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Ultrasound during pregnancy for predicting differences in birth weight between twins

Authors: Jahanfar S, Ho JJ, Jaafar SH, Abraha I, Noura M, Ross CR, Pammi M

Background

Birth weight differences of more than 20% in twins is associated with poor outcomes for the mother and baby. Clinicians measure the estimated fetal weight differences by ultrasound before birth and compare it to differences in birth weight after the babies are born. In this review, we summarized data on whether the ultrasound measurements are accurate enough to predict birth weight differences in twins.

Study characteristics

We searched medical databases to March 2019 for studies comparing ultrasound measurements to birth weight differences and we identified 39 studies. Twenty-two studies provided data on birth weight differences of 20% and 18 studies provided data on birth weight differences of 25%.

Quality of the evidence

We assessed the quality of individual studies using a tool called "Quality Assessment of Diagnostic Accuracy Studies" (QUADAS-2) and the overall quality by a recommended method called GRADE to find out the reliability of the evidence.

Key results

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We found that ultrasound estimation of fetal weight differences compared to birth weight differences was not reliable. On average, ultrasound detected birth weight differences of 20% and 25% only half the time. The quality of evidence was very low.

There is insufficient evidence to support the use of ultrasound as the sole measure for detecting birth weight differences in twins, or poor outcomes. The diagnostic accuracy of other measures including amniotic fluid volume (the fluid surrounding the babies in the womb) or Doppler studies (which use sound waves to detect the movement of blood in the babies' blood vessels and the umbilical cord) in combination with ultrasound to inform clinical decisions needs to be evaluated. Future well-designed studies could also research the impact of whether the babies share a placenta (or not), the sex of the babies, and gestational age (time from woman's last menstrual period), in the diagnostic accuracy of ultrasound for estimated birth weight differences.

Preventing venous thromboembolism in women during pregnancy, childbirth and after birth

Authors: Middleton P, Shepherd E, Gomersall JC

We set out to determine from randomised controlled trials the benefits and harms of treatments during pregnancy, childbirth, and after birth to prevent deep vein clots in women who are at increased risk.

What is the issue?

A blood clot can form in a deep vein , usually in the legs. This is known as deep vein thrombosis (DVT). If part of the clot breaks off it can be carried in the blood to the lungs and block blood vessels there. This is called a pulmonary embolism (PE), and can cause death, although this is rare. Together these are known as venous thromboembolism (VTE) disease. A women's clotting system is more active during pregnancy to protect her from excessive bleeding during birth. Some women are at a higher risk of VTE during pregnancy and around the time of childbirth including women with previous VTE, thrombophilia (a condition which makes people more likely to develop clots) and following a caesarean birth.

Why is this important?

Women at increased risk of VTE during pregnancy and in the six weeks following childbirth are commonly given treatments to prevent blood clots. Treatments vary due to lack of clear guidelines. The treatments to prevent VTE include heparin type drugs, aspirin and the wearing of compression stockings to improve blood flow in the legs. Some of the treatments can potentially harm women, for example, by increasing blood loss after childbirth or interfering with wound healing.

What evidence did we find?

This is an update of a Cochrane Review published in 2014. We searched for new evidence in October 2019. Twenty-nine randomised controlled studies, involving 3839 women, are now included. The studies were published from 1975 to 2016 and were mainly carried out in high-income countries. They included women at

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increased risk of VTE who were pregnant, in childbirth, and after the birth. Treatments assessed included different types and doses of heparin (of low molecular weight heparin and unfractionated heparin), and compression stockings or devices. No deaths occurred. The reported findings were supported by very low-certainty evidence.

Starting treatment during pregnancy (with or without treatment after childbirth): we looked at the occurrence of symptomatic VTE and adverse effects that caused women to stop treatment. Any benefits of heparin were unclear when compared with no treatment or a placebo (assessed in up to four studies with 476 women). Similarly, for different types of heparin (assessed in up to four studies with 404 women), different doses of low molecular weight heparin (in one study with 144 women), and for compression stockings compared with no stockings (in one study with 44 women).

For treatment during and following vaginal or caesarean birth: we are very uncertain about the effects of heparin when compared with no treatment on the occurrence of symptomatic VTE (assessed in one study with 210 women). This study did not report on adverse effects that led women to stop treatment.

For treatment during and following caesarean birth: we are very uncertain about the effects of heparin compared with no treatment or a placebo (assessed in up to five studies with 1140 women). The studies looked at different types or doses of heparin, and compression devices compared with bed rest (in one study of 49 women). No adverse effects stopping treatment were reported.

Looking at treatment following vaginal or caesarean birth: no symptomatic VTEs were reported in women receiving either heparin or no treatment or placebo in two studies (58 women). No study reported on adverse effects leading to women stopping treatment.

What does this mean?

We are very uncertain if the benefits of treatments used to prevent deep vein clots in high-risk women during pregnancy and around the time of childbirth outweigh any harms. Small numbers of studies were included in the comparisons with a range of outcomes measured and low numbers of events. Some studies had design limitations and definitions of blood clotting risk factors and outcomes were not always clear. More, large, high-quality studies are needed.

Probiotics to prevent gestational diabetes mellitus

Authors: Davidson SJ, Barrett HL, Price SA, Callaway LK, Dekker Nitert M

We analysed evidence from randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups) investigating probiotic supplements alone or in combination with drug or non-drug interventions for preventing gestational diabetes mellitus (GDM).

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What is the issue?

GDM is a condition where the mother develops high blood sugar levels, usually after 13 weeks of pregnancy. GDM is different from type 2 diabetes in that blood sugar levels are normal before pregnancy, and the levels usually return to normal after pregnancy. GDM is associated with an increased risk of developing type 2 diabetes later in life. Women with GDM are at increased risk of high blood pressure with protein in the urine (pre-eclampsia) and instrumental delivery or caesarean section. Their infants are more likely to be born large for their gestational age. Probiotics are 'good bacteria' that are usually taken in the form of capsules or drinks to add to the gut bacteria. We are dependent on our gut bacteria to help digest our food, produce certain vitamins, regulate our immune system and keep us healthy by protecting us against disease-causing bacteria. Probiotics could change a person's metabolism and play a role in the prevention of GDM.

Why is this important?

Women who are overweight or obese, had GDM in a previous pregnancy or have an immediate family member with diabetes are at increased risk of GDM. Current treatment for GDM includes diet with or without medication but does not always prevent the problems associated with GDM. Probiotics could be a simple method for preventing GDM. This review looked at whether there is evidence to show if this is true.

What evidence did we find?

We searched for evidence from randomised controlled trials in March 2020 and identified seven studies with 1647 pregnant women comparing probiotics with inactive placebo (pretend treatment). Two studies were in overweight and obese women, two in obese women and three did not exclude women based on their weight. The overall risk of bias was low except for one study where the risk of bias was unclear.

It is unclear how probiotics affect the risk of developing **GDM** due to the wide variation in the results of six studies (1440 women, low-quality evidence). Probiotics increase the risk of developing **pre-eclampsia** (4 studies, 955 women; high-quality evidence). Probiotics make little to no difference to the risk of needing a **caesarean section** (6 studies, 1520 women; high-quality evidence), and probably make little to no difference to weight gain during pregnancy (4 studies, 853 women; moderate-quality evidence) or to the risk of giving birth to a **big baby** (4 studies, 919 women; moderate-quality evidence). None of the studies reported information about the risk of perineal trauma (tears during vaginal birth or a surgical incision (episiotomy)), postnatal depression or developing subsequent diabetes.

We do not know if probiotics affect the infant having **medical problems after birth** because of the variation in results between studies (2 studies, 623 infants; low-quality evidence). It is also uncertain how probiotics affect **infant death** (either before birth or as a newborn) (3 studies, 709 infants; low-certainty evidence), **low blood sugar** (2 studies, 586 infants; low-certainty evidence) or **body fat** (2 studies, 320 infants; low-certainty

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evidence). None of the studies reported information about the risk of infants developing diabetes or long-term conditions that affect brain development.

What does this mean?

Low-quality evidence from six trials has not clearly identified the effect of probiotics on the risk of GDM. However, high-quality evidence suggests that probiotics probably increase the risk of pre-eclampsia. Therefore, there is currently evidence of possible harm with little observed benefit for widespread use of probiotics in pregnancy.

There are eight studies currently ongoing that may help to provide more clarity on the effects of probiotics. It is also important to explore the relationship between probiotics and pre-eclampsia further.

Are progestogen treatments effective in preventing miscarriage?

Authors: Devall AJ, Papadopoulou A, Podesek M, Haas DM, Price MJ, Coomarasamy A, Gallos ID

We set out to find out which progestogen treatment is most effective, safe, and has fewer side-effects for preventing miscarriage in women with threatened and with recurrent miscarriage, using evidence from randomised controlled trials. We looked at the number of women who went on to have a live birth, or miscarriage.

What is the issue?

Miscarriage is the most common cause of early pregnancy loss in the first 24 weeks and one of the most common complications in early pregnancy. An estimated 15% to 20% of pregnancies will end in a miscarriage, with 25% of women experiencing a miscarriage in their lifetime. Women can be at risk of a miscarriage if they experience early pregnancy bleeding, or if they have a history of previous miscarriages.

Why is this important?

Progesterone is an important pregnancy hormone that helps to maintain a pregnancy. A variety of different progesterone-like treatments (known as progestogens) have been used to treat women with early pregnancy bleeding. They are also used to prevent miscarriage in women with a history of previous miscarriages. There is uncertainty about the effectiveness, safety, and side-effects of the available progestogens for preventing miscarriage in these different groups of women. We wanted to find out which, if any, of the treatments is the most effective and safest. We collected and analysed all the relevant studies to answer this question.

What evidence did we find?

We searched for evidence in December 2020 and identified seven studies involving 5,682 women. All women were managed in hospitals. Women were diagnosed with early pregnancy bleeding (known as threatened miscarriage), or had a history of three or more previous miscarriages (known as recurrent miscarriage). Four

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different progestogen treatments were used: vaginal micronized progesterone, oral dydrogesterone, oral micronized progesterone and 17-α-hydroxyprogesterone injected into muscle. In six of the studies the treatments were compared to inactive placebo.

Three studies involved 4496 women with threatened miscarriage, some of whom had previously experienced a miscarriage. Overall, vaginal micronized progesterone (high-quality evidence) and oral dydrogesterone (moderate-quality evidence) made little difference to the number of women who went on to have a live birth when compared with placebo. We further studied the women who had experienced a previous miscarriage, were now presenting with a threatened miscarriage, and were given vaginal micronized progesterone or placebo. For women with one or more previous miscarriages, vaginal micronized progesterone increased the live birth rate compared to placebo (high-quality evidence). Those women who had no previous miscarriages, but were now presenting with early pregnancy bleeding showed no improvement in live birth rate (high-certainty evidence).

For women with recurrent miscarriage, we based our findings on one study involving 826 women. Overall, vaginal micronized progesterone made little difference to the live birth rate when compared with placebo. The evidence for dydrogesterone compared with placebo for women with recurrent miscarriage is of very low-certainty evidence, therefore the effects remain unclear. No data are available to assess the effectiveness of 17-α-hydroxyprogesterone or oral micronized progesterone for the outcome of live birth in women with recurrent miscarriage.

From the available data, there are likely no differences in adverse events associated with vaginal micronized progesterone. There was no difference in birth defects and side effects with vaginal micronized progesterone when compared with placebo. There was not enough information about safety and birth defects for us to analyse for all the other treatments.

What does this mean?

The overall available evidence suggests that progestogens probably make little or no difference to live birth rate for women with threatened or recurrent miscarriage. Vaginal micronized progesterone may increase the live birth rate for women who are experiencing early pregnancy bleeding and have a history of one or more previous miscarriages, with likely no difference in adverse events. There is still uncertainty over the effectiveness and safety of alternative progestogen treatments for threatened and recurrent miscarriage.

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

Kind regards

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