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Interventions for improving outcomes in pregnancies that follow stillbirth

Authors: Wojcieszek AM, Shepherd E, Middleton P, Lassi ZS, Wilson T, Murphy MM, Heazell AEP, Ellwood DA, Silver RM, Flenady V

We aimed to compare the effectiveness of different interventions or models of care in improving pregnancy outcomes for parents who have had a previous stillbirth at 20 weeks' gestation or more. The care could be initiated before pregnancy, or during pregnancy, labour, or birth.

What is the issue?

Every year at least 2.6 million families experience the tragedy of stillbirth. This is a devastating event that can have long-term consequences and change parents' attitudes to future pregnancies. Many different causes can lead to stillbirth, and sometimes multiple causes occur together. Causes such as long-term health problems in the mother are still present in subsequent pregnancies. The parents may therefore benefit from special care before becoming pregnant again. Such care may be highly diverse, addressing a range of risk factors, conditions, and other considerations. This care can take the form of counselling or social support programmes to assist with dealing with grief, anxiety and depression; better managing a mother's health before conception to address health issues; and assisting with high-risk behaviours or risk factors such as being overweight, smoking, or alcohol use. Once pregnant, the mother can be closely watched, possibly with extra antenatal visits or by attending special antenatal clinics. A planned early birth may also be considered.

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Why is this important?

Parents who have had a stillborn baby are more likely to have another stillbirth than parents who have not had a stillborn baby before. In their next pregnancy, parents often experience anxiety and depression, and ongoing worry about whether their baby will survive. It is important to be able to work out from high-quality clinical studies which interventions are helpful in preventing stillbirth from happening again, and in improving the health and well-being of these parents and families.

What evidence did we find?

We searched for evidence from randomised controlled trials published up to June 2018. We included 10 studies at low to moderate risk of bias. All but one study were from high-income countries, mainly in developed areas of Europe. The women in the studies were either pregnant or attempting to conceive after having a miscarriage, a stillborn baby, or a serious complication in a previous pregnancy. The interventions included two types of drugs (low-dose aspirin and low-molecular-weight heparin) that reduce blood clotting and may help the placenta to function (six trials), pre-conception injection of blood cells (third-party leukocyte immunisation) to help mothers' immune systems to cope with pregnancy (one trial), a special type of antibody (intravenous immunoglobulin) given into a vein to improve the functioning of the pregnant woman's immune system (two trials), and injections of a medication (progestogen) that acts like the pregnancy hormone progesterone (one trial). We evaluated data from 222 women who had previously had a stillborn baby at 20 weeks' gestation or more.

We were unable to determine whether any of these interventions reduced the chance of having another stillborn baby in the subsequent pregnancy; or whether the interventions reduced the chances of babies dying or having serious complications in the first month of life, because the studies not large enough for us to have confidence in the findings. Largely because of this, we judged the quality of evidence in this review to be very low to low. Two interventions (low-dose aspirin and third-party leukocyte immunisation) appeared to increase the birthweight of babies, but these findings are not reliable due to the small numbers of babies included.

The included studies provided very little information about psychological outcomes of parents or longer-term outcomes of children and families.

What does this mean?

There is insufficient evidence from the studies included in this review to know which interventions are helpful in preventing subsequent stillbirths and improving the health and well-being of parents and families in pregnancies that follow a stillbirth. More targeted studies are needed, which include larger numbers of women/parents who have previously experienced a stillbirth. We urgently need studies testing what forms of

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psychological support are most helpful in reducing anxiety and depression for these parents. Any studies carried out in future should measure the financial costs of interventions, and longer-term health outcomes of families and children.

Which drug is best for reducing excessive blood loss after birth?

Authors: Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, Williams MJ, Diaz V, Pasquale J, Chamillard M, Widmer M, Tunçalp Ö, Hofmeyr G, Althabe F, Gülmezoglu A, Vogel JP, Oladapo OT, Coomarasamy A

What is the issue?

The aim of this Cochrane Review was to find out which drug is most effective in preventing excessive blood loss at childbirth and has the least side effects. We collected and analysed all the relevant studies to answer this question (date of search: 24 May 2018).

Why is this important?

Excessive bleeding after birth is the most common reason why mothers die in childbirth worldwide. Although most women will have moderate bleeding at birth, others may bleed excessively, and this can pose a serious risk to their health and life. To reduce excessive bleeding at birth, the routine administration of a drug to contract the uterus (uterotonic) has become standard practice across the world.

Different drugs given routinely at birth have been used for reducing excessive bleeding. They include oxytocin, misoprostol, ergometrine, carbetocin, injectable prostaglandins and combinations of these drugs, each with different effectiveness and side effects. Some of the side effects identified include: vomiting, high blood pressure and fever. Currently, oxytocin is recommended as the standard drug to reduce excessive bleeding. We analysed all the available evidence to compare the effectiveness and side-effect profiles for each drug.

What evidence did we find?

We found 196 studies involving 135,559 women. We compared seven uterotonic agents against each other and against women receiving no uterotonic. Studies were conducted across 53 countries. In most studies women were giving birth normally and in a hospital.

The analysis suggests that all drugs are effective for preventing blood loss that equals or exceeds 500 mL when compared with no routine uterotonic treatment. Compared with oxytocin (the standard recommended drug), the three best drugs for this outcome were a combination of ergometrine plus oxytocin, carbetocin, and a combination of misoprostol plus oxytocin. We found the other drugs misoprostol, injectable prostaglandins, and ergometrine may make little or no difference to this outcome compared with oxytocin.

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All drugs except ergometrine and injectable prostaglandins are effective for preventing blood loss that equals or exceeds 1000 mL when compared with no treatment. Ergometrine plus oxytocin and misoprostol plus oxytocin make little or no difference in this outcome compared with oxytocin. It is uncertain whether carbetocin and ergometrine alone make any difference to this outcome. However, misoprostol is less effective in preventing blood loss that equals or exceeds 1000 mL compared with oxytocin.

Misoprostol plus oxytocin reduces the use of additional uterotonics and probably also reduces the risk of blood transfusion when compared with oxytocin. Carbetocin, injectable prostaglandins and ergometrine plus oxytocin may also reduce the use of additional uterotonics but the certainty of the evidence is low. No meaningful differences could be detected between all agents for maternal deaths or severe birth complication as these are rare in such studies.

The two combinations of drugs were associated with important side effects. When compared with oxytocin, women receiving misoprostol plus oxytocin combination are more likely to suffer vomiting and fever. Women receiving ergometrine plus oxytocin are also more likely to suffer vomiting and may make little or no difference to the risk of hypertension, however the certainty of the evidence was low for this outcome.

The analyses gave similar results irrespective of whether women were giving birth normally or by caesarean, in a hospital or in the community, were at high or low risk for bleeding excessively after birth, whether they received a high or a low dose of misoprostol and whether they received a bolus or an infusion of oxytocin or both.

What does this mean?

All agents were generally effective for preventing excessive bleeding when compared with no uterotonic drug treatment. Ergometrine plus oxytocin combination, carbetocin, and misoprostol plus oxytocin combination may have some additional benefits compared with the current standard oxytocin. The two combination drugs, however, are associated with significant side effects that women might find disturbing compared with oxytocin. Carbetocin may have some additional benefits compared with oxytocin and appears to be without an increase in side effects.

Delivering the placenta in the third stage of labour

Authors: Begley CM, Gyte GML, Devane D, McGuire W, Weeks A, Biesty LM

What is the issue?

The aim of this Cochrane Review was to look at different ways of delivering the placenta after the birth of the baby; expectant, active or mixed management. We asked, what are the benefits and harms for all women, but

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specifically for women at low risk of severe bleeding (haemorrhage)? We collected and analysed all relevant studies to answer this question (22 January 2018).

Why is this important?

Once a baby is born, the womb (uterus) continues to contract, causing the placenta to separate from the wall of the uterus. The mother then delivers the placenta, or 'after-birth'. This is called expectant management of third stage of labour. Active management of third stage involves three components: 1) giving a drug (a uterotonic) to help contract the uterus; 2) clamping the cord early (usually before, alongside, or immediately after giving the uterotonic); 3) traction is applied to the cord with counter-pressure on the uterus to deliver the placenta (controlled cord traction). Mixed management uses some, but not all, of the three components. Active management was introduced to try to reduce severe blood loss at birth. This is a major cause of women dying in low-income countries where women are more likely to be poorly nourished, anaemic and have infectious diseases. In high-income countries, severe bleeding occurs much less often, yet active management has become standard practice in many countries.

What evidence did we find?

We found eight studies that contributed data and involved 8892 women and their babies. All studies were undertaken in hospital settings, seven in higher-income countries and one in a lower-income country. Four studies compared active with expectant management and four compared active with mixed management. Overall, the quality of the evidence was generally low or very low and we need more data to be confident in the findings. For all women, irrespective of their risk of severe bleeding, active management may reduce severe bleeding and anaemia. However, it also may reduce the baby’s birthweight and increase the mother's blood pressure, afterpains, vomiting, and the number of women returning to hospital with bleeding. Findings were similar for women at low risk of bleeding, though it was unclear if there was any difference in the incidence of severe bleeding or anaemia.

What does this mean?

Women should be given information before they give birth to help them make informed choices. Some adverse effects experienced by mothers may possibly be avoided by using specific drugs. Delaying cord clamping may benefit the baby by preventing the reduction in birthweight from early cord clamping, but more research is needed. Also, it may be that just giving a uterotonic might reduce severe bleeding, without using the other parts of active management. More research is needed, particularly in low-income countries.

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Desmopressin acetate (DDAVP) for preventing and treating acute bleeds during pregnancy in women with congenital bleeding disorders

Authors: Karanth L, Barua A, Kanagasabai S, Nair N

Review question

We reviewed the evidence about the effect and safety of desmopressin acetate (DDAVP) in preventing and treating acute bleeding in pregnant women with bleeding disorders. This is an update of previously published versions of this Cochrane Review.

Background

Congenital bleeding disorders cause problems with bleeding during pregnancy, labour and delivery. Bleeding complications in women with congenital bleeding disorders are an important cause of disease and death linked to childbirth. Agents to stop the flow of blood are used for women with these bleeding disorders during pregnancy. DDAVP is a drug used to effectively increase the concentration of factor VIII in the blood and to increase the clumping together of platelets to stop bleeding. It does not come from human plasma and it carries no risk of infection. It might be a precious resource in people with von Willebrand disease, haemophilia A or congenital platelet disorders to prevent and treat bleeding episodes related to pregnancy.

Search date

The evidence is current to: 01 October 2018.

Study characteristics

We did not find any randomised controlled trials assessing desmopressin acetate in this group of women.

Key results

There were no trials included in the review. Given the ethical considerations, future randomised controlled trials are unlikely. Evidence is needed to show the risks and benefits of DDAVP when used to prevent and treat bleeding during pregnancy in women with congenital bleeding disorders. While there is evidence from observational trials that shows the drug is effective in stopping and preventing bleeding, we conclude that there is still a need to generate other high-quality controlled evidence. Given that there are unlikely to be any trials published in this area, this review will no longer be regularly updated.

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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