discussions with the parturient and her family.

Recommendations

1. Women facing decisions regarding obstetric and neonatal management at extremely preterm gestations should be counselled by an expert multidisciplinary team. Neonatal survival data vary globally, and national and local data are important elements of counselling. The data should be interpreted with the understanding that perinatal management has a role to play in these results (Weak, Moderate).
2. Whenever possible, women at periviable gestations should be offered transfer to a level 3 centre. If a clear, informed decision has been reached not to provide the infant with intensive care if delivered, and if specialized comfort care can be provided at the referring centre, the transfer may not be necessary. Decision to transfer should factor in gestational age, estimated fetal weight, and parental preferences. Practitioners should be educated about the management options for extreme prematurity and should have the option to call specialist practitioners for advice in managing these cases. Care providers should acknowledge the

difficulty and disruption associated with transfer and should prepare women and their families for the process and potential outcomes (Strong, Moderate).

GA AND EFW

The discussion about intervention at periviability is limited by accurate GA prediction. Other than in pregnancies conceived using IVF, accurate first trimester dating of pregnancies remains a challenge. Decisions to intervene for fetal benefit are largely made on the basis of prediction of survival, which in turn are based largely on GA.

The SOGC recommends accurate dating of all pregnancies.¹¹ It is believed that the crown-rump length measured at the earliest stage of the pregnancy, after 7 weeks' gestation, is the most accurate and should be used when available.

Birth weight plays an important prognostic role in the prediction of outcomes, but this information is not available antenatally and therefore cannot be used when the decision to pursue interventions for fetal and neonatal benefit is made.¹² EFW has traditionally been described as unreliable at the extremes of viability. A recent study supports the use of EFW in prediction of birth weight in the periviable population, describing a clinically insignificant error of 9.4%, between ultrasound EFW and birth weight.¹³ This study further suggests that if delivery occurs within 1 week of measurement, the value of EFW may be helpful in predicting neonatal outcome. Another study, however, cautioned that this difference is greater in SGA fetuses.¹⁴ Error ranges also vary based on formulae used.¹⁵ Additional studies are needed to validate the accuracy of ultrasound in this population and to study the possible benefits of increasing the frequency of ultrasound in women likely to deliver at borderline viability.

Although survival and morbidity data are often presented as if changes occur in a stepwise fashion, in reality, there is continuous improvement in outcomes over time. With all other variables being equal, a birth at 23+6 will generally have a better outcome compared with one at 23+0 weeks.

Recommendation

3. First trimester ultrasound should be offered in all pregnancies, especially when risk factors for preterm birth are present. The value of ultrasound-measured estimated fetal weight in decision-making around obstetric interventions requires study (Strong, Low).

ADMINISTRATION OF ACS

ACS are a mainstay in the management of threatened spontaneous or iatrogenic preterm delivery. Initial evidence supports their use in the prevention of respiratory and extrapulmonary neonatal complications when administered to women after 25+0 weeks' gestation.^{16,17} This recommendation has since been extrapolated to the 24-week population, and administration at this stage is generally the standard of care across Canada. Neonatologists caring for very preterm infants recognize that the advantages conveyed by maternal treatment with corticosteroids may provide the edge needed for these very vulnerable infants to experience fewer complications and improved survival.

RCTs have not been conducted in the periviable population, but observational evidence suggests benefit. A retrospective cohort showed that ACS administration was associated with lower rates of mortality or neurodevelopmental impairment in those born prior to 24+6 weeks.¹⁸ This study included all those born weighing >400 g but excluded any newborns who died before 12 hours of age. There were higher rates of Caesarean deliveries among the exposed group, which could potentially overestimate the benefit. Dose and timing of ACS administration, length of hospitalization, and fetal monitoring were not discussed. Other studies have shown trends to benefit in the reduction of RDS and severe IVH and increased survival to discharge in neonates whose mothers received ACS. Increased survival to 1 year of life has been shown with the use of corticosteroids in this population.^{19–21}

A recent meta-analysis of observational studies examining the benefit of steroid administration before 24+0 weeks showed benefit when active resuscitation was planned (OR 0.48, 95% CI 0.36 to 0.61), particularly when given between 23+0 and 23+6 weeks (OR 0.45, 95% CI 0.33 to 0.60).²² Although these data are promising, they are limited by their observational nature and the lack of information about dosing, mode of delivery, conditions of delivery, and other potentially confounding variables.

Decisions around the lower limit of ACS administration should be made in conjunction with local NICU practices. When resuscitation is planned for 23+0 weeks and earlier, benefit may be obtained by prior ACS administration. Counselling around the perceived benefit and the lack of RCT data is necessary.

Evidence suggests that the greatest benefit of the administration of ACS is achieved when delivery occurs within 7 days after the initiation of the course.²³ RCT data show

that multiple courses, when initiated after 25 weeks, do not confer benefit and may have adverse effects.²⁴

Because we do not recommend repeated courses of ACS in this population, the following question remains: if ACS are administered prior to 25 weeks and the delivery does not occur as expected, has the opportunity to administer ACS later been wasted? More information is needed regarding the optimal interval between steroid administration and delivery in general. A retrospective study examining extremely low birth weight infants (401–1000 g) showed no difference in outcomes between those who were delivered before versus after 7 days of ACS administration.²⁵ Another retrospective cohort study examined the need for intubation depending on time from ACS administration when the interval was less than 28 days. Differences in intubation were dependent on GA more so than on timing from ACS administration.²⁶ However, in those born during the 28- to 29+6-week GA period, the OR for RDS and need for continuous positive airway pressure were higher in those with longer intervals since ACS administration, although these results were not statistically significant. Similarly, another retrospective cohort study failed to show a difference in composite outcomes in those born 14 days or more after administration of ACS, although a trend towards severity of respiratory morbidity was seen.²⁷

Because concerns exist around the loss of efficacy of ACS after a prolonged interval between administration and delivery, the question of a rescue dose emerges. Rescue doses have not been studied to the same extent as multiple courses. In one study, the administration of a single rescue dose of betamethasone given 24 hours prior to delivery, when the initial course was given prior to 28 weeks, decreased the risk of RDS (OR 0.44, 95% CI 0.2 to 0.9).²⁸ Increased respiratory compliance, and therefore less pulmonary morbidity, has been demonstrated in newborns whose mothers received a rescue dose of betamethasone when the initial course was given more than 14 days prior to delivery.²⁹ An RCT found improved neonatal outcomes in women who received a single rescue dose of betamethasone after being given their initial course of steroid prior to 30 weeks gestation. The results were found to be significant in those who delivered before 34 weeks. No increased rates of immediate adverse outcomes were found.³⁰

Caution in extrapolating these data to the 23- to 24+6-week population is necessary because the fundamental efficacy of ACS at this early stage has not been proven through RCTs.

The consensus from the meeting reinforces the judicious use of ACS at 23+0 weeks based on a discussion around planned resuscitation and a more widespread administration of ACS after 24+0 weeks. Although risks associated with repeated courses have been shown, the risks and benefits of a rescue dose in this population have not been established.

Recommendations

4. In the periviable periods, antenatal corticosteroids should be administered after careful consideration of the likelihood of delivery and the resuscitation wishes of the family. If delivery is expected within 7 days, and if full resuscitation is planned, a single course of antenatal corticosteroids should be administered to women (Strong, Moderate).
5. A rescue dose of corticosteroid, when the initial course of corticosteroid was given before 25 weeks, should not currently be recommended because benefit or harm of such additional dose is not proven. Further study is required (Strong, Moderate).

MgSO₄ FOR NEUROPROTECTION

The benefits of MgSO₄ for the prevention of cerebral palsy in infants with birth weight under 1500 g were initially shown in a case-control study published 2 decades ago.³¹ Since then, RCTs and meta-analyses have supported the use of MgSO₄ for neuroprotection in preterm deliveries.^{32,33} The SOGC recommends administration in the case of imminent birth at less than 31+6 weeks' GA.³⁴

The extremely preterm gestations comprised only a small portion of the infants enrolled in the sentinel studies supporting MgSO₄ administration for neuroprotection. The Australasian Collaborative Trial of MgSO₄ study recruited as early as 24 weeks and administered MgSO₄ to women who were believed to deliver imminently.³⁵ Although the study did not show a significant reduction in rates of cerebral palsy, there was a significant decrease in severe gross motor dysfunction by 2 years of age. In a follow-up study examining the now school-aged children from the initial cohort, a difference in cognitive or behavioural outcomes between the groups was not demonstrated.³⁶ There was also no difference seen in any adverse long-term outcomes.

Theoretical concerns of respiratory depression in neonates born to women who received MgSO₄ have not been seen clinically. Higher rates of intestinal perforation in neonates from women who were given MgSO₄ as early as 22 weeks were shown in one study but not reproduced.³⁷ A

suggestion from that study was that the effects were dose-dependent. Indeed, the regimens of the primary MgSO₄ trials were all different, and little is known about the dose-dependent effects of MgSO₄ administration. Although long-term studies have not shown any concerning effects of MgSO₄, there is a dearth of studies specifically assessing benefit and harm in the population at borderline viability.

With the current evidence available, both the Society for Maternal-Fetal Medicine and the Royal College of Obstetricians and Gynaecologists recommend maternal administration of intravenous MgSO₄ as early as 23 weeks when full intervention is planned.^{6,7} Based on the working group discussion, a decision was made to recommend administration as early as 23 weeks, when full intervention is intended and delivery is believed to be imminent. This should be administered in accordance with local hospital protocols and current SOGC guideline recommendations.³⁴

There is insufficient evidence to support retreatment, and given the usual short time frame in these clinical cases, it will likely not be an issue for those who deliver in the borderline viability group. We recommend administering intravenous maternal MgSO₄ only in the case of imminent delivery and hope this will limit unnecessary administration to those who do not deliver. In the case pregnancy is prolonged, however, it is difficult to assess whether retreatment is necessary or warranted.

Additional research should focus on the long-term efficacy and potential adverse outcomes of MgSO₄ when administered in the 23- to 24+6-week population. Other interventions for neuroprotection currently being considered, such as melatonin, N-acetylcysteine, and erythropoietin, with their antioxidant and/or angiogenic mechanisms, have started to show promise and warrant further investigation but are not yet recommended.³⁸

Recommendation

6. Magnesium sulfate for neuroprotection should be given after careful consideration of the likelihood of delivery and the benefits of treatment. If delivery is expected imminently, and if full resuscitation is planned, magnesium sulfate should be administered in the extreme preterm population in accordance with local protocols and the existing SOGC guideline (Strong, Moderate).

MODE OF DELIVERY

Although debate exists about a neonatal benefit of Caesarean delivery, there is little question about the

increased maternal risks, especially at early gestations. In the 23- to 24+6-week period, there is little differentiation of a developed lower segment, and classical or high transverse uterine incisions are usually required.

A retrospective cohort of women who underwent periviable Caesarean deliveries showed that their subsequent pregnancies had a higher rate of uterine rupture compared with women who delivered vaginally.³⁹ The newborns in the subsequent pregnancy were born earlier and had lower birth weights. However, this large cohort did not show a difference in maternal outcomes in the index pregnancy. The findings of this study may not be completely applicable to the general population because women have different reproductive futures planned. Future pregnancy planning should be a point of discussion when making informed decisions around mode of delivery in this periviable population.

The value of routine Caesarean delivery for all preterm births has been refuted widely. A meta-analysis of four studies⁴⁰ failed to show an improvement in neonatal outcome, whereas cohort studies showed no decrease in neonatal mortality and no clear benefit of routine Caesarean delivery for preterm deliveries in vertex presentation.^{20,41}

The question of optimal delivery with breech presentation remains. It is generally accepted that, in most cases, Caesarean delivery for the breech presentation at term leads to improved neonatal outcomes, and evidence from cohort studies and systematic reviews exists to support extending this practice to the preterm population.^{41–43} A small, retrospective study did not show significantly higher rates of neonatal head entrapment in breech presentation at 24 to 27 weeks' GA, with four cases occurring in 43 vaginal deliveries.⁴⁴ Higher rates were found to occur with increasing weight and increasing GA. Interestingly, five cases of head entrapment occurred in 83 Caesarean deliveries,⁴⁴ suggesting that Caesarean delivery is not inherently atraumatic and that surgical considerations should be made to promote the easiest delivery possible. There have not been robust studies assessing fetal outcomes with classical compared with transverse uterine incisions. Similarly, en caul delivery, although recommended generally, has not been rigorously studied in relation to newborn outcomes.^{7,45}

The evidence about Caesarean delivery is limited, in that it does not include the extreme preterm population and recommendations are based on extrapolation and expert opinion. The consensus at the meeting was that given the information currently available, Caesarean delivery in

the extreme preterm population should be reserved for maternal or obstetric indications when active neonatal management is planned. This is consistent with recommendations from the Society for Maternal-Fetal Medicine and the Royal College of Obstetricians and Gynaecologists.^{7,46}

Because of the uncertainty surrounding Caesarean delivery and fetal outcomes in this population, an early discussion with the family is warranted. The risks of Caesarean, impact on future pregnancies, and uncertainty with respect to the outcome should all be discussed with a multidisciplinary team as soon as possible and ideally well before the time a Caesarean delivery is acutely needed.

Recommendation
7. Other than for maternal indications, routine Caesarean delivery in the extreme preterm population should be avoided (Strong, High). In cases of fetal malpresentation or other obstetric indications, the limitations of evidence should be discussed and a multidisciplinary approach should be used to come to a decision that considers both maternal and fetal outcome when active neonatal management is planned (Strong, Moderate).

INTRAPARTUM FETAL MONITORING

EFM is an important component of intrapartum care in complex pregnancies. The purpose of EFM in periviable gestations is two-fold:

1. To alert obstetricians to possible signs of fetal compromise in labour in cases in which surgical intervention would be considered to expedite delivery. It should be recognized that survival figures for extremely preterm infants are likely to be reduced in the presence of acidemia but unlikely to be completely recoverable by Caesarean delivery. Furthermore, our ability to accurately diagnose intrapartum fetal compromise is questionable. Most of our knowledge around the parameters of intrapartum monitoring has been based on physiologic fetal responses at term and near term. Extrapolation to preterm gestation has been suggested, but parameters specific to the borderline viability population have not been developed.
2. To inform neonatologists about the likely condition of the fetus during labour, particularly in the 30 minutes prior to delivery, because this can influence the extent or duration of intensive support offered. Some parents will choose not to undertake Caesarean delivery for fetal indications but request initial neonatal intensive support.

In such cases, there should be clarity around the issue of abnormal fetal heart rate patterns or a decision not to apply EFM at all. The possibility of fetal intrapartum demise needs to be frankly discussed.

Guidelines recommend using EFM when active neonatal management is planned. The discussion at the consensus meeting suggested the same action. Intrapartum fetal compromise should be assessed under the supervision of practitioners experienced in the care of extremely preterm gestations. Recognition that this interpretation is based on experience and that it is difficult to accurately measure fetal status under these conditions should be acknowledged and discussed with the parturient. Obvious signs of abnormal fetal surveillance such as prolonged bradycardia; repetitive, severe abnormal fetal heart rate decelerations; or fetal tachycardia should be used to guide ongoing management and plans for delivery, in accordance with SOGC guidelines.⁴⁷ Acknowledgement of differences in physiology at preterm gestations should be made, and recognition that some parameters may provide more indication of distress in the preterm versus term fetus is important.^{48,49}

When active neonatal intervention is not desired, there is no role for continuous EFM. Some patients may like to know of the current fetal status during the labour process, and in these cases intermittent auscultation is appropriate.

Additional research is needed into tools to predict ongoing intrapartum fetal status in this population. Parameters based on EFM can be developed, and the role of other technologies should be explored.

Recommendation

8. Intrapartum continuous fetal monitoring should be used when active neonatal management is planned. Interpretation parameters should be used cautiously by those experienced in the care of preterm and extremely preterm gestations (Weak, Low).

DELAYED CORD CLAMPING, CORD MILKING, AND DELIVERY ROOM TEMPERATURE

Delayed cord clamping has been adopted as an intervention to help minimize blood transfusion and improve outcomes in preterm births. Several studies and meta-analyses have shown improvement in short-term outcomes, significantly lower rates of blood transfusion, and trends towards decreased rates of IVH and sepsis in infants who underwent delayed cord clamping or cord milking.^{50,51} Studies reporting benefit with delayed cord clamping report protocols ranging from 20 to 180 seconds

of delay.^{52,53} A recent RCT failed to show a change in neonatal systemic blood flow but did show an increased hemoglobin level (0.9 g/dL) at 6 hours of life after 60 seconds of delayed cord clamping.⁵⁴ Additional RCT data are necessary to justify the delay in provision of resuscitative measures.

Cord milking is of increasing interest given the time saving that can be achieved and the expedition of neonatal resuscitation measures. To date, no adverse effects have been found with cord milking.⁵¹ Improvement in long-term outcomes have not yet been demonstrated with this strategy, but its ease and safety make it an attractive intervention for improving short-term outcomes in the NICU.

Neonatal hypothermia is known to be associated with worse outcomes in the extremely preterm population, and optimal NICU admission temperatures correlate with lower rates of adverse outcomes.⁵⁵ Neonates born at this stage have fewer mechanisms to compensate for any cold ambient temperatures. A quality improvement initiative showed a reduction in neonatal hypothermia with a slight increase in operating room temperature to an ambient 21°C.⁵⁶ Warmer operating rooms have also been shown to decrease surgical site infections and may play a role in improving maternal outcomes as well.⁵⁷

The consensus from the meeting supported the use of delayed cord clamping and the further exploration of cord milking. Recommendations to keep ambient temperatures higher in the delivery room to ensure maternal normothermia were also made.

Recommendation

9. Delayed cord clamping in the extreme preterm population is recommended. When this is not feasible, cord milking should be considered (Strong, Moderate).

DISCUSSION

A multidisciplinary team plan should be in place when women present at risk for delivery prior to 25 weeks. Accurate pregnancy dating is important to appropriately counsel regarding maternal, fetal, and newborn management options and to develop the optimal obstetric management plan, with the family's wishes taken into account.

Practitioners should acknowledge uncertainty around our knowledge of best practices and the limitations in the evidence available. We should also be aware of our inherent biases and recognize that these biases may affect our ability

to counsel objectively. Medical providers are prone to paint a grim picture of outcomes at this stage in gestation,⁵⁸ and we should acknowledge that much of our information stems from an era in which active obstetric interventions were often not performed in the face of planned neonatal resuscitation. Counselling should be consistent, both within and across caregiver groups. This requires agreed-upon guidelines, careful documentation, and standardized protocols.

There is much research needed in this area. Protocols and guidelines on the management of extremely preterm births, based upon variable levels of evidence, are emerging from many countries and extrapolation into Canadian practice may be challenging due to differences in health care resources and geographic considerations.³⁹ Therefore, practitioners should be aware of their local referral pathway systems for perinatal complications and should remain alert to new research in this area. Areas of additional research should include the following: impact of antenatal steroids, benefit or harms of a rescue dose, optimal mode of delivery in fetal malpresentation, correlation of EFW with birth weight and neonatal outcomes, and the benefits and harms of MgSO₄ administration. Qualitative work examining women's and their families' experiences would allow for us to assess the efficacy and benefit of antenatal counselling. Regional differences will allow us to compare different methods and technologies involved in counselling. Given the rarity of these cases, we would benefit from nationwide prospective studies to answer the many unanswered questions that exist for the optimal care of a woman delivering at borderline viability.

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REFERENCES

- Shah PS, Yoon EW, Chan P. The Canadian Neonatal Network Annual Report 2015. Toronto, ON: Canadian Neonatal Network; 2016. Available at: <http://www.canadianneonatalnetwork.org/Portal/LinkClick.aspx?fileticket=Bb8nbmxDkRs%3d&tabid=39>. Accessed on 28 November 2016.
- Shah PS, Yoon EW, Chan P. The Canadian Neonatal Network, Annual Report 2013. Toronto, ON: Canadian Neonatal Network; 2014. Available at: <http://www.canadianneonatalnetwork.org/Portal/LinkClick.aspx?fileticket=IreR0871sjA%3D&tabid=39>. Accessed on 13 March 2015.
- Crane JM, Magee LA, Lee T, et al. Maternal and perinatal outcomes of pregnancies delivered at 23 weeks' gestation. *J Obstet Gynaecol Can* 2015;37:214–24.
- Lemyre B, Daboval T, Dunn S, et al. Shared decision making for infants born at the threshold of viability: a prognosis-based guideline. *J Perinatol* 2016;36:503–9.
- Raju TN, Mercer BM, Burchfield DJ, et al. Periviable birth: executive summary of a joint workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2014;123:1083–96.
- Royal College of Obstetricians and Gynaecologists. Perinatal Management of Pregnant Women at the Threshold of Infant Viability—The Obstetric Perspective (Scientific Impact Paper 41). London, UK: Royal College of Obstetricians and Gynaecologists; 2014. Available at: <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/sip41/>. Accessed on 13 February 2014.
- Schünemann H, Brożek J, Guyatt G, et al. The GRADE Handbook. GradePro:GDT. Available at: <http://gdt.guidelinedevelopment.org/app/handbook/handbook.html>; 2013. Accessed on 16 December 2016.
- Lee SK, McMillan DD, Ohlsson A, et al. The benefit of preterm birth at tertiary care centers is related to gestational age. *Am J Obstet Gynecol* 2003;188:617–22.
- Hossain S, Shah PS, Ye XY, et al. Outborns or inborns: where are the differences? A comparison study of very preterm neonatal intensive care unit infants cared for in Australia and New Zealand and in Canada. *Neonatology* 2016;109:76–84.
- Jefferies AL, Kirpalani H, Albersheim SG, et al. Counselling and management for anticipated extremely preterm birth. *Paediatr Child Health* 2014;19:25–6.
- Butt K, Lim K. Society of Obstetricians and Gynaecologists of Canada. Determination of gestational age by ultrasound. *J Obstet Gynaecol Can* 2014;36:171–83.
- Tyson JE, Parikh NA, Langer J, et al. Intensive care for extreme prematurity—moving beyond gestational age. *N Engl J Med* 2008;358:1672–81.
- Ethridge Jr JK, Louis JM, Mercer BM. Accuracy of fetal weight estimation by ultrasound in periviable deliveries. *J Matern Fetal Neonatal Med* 2014;27:557–60.
- Stefanelli S, Groom KM. The accuracy of ultrasound-estimated fetal weight in extremely preterm infants: a comparison of small for gestational age and appropriate for gestational age. *Aust N Z J Obstet Gynaecol* 2014;54:126–31.
- Abele H, Hoopmann M, Wagner N, et al. Accuracy of sonographic fetal weight estimation of fetuses with a birth weight of 1500 g or less. *Eur J Obstet Gynecol Reprod Biol* 2010;153:131–7.
- Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. *Pediatrics* 1972;50:515–25.
- Effect of corticosteroids for fetal maturation on perinatal outcomes. NIH Consensus Development Panel on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. *JAMA* 1995;273:413–8.
- Carlo WA, McDonald SA, Fanaroff AA, et al. Association of antenatal corticosteroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. *JAMA* 2011;306:2348–58.
- Mori R, Kusuda S, Fujimura M. Neonatal Research Network Japan. Antenatal corticosteroids promote survival of extremely preterm infants born at 22 to 23 weeks of gestation. *J Pediatr* 2011;159:110–114.e1.
- Group E, Fellman V, Hellstrom-Westas L, et al. One-year survival of extremely preterm infants after active perinatal care in Sweden. *JAMA* 2009;301:2225–33.
- Hayes EJ, Paul DA, Stahl GE, et al. Effect of antenatal corticosteroids on survival for neonates born at 23 weeks of gestation. *Obstet Gynecol* 2008;111:921–6.
- Park CK, Isayama T, McDonald SD. Antenatal corticosteroid therapy before 24 weeks of gestation: a systematic review and meta-analysis. *Obstet Gynecol* 2016;127:715–25.

23. Crowley P, Chalmers I, Keirse MJ. The effects of corticosteroid administration before preterm delivery: an overview of the evidence from controlled trials. *Br J Obstet Gynaecol* 1990;97:11–25.
24. Murphy KE, Hannah ME, Willan AR, et al. Multiple courses of antenatal corticosteroids for preterm birth (MACS): a randomised controlled trial. *Lancet* 2008;372:2143–51.
25. Chawla S, Natarajan G, Rane S, et al. Outcomes of extremely low birth weight infants with varying doses and intervals of antenatal steroid exposure. *J Perinat Med* 2010;38:419–23.
26. Wilms FF, Vis JY, Pattinaja DA, et al. Relationship between the time interval from antenatal corticosteroid administration until preterm birth and the occurrence of respiratory morbidity. *Am J Obstet Gynecol* 2011;205:49.e1–7.
27. Ring AM, Garland JS, Stafel BR, et al. The effect of a prolonged time interval between antenatal corticosteroid administration and delivery on outcomes in preterm neonates: a cohort study. *Am J Obstet Gynecol* 2007;196:457.e1–6.
28. Vermillion ST, Bland ML, Soper DE. Effectiveness of a rescue dose of antenatal betamethasone after an initial single course. *Am J Obstet Gynecol* 2001;185:1086–9.
29. McEvoy C, Schilling D, Peters D, et al. Respiratory compliance in preterm infants after a single rescue course of antenatal steroids: a randomized controlled trial. *Am J Obstet Gynecol* 2010;202:544.e1–9.
30. Garite TJ, Kurtzman J, Maurel K, et al. Impact of a ‘rescue course’ of antenatal corticosteroids: a multicenter randomized placebo-controlled trial. *Am J Obstet Gynecol* 2009;200:248.e1–9.
31. Nelson KB, Grether JK. Can magnesium sulfate reduce the risk of cerebral palsy in very low birthweight infants? *Pediatrics* 1995;95:263–9.
32. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks’ gestation: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2009;200:595–609.
33. Doyle LW, Crowther CA, Middleton P, et al. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database Syst Rev* 2009;CD004661.
34. Magee L, Sawchuck D, Synnes A, et al. SOGC Clinical Practice Guideline. Magnesium sulphate for fetal neuroprotection. *J Obstet Gynaecol Can* 2011;33:516–29.
35. Crowther CA, Hiller JE, Doyle LW, et al. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. *JAMA* 2003;290:2669–76.
36. Doyle LW, Anderson PJ, Haslam R, et al. School-age outcomes of very preterm infants after antenatal treatment with magnesium sulfate vs placebo. *JAMA* 2014;312:1105–13.
37. Rattray BN, Kraus DM, Drinker LR, et al. Antenatal magnesium sulfate and spontaneous intestinal perforation in infants less than 25 weeks gestation. *J Perinatol* 2014;34:819–22.
38. Chang E. Preterm birth and the role of neuroprotection. *BMJ* 2015;350:g6661.
39. Lannon SM, Guthrie KA, Reed SD, et al. Mode of delivery at periviable gestational ages: impact on subsequent reproductive outcomes. *J Perinat Med* 2013;41:691–7.
40. Alfirevic Z, Milan SJ, Livio S. Caesarean section versus vaginal delivery for preterm birth in singletons. *Cochrane Database Syst Rev* 2012;6:CD000078.
41. Reddy UM, Zhang J, Sun L, et al. Neonatal mortality by attempted route of delivery in early preterm birth. *Am J Obstet Gynecol* 2012;207:117.e1–8.
42. Hannah ME, Hannah WJ, Hewson SA, et al. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. *Lancet* 2000;356:1375–83.
43. Bergenhenegouwen LA, Meertens LJ, Schaaf J, et al. Vaginal delivery versus caesarean section in preterm breech delivery: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2014;172:1–6.
44. Robertson PA, Foran CM, Croughan-Minihane MS, et al. Head entrapment and neonatal outcome by mode of delivery in breech deliveries from twenty-four to twenty-seven weeks of gestation. *Am J Obstet Gynecol* 1995;173:1171–6.
45. Blagaic V, Stanojevic M, Jelcic A. Amnion protective cesarean section—method for gentle delivery of preterm and/or VLBW neonates. *J Matern Fetal Neonatal Med* 2014;27:393–6.
46. Ecker JL, Kaimal A, Mercer BM, et al. Obstetric Care Consensus: Periviable Birth. American Congress of Obstetricians and Gynecologists. Available at: <http://www.acog.org/Resources-And-Publications/Obstetric-Care-Consensus-Series/Periviable-Birth>; 2016. Accessed on 30 May 2017.
47. Liston R, Sawchuck D, Young D. SOGC Clinical Practice Guideline. Fetal health surveillance: antepartum and intrapartum consensus guideline. *J Obstet Gynaecol Can* 2007;29:S3–56.
48. Afors K, Chandraran E. Use of continuous electronic fetal monitoring in a preterm fetus: clinical dilemmas and recommendations for practice. *J Pregnancy* 2011;2011:848794.
49. Freeman RK, Garite TJ, Nageotte MP, et al. Fetal heart rate monitoring, ed 4. Philadelphia, PA: Lippincott Williams & Wilkins; 2012. p. 270.
50. Al-Wassia H, Shah PS. Efficacy and safety of umbilical cord milking at birth: a systematic review and meta-analysis. *JAMA Pediatr* 2015;169:18–25.
51. Krueger MS, Eyal FG, Peevy KJ, et al. Delayed cord clamping with and without cord stripping: a prospective randomized trial of preterm neonates. *Am J Obstet Gynecol* 2015;212:394.e1–5.
52. Ghavam S, Batra D, Mercer J, et al. Effects of placental transfusion in extremely low birthweight infants: meta-analysis of long- and short-term outcomes. *Transfusion* 2014;54:1192–8.
53. Chiruvolu A, Tolia VN, Qin H, et al. Effect of delayed cord clamping on very preterm infants. *Am J Obstet Gynecol* 2015;213:676.e1–7.
54. Popat H, Robledo KP, Sebastian L, et al. Effect of delayed cord clamping on systemic blood flow: a randomized controlled trial. *J Pediatr* 2016;178:81–86.e2.
55. Lyu Y, Shah PS, Ye XY, et al. Association between admission temperature and mortality and major morbidity in preterm infants born at fewer than 33 weeks’ gestation. *JAMA Pediatr* 2015;169:e150277.
56. Billimoria Z, Chawla S, Bajaj M, et al. Improving admission temperature in extremely low birth weight infants: a hospital-based multi-intervention quality improvement project. *J Perinat Med* 2013;41:455–60.
57. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med* 1996;334:1209–15.
58. Schenone MH, Aguin E, Li Y, et al. Prenatal prediction of neonatal survival at the borderline viability. *J Matern Fetal Neonatal Med* 2010;23:1413–8.