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Formula versus maternal breast milk for feeding preterm or low birth weight infants

Fetal measurements for guiding the medical management of women with diabetes in pregnancy to improve outcomes for mother and baby

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Interventions to support women who are overweight or obese to start and continue breastfeeding

Cervical assessment by ultrasound for preventing preterm delivery

Regimens of vitamin D supplementation for women during pregnancy

Formula versus maternal breast milk for feeding preterm or low birth weight infants

Authors: Brown J, Walsh V, McGuire W

Review question

Does feeding preterm or low birth weight infants with formula rather than maternal breast milk affect growth and development?

Background

Artificial formulas can be manipulated to contain higher amounts of important nutrients such as protein than maternal breast milk but newborn infants often find formula difficult to digest. Artificial formulas, furthermore, do not contain the antibodies and other substances present in breast milk that protect the immature gut of preterm or low birth weight infants and reduce the risk of infection and severe bowel problems. If preterm infants are fed with formula rather than maternal breast milk (breast-fed directly or mother's own expressed breast milk), this might increase the risk of these problems and adversely affect growth and development.

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Given these concerns, we planned to review the evidence from clinical trials that compared formula versus maternal breast milk for feeding preterm or low birth weight infants.

Study characteristics

In searches up to October 2018, we did not find any eligible randomised controlled trials.

Key results and conclusions

There are no trial data to answer this question. Since another Cochrane Review showed that feeding with formula compared to donor breast milk increases the risk of serious gut problems in preterm or low birth weight infants, it is unlikely that families and clinicians would consider it acceptable to allocate an infant to receive formula as an alternative to maternal breast milk when it is available.

Fetal measurements for guiding the medical management of women with diabetes in pregnancy to improve outcomes for mother and baby

Authors: Rao U, de Vries B, Ross GP, Gordon A

What is the issue?

Diabetes during pregnancy affects between one and three in ten pregnant women (10% to 30%), and is associated with an increased risk of adverse outcomes. The baby may grow to a large size, leading to injury of the baby during birth, or the need for caesarean delivery. It is known that carefully controlling the mother's blood glucose levels during pregnancy reduces the risk of these and other adverse outcomes. All women with diabetes during pregnancy have their glucose levels closely monitored, and are treated using dietary changes, exercise or medications such as insulin or oral medication, even when their babies are not showing signs of being affected.

The most common sign of being affected by high glucose and insulin levels is a baby who is larger than expected, and so at risk of macrosomia (weighing more than 4000 g at birth).

Why is this important?

Only 14% to 22% of women with diabetes during pregnancy have macrosomic babies (babies weighing more than 4000 g at birth). At present, all women with diabetes during pregnancy, even those whose babies are not showing signs of being larger, are closely monitored. This costs time and money for both the women and the health services. If we are able to prove that targeting intensive monitoring and treatment to those women whose unborn babies are affected by overgrowth does not increase the risk of adverse outcomes, we may be able to save time, resources and anxiety.

What evidence did we find?

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We searched for evidence on the 29th of January 2019 and identified three small randomised controlled trials (involving a total of 524 women) for inclusion in our review. The overall trial quality was low to moderate. The trials did not report the majority of outcomes of interest in this review, including outcomes relating to cost or use of resources.

Compared with monitoring the mothers' blood glucose levels alone, the addition of ultrasound may make little or no difference to the risk of having a caesarean birth (2 trials, 428 women, low-certainty evidence). Very low-certainty evidence means that we are unclear about the results relating to the risks of the mother having blood pressure disorders during pregnancy (2 trials, 325 women). The included trials did not report on the important maternal outcomes of low blood glucose, or development of type 2 diabetes.

Using ultrasound in addition to monitoring the mother's blood glucose levels may make little or no difference to the risk of the newborn baby having low blood glucose levels (3 trials, 524 women, low-certainty evidence). Very low-certainty evidence means that we are unclear about results relating to the risks of: having a baby that is large for gestational age (3 trials, 524 women); the baby's shoulders becoming entrapped in the birth canal (1 trial, 96 women); death or illness in the newborn baby (1 trial, 96 women); or the baby dying during pregnancy or birth (1 trial, 96 women).

What does this mean?

This review was based on limited evidence from three trials (involving 524 women). The trials did not report some important outcomes of interest to this review, and the majority of our secondary outcomes were also unreported. The certainty of the available evidence ranged from low to very low. There was insufficient evidence to evaluate the use of ultrasound (in addition to maternal blood glucose concentration values) to assist in guiding the medical management of GDM, and the effect on important short- and long-term outcomes for the mother or her baby, or the associated costs.

Large, randomised trials are needed. Such trials could consider important short- and long-term outcomes (as listed in this review) for the mother, her baby, and resource use.

Does delaying cord clamping or using cord milking at birth improve the health of babies born too early?

Authors: Rabe H, Gyte GML, Díaz-Rossello JL, Duley L

What is the issue?

In this Cochrane Review, we set out to determine if delayed cord clamping or umbilical cord milking improves the health outcomes for babies born before 37 weeks' gestation. These interventions were compared with early cord clamping.

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Why is it important?

Babies born before 37 weeks, or preterm, have poorer health outcomes than babies born at term, particularly if they are born before 32 weeks. Babies born preterm can experience problems with the functioning of many of their major organs including their lungs, gut and hearts. They have a greater risk of dying or having long-term problems such as cerebral palsy. After birth, the babies may need blood transfusions and drugs to strengthen their heart contractions (inotropes) and to raise their blood pressure. It is important to try to find ways of improving the health of these tiny babies.

Early clamping of the umbilical cord has been standard practice over many years. It allows the baby to be transferred quickly to care from a specialised team of doctors either at the side of the room or in another room. Yet, delayed clamping for half to three or more minutes allows continuing blood flow between the mother and her baby, and this may help the baby to adjust to breathing air. Squeezing blood along the umbilical cord towards the baby (milking the cord), can boost the baby's blood volume, and this may improve the baby's health. We wanted to see if there are any benefits or harms from either waiting to clamp or milking the cord.

What evidence did we find?

We collected and analysed all relevant studies to answer this question (date of search: November 2017). Our updated review included 40 studies which provided data on 4884 babies and their mothers. Studies were undertaken across the world, but mostly in high-income countries. Births were in hospitals which practiced early clamping. For many outcomes there were insufficient data to be really confident of our findings.

1) For delayed cord clamping (with immediate care of the baby after cord clamping) compared with early cord clamping, we found it likely that fewer babies died before discharge (20 studies, 2680 babies). Also, fewer babies may have had any bleeding in the brain (15 studies, 2333 babies), but there was probably no difference in the numbers of babies with very serious brain bleeds (10 studies, 2058 babies).

2) Only one study of 276 babies and their mothers provided data on delayed cord clamping with immediate care of the baby beside the mother with cord intact compared with early cord clamping. This study was small and did not identify any marked differences in health outcomes.

3) For delayed cord clamping (with immediate care of the baby after cord clamping) versus cord milking, there were insufficient data (three studies, 322 babies) to make comparisons between outcomes.

4) For cord milking versus early cord clamping, we found 11 studies providing data with 1183 babies and their mothers. Again, there were insufficient data to make clear comparisons on outcomes.

What does this mean?

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Delayed cord clamping probably reduced the risk of death for babies born preterm. Early cord clamping probably causes harm. No studies showed what length of delay was best, and only a few studies followed babies for health outcomes in early childhood. There is insufficient evidence for reliable conclusions on providing immediate care for the baby beside the mother with the cord intact. Similarly, there is insufficient evidence for reliable conclusions on cord milking. Further studies are in progress.

Interventions to support women who are overweight or obese to start and continue breastfeeding

Authors: Fair FJ, Ford GL, Soltani H

What is the issue?

Breastfeeding is important for the health of mothers and their infants. Current advice is for exclusive breastfeeding to continue until babies are six months of age. Infants fed with formula milk are at greater risk of infections, asthma and sudden infant death syndrome. Mothers who do not breastfeed are at greater risk of female cancers and type 2 diabetes. Women who are overweight or obese are less likely to start breastfeeding than other women and tend to breastfeed for a shorter length of time. Suggested reasons include physical factors such as larger breasts, which make traditional breastfeeding positions more difficult, and a delay in their milk coming in (normally around 72 hours). This can decrease mothers' confidence in their milk supply and ability to breastfeed. Cultural factors may also influence women's decision making about starting and continuing breastfeeding, for example, how the woman's family and friends fed their babies, how confident the mother is in reaching her breastfeeding goals and how the woman views her own body.

Why is this important?

Women who are overweight or obese can experience challenges with breastfeeding that could be overcome with additional encouragement and support. We wanted to find out what types of support are provided and what works best, both before and after birth. Interventions included education, social support and physical methods such as milk expression.

What evidence did we find?

We searched for evidence (January 2019) and identified seven randomised controlled trials (RCTs), involving 831 women (range 36 to 226 women), conducted in high-income countries (USA, Denmark, Australia) between 2006 and 2015. Three trials only included women who were obese prior to pregnancy and four trials included women who were overweight and women who were obese.

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The trials compared different types of breastfeeding support to usual care. There were a limited number of trials for each type of support, and differences in how much support the women received in the support and usual care groups.

One trial (39 women) used a physical support intervention through the loan of an electric or manual breast pump versus usual care (no pump). Very low-certainty evidence means it is unclear whether physical support improves exclusive breastfeeding at four to six weeks; or any breastfeeding at four to six weeks. The trial did not report other important outcomes of interest: non-initiation of breastfeeding, and exclusive or any breastfeeding at six months after birth.

Six trials (792 women) used multiple methods of support (including education and social support through telephone or face-to-face contact) versus usual care. One trial (174 women) did not report on any of our main outcomes of interest. One of the trials also provided physical support through providing a breast pump and a baby sling, and another provided a small gift to the women at each trial visit. Support in these trials was provided by a professional (four trials) or a peer (two trials), either in a group (one trial) or individually (five trials).

For women receiving an intervention that incorporated multiple methods of support (including social, educational or physical support) versus usual care, we are unclear about the effects of the intervention because we identified very low-certainty evidence for all of the important outcomes in this review: rate of non-initiation of breastfeeding; exclusive breastfeeding at four to six weeks; any breastfeeding at four to six weeks; rate of exclusive breastfeeding at six months after birth; and any breastfeeding at six months after birth.

What does this mean?

The effectiveness of interventions for supporting women who are overweight or obese to start and continue breastfeeding remains unclear. The methods used by the available trials varied in quality, with small numbers of participants. No trials compared one type of support to another.

We need high-quality trials to evaluate whether social, educational, physical support, or any combination of these interventions can give mothers who are overweight or obese the best chance of starting and continuing to breastfeed. The interventions need to be designed specifically for this group of women and delivered by people who understand the challenges these women face when establishing and maintaining breastfeeding.

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Cervical assessment by ultrasound for preventing preterm delivery

Authors: Berghella V, Saccone G

We set out to assess the effectiveness of knowing the cervical length, measured with ultrasound, for preventing preterm birth compared with not knowing the cervical length.

What is the issue?

The cervix is the lower part of the uterus that connects to the vagina. When women are not pregnant, it is normally at least 3 cm long. During pregnancy, a short cervical length is associated with a risk of spontaneous preterm birth. The shorter the cervical length, the greater the risk. Therefore, measuring cervical length by ultrasound can help predict spontaneous preterm birth. The cervical length is measured by an ultrasound scan through the vagina (transvaginal or TVU), abdomen (transabdominal), or the perineum (transperineal). The most common causes of spontaneous preterm birth are preterm labour or preterm premature rupture of the membranes. Many of the interventions used to prevent preterm birth are used once symptoms develop.

Why is this important?

Preterm birth before 37 weeks is the main cause of a newborn baby being sick and disabled, or dying. The cervix is the opening or passage through which the baby must pass before being born vaginally. Ultrasound can detect early changes of the cervix, such as shortening of the cervical length, to predict preterm birth. On identifying a short cervical length, interventions can be applied to prevent preterm birth. These interventions include giving the expectant mother progesterone to relax the uterus, or applying a stitch, known as a cerclage, to tighten the opening of the cervix.

What evidence did we find?

This review assessed if knowing the cervical length can prevent preterm birth. We included seven randomised controlled studies, which involved 923 pregnant women at 14 to 32 weeks' gestation. One study included expectant mothers with twins, without any symptoms of preterm birth or labour, and looked at the number of babies born prematurely before 36 weeks. Four studies included expectant mothers of single babies with threatened preterm labour, and one study involving women with premature rupture of the membranes looked at the safety of transvaginal ultrasound. One trial included expectant mothers with singleton pregnancies who did not have any symptoms of preterm birth or labour to look at the efficacy of transvaginal ultrasound cervical length screening. All studies used transvaginal ultrasound to assess cervical length.

For women with twin pregnancies and not showing symptoms of preterm birth, we are unclear of the impact of knowing the cervical length on whether babies are born before 34 weeks' gestation, or their gestational age at birth (1 study, 125 women), because we assessed the quality of the evidence to be very low. For women with a single baby and threatened preterm labour, knowledge of their cervical length may have led to a longer

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pregnancy by about four days (4 studies, 410 women), but the evidence on the number of babies born before 37 weeks was unclear (2 studies, 242 women). For women whose waters had broken, it is unclear whether healthcare provider knowledge makes any difference to whether the women gave birth preterm, or on the number of infections, again because we judged the quality of evidence as very low. For women with singleton pregnancies not showing symptoms of preterm birth, it is unclear whether an ultrasound to measure cervical length made any difference to whether their babies were born before 37 weeks' gestation (1 study, 296 women; very low-quality evidence).

What does this mean?

We found a limited number of studies including small numbers of women. The studies varied in their design and had a broad spread of results. Women were not blinded to whether they had an ultrasound or not. Currently, there is not enough high quality research to show if knowledge of cervical length in women with twin or singleton pregnancies has any effect. Future studies could include ways of managing women as a result of the cervical length results, and it would be useful to look at specific populations separately, such as single babies versus twins and women with and without symptoms of preterm labour. They could also report on all important maternal and perinatal outcomes, and include cost-effectiveness analyses.

Regimens of vitamin D supplementation for women during pregnancy

Authors: Palacios C, Trak-Fellermeier M, Martinez RX, Lopez-Perez L, Lips P, Salisi JA, John JC, Peña-Rosas J

What is the issue?

This review evaluated if there are beneficial effects of supplementing pregnant women with more than the current vitamin D recommendation (200 international units/day (IU/d) to 600 IU/d) on pregnancy and neonatal health outcomes and to evaluate if there are negative health effects when using more than the current upper limit recommendation (4000 IU/d).

Why is this important?

Vitamin D supplementation in pregnancy compared to no supplementation appears to decrease the risk of pre-eclampsia, gestational diabetes, low birthweight and may reduce the risk of severe postpartum haemorrhage. However, it is not clear if doses greater than the currently recommended level are needed to observe these health benefits, and if giving more than the upper limit is related to adverse events.

What was studied in the review?

This review included trials evaluating the effect of different vitamin D regimens (doses, frequencies, duration, and times of commencement) to compare the effects of 601 IU/d or more versus 600 IU/d or less and 4000 IU/d

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or more versus 3999 IU/d or less, of vitamin D alone or with any other nutrient on pregnancy and neonatal health outcomes.

What evidence did we find?

Evidence from 19 trials involving 5214 women suggest that supplementation with 601 IU/d or more of vitamin D during pregnancy may reduce the risk of gestational diabetes but may make little or no difference to the risk of pre-eclampsia, preterm birth or low birthweight compared to women receiving 600 IU/d or less.

Evidence from 15 trials involving 4763 women suggests that supplementation with 4000 IU/d or more of vitamin D during pregnancy may make little or no difference to the risk of pre-eclampsia, gestational diabetes, preterm birth or low birthweight compared to women receiving 3999 IU/d or less.

Adverse events were reported differently in most trials; in general, there was little to no side effects reported or similar cases between groups.

What does this mean?

Supplementing pregnant women with more than the current vitamin D recommendation may reduce the risk of gestational diabetes; however, it may make little or no difference in the risk of the other outcomes.

Supplementing pregnant women with more than the current upper limit for vitamin D seems not to increase the risk of the outcomes evaluated. Vitamin D supplementation appears to be safe.

If you have any questions or comments with regard to the above document please feel free to contact me.

Kind regards

Dr Vanessa Jordan PhD

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