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Imaging techniques for antenatal detection of morbidly adherent placenta (Protocol)

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[Intervention Protocol]

Imaging techniques for antenatal detection of morbidly adherent placenta

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To evaluate the impact of ultrasound and MRI imaging on the outcome of pregnancy for women at risk of morbidly adherent placenta.

BACKGROUND

Description of the condition

The chorionic villi of the human placenta are normally attached to the thin layer of uterine decidua. This allows easy detachment of the placenta following delivery of the fetus. In abnormally adherent placentation, the chorionic villi grow through the uterine decidua and can be found attached directly to uterine myometrium (placenta accreta). The villi can invade into the myometrium (placenta accreta) or penetrate the uterine serosa or nearby organs (placenta percreta). Abnormally adherent placenta is also known under different names; morbidly adherent placenta, abnormal placental invasion and placenta accrete.

Morbidly adherent placenta is associated with low-lying placenta. Low-lying placenta or placenta praevia exist when the placenta is inserted wholly or in part into the lower segment of the uterus. Low-lying placenta is diagnosed when placenta appears on the lower segment of the uterus on ultrasound scan before 20 weeks of gestation. If the placenta is in the lower segment of uterus after 20 weeks of gestation it is known as placenta praevia. This condition is diagnosed as major placenta praevia if the placenta lies over the cervical os and as minor praevia if the placenta does not cover the os (RCOG 2005).

Morbidly adherent placenta can cause major obstetric complications during the third stage of labour and in the postnatal period. Presence of the placental tissue in the uterine cavity prevents the uterus from normal sustained contraction following delivery of the baby. Therefore, women with abnormally adherent placenta tend to have intractable postpartum haemorrhage. Various medical and surgical therapeutic interventions including uterotonics, uterine tamponade devices, ligation of pelvic blood vessels, hysterectomy and uterine artery embolisation can be used to stop bleeding. Despite availability of all these interventions, the risk of maternal death in women with abnormal placentation remains as high as 10% (Chou 2000). Morbidly adherent placenta can also be managed conservatively, which involves leaving the placenta in situ and using prophylactic antibiotics.

The incidence of abnormal placental invasion is believed to be one per 533 deliveries (Price 1991; Wu 2005). Previous caesarean section, low lying placenta, and previous uterine surgeries are the major risk factors for abnormal placentation. It is believed that the incidence of placenta praevia is increasing due to the rising caesarean section rate. Solheim and colleagues forecast that if rates of caesarean section continue to rise as they have in recent years, by 2020, the rate of caesarean section will be 46.2% and there will be an additional 3728 cases of placenta praevia, 2524 cases of placenta accreta and 52 maternal deaths annually in the United States (Solheim 2008).

The main screening tool for antenatal detection of morbidly adherent placenta is taking detailed history during antenatal visits. The patient's history of prior uterine surgery, retained placenta following previous deliveries and diagnosis of placenta praevia on ultrasound scan should increase the clinician's suspicion and prompt further investigation to establish if the patient has placenta accrete.

Although antenatal detection of morbidly adherent placenta is important determinant of maternal and neonatal outcomes, it is difficult to assess the extent of its effect in the outcomes. Use of other important pharmacological, surgical and radiological interventions and level of expertise of health care providers may influence the outcomes.

Description of the intervention

Ultrasound scanning and magnetic resonance imaging (MRI) are two main imaging modalities for detection of morbidly adherent placenta.

Greyscale, two-dimensional ultrasound scanning is the most widely used diagnostic test for antenatal detection of morbidly adherent placenta. Certain ultrasound features such as large placental lagoons, loss of the retroplacental hypoechogenic zone and progressive thinning of retroplacental myometrium have been described as signs of morbidly adherent placenta on ultrasound scanning. One study estimated that grey-scale ultrasound had 87% sensitivity, 98% specificity, 93% positive predictive value and 98% negative predictive value (Haratz-Rubinstein 2002). However, some other studies reported that sensitivity of this test was as low as 33% (Finberg 1992).

Power or colour doppler in conjunction with grey scale ultrasound may improve diagnostic accuracy. Doppler ultrasonography may show increased vascularity at the site of placental invasion in the presence of a morbidly adherent placenta (Chou 2000).

Three-dimensional ultrasound scanning allows multiplanar images of the uteroplacental region and adjacent organs which may improve the diagnostic capability of ultrasound scanning. Three-dimensional ultrasound is found to be more sensitive when compared to two-dimensional scanning in the assessment of placental invasion of the bladder (Chou 2009).

Magnetic resonance tomography can show a larger field of view in more detail. Some studies suggest that magnetic resonance imaging (MRI) is superior to ultrasound imaging in diagnosis of abnormal placental invasion (Warshak 2006). Others argue that these two imaging modalities are comparable in accuracy and that MRI should be used when resolution of ultrasound is limited, for example in conditions such as maternal obesity or posterior placenta (Dwyer 2008).

How the intervention might work

Antenatal detection of morbidly adherent placenta allows healthcare professionals to make necessary preparations for management of severe postpartum bleeding. Planned caesarean delivery by experienced surgeons and theatre staff with access to blood products may significantly improve maternal outcome. Multidisciplinary surgical teams can be summoned in anticipation of severe intractable bleeding or injury to adjacent organs.

On the other hand, availability of imaging techniques can lead to reporting of false negative results which can give false reassurance to clinical teams. This over reliance on the imaging test may lead to inadequate preparation for delivery and poor management of severe complications of morbidly adherent placenta.

The prospect of a difficult caesarean delivery, with risk of severe bleeding, can cause significant stress to pregnant women. This

may lead to anxiety, depression and fear of childbirth. Many women diagnosed with morbidly adherent placenta may be offered elective caesarean section before 39 weeks when the risk of neonatal respiratory morbidity is higher (Morrison 1995).

Some studies suggest that imaging techniques are not very accurate in estimating the degree of invasion. Mildly adherent placenta may be managed by manual removal of placenta. Antenatal diagnosis of morbidly adherent placenta can decrease the threshold for, and sometimes even lead to, overzealous surgical interventions.

Some have suggested use of dynamic gadolinium contrast enhanced MRI to distinguish myometrium from placenta and to differentiate maternal and fetal portions of placenta. However, gadolinium crosses the placenta and its safety has not been assessed.

Why it is important to do this review

Use of imaging techniques remains the main diagnostic tool in the antenatal detection of this condition. Antenatal diagnosis of a morbidly adherent placenta is believed to be the key element of providing safer birth for the women with this pathology. However, there is a possibility of harm caused by false positive and false negative scans. Cost-effectiveness may also be an important issue, as both ultrasound and MRI require expensive medical equipment and specialist expertise.

OBJECTIVES

To evaluate the impact of ultrasound and MRI imaging on the outcome of pregnancy for women at risk of morbidly adherent placenta.

METHODS

Criteria for considering studies for this review

Types of studies

We will include all randomised controlled trials. We will not include quasi-randomised, cluster-randomised studies or crossover trials.

If potentially eligible studies are available in abstract form, we will contact the authors for further information for the review and the study will be identified as awaiting further assessment.

Types of participants

Pregnant women with suspected abnormally adherent placenta (low lying placenta, previous caesarean section).

Types of interventions

Interventions

- Two-dimensional ultrasound
- Three-dimensional ultrasound
- MRI

Comparison

- Two-dimensional ultrasound versus three-dimensional ultrasound
- Two-dimensional ultrasound versus MRI
- Three-dimensional ultrasound versus MRI
- Two-dimensional ultrasound versus no imaging
- Three-dimensional ultrasound versus no imaging
- MRI versus no imaging

Types of outcome measures

Primary outcomes

Maternal

1. Severe postpartum haemorrhage (blood loss more than 1500 ml)
2. Caesarean hysterectomy
3. Maternal death

Secondary outcomes

Maternal

1. Caesarean section
2. Admission to intensive treatment unit (ITU)
3. Anxiety
4. Postnatal sepsis
5. Prolonged hospitalisation due to conservative management of morbidly adherent placenta
6. Cost of investigations

Neonatal

1. Neonatal respiratory distress syndrome
2. Significant neonatal morbidity as defined by trialists
3. Neonatal mortality

Search methods for identification of studies

Electronic searches

We will contact the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register.

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We will not apply any language restrictions.

Data collection and analysis

Selection of studies

O Rustamov (OR) and R Arora (RA) will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult I Siddique (IS).

Data extraction and management

We will design a form to extract data. For eligible studies, OR and IS will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult RA. We will enter data into Review Manager software (RevMan 2008) and check for accuracy.

When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

OR and RA will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2009). We will resolve any disagreement by discussion or by involving ZA.

(1) Sequence generation (checking for possible selection bias)

We will describe for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We will assess the method as:

- adequate (any truly random process, e.g. random number table; computer random number generator);
- inadequate (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear.

(2) Allocation concealment (checking for possible selection bias)

We will describe for each included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We will assess the methods as:

- adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear.

(3) Blinding (checking for possible performance bias)

We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will judge studies at low risk of bias if they were blinded, or if we judge that the lack of blinding could not have affected the results. We will assess blinding separately for different outcomes or classes of outcomes.

We will assess the methods as:

- adequate, inadequate or unclear for participants;
- adequate, inadequate or unclear for personnel;
- adequate, inadequate or unclear for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake. We will assess methods as:

- adequate (10% or less missing data);
- inadequate (incomplete outcome data more than 10%);
- unclear (information on incomplete outcome data not available).

(5) Selective reporting bias

We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We will assess the methods as:

- adequate (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- inadequate (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear.

(6) Other sources of bias

We will describe for each included study any important concerns we have about other possible sources of bias.

We will assess whether each study was free of other problems that could put it at risk of bias:

- yes;
- no;
- unclear.

(7) Overall risk of bias

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2009). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we will present results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardised mean difference to combine trials that measure the same outcome, but use different methods.

Unit of analysis issues

We will not include cluster-randomised studies or crossover trials.

Dealing with missing data

For included studies, we will note levels of attrition. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and analyse all participants in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We will assess statistical heterogeneity in each meta-analysis using the T^2, I^2 and Chi^2 statistics. We will regard heterogeneity as substantial if I^2 is greater than 30% and either T^2 is greater than zero, or there is a low P value (< 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

If there are 10 or more studies in the meta-analysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually, and use formal tests for funnel plot asymmetry. For continuous outcomes we will use the test proposed by Egger 1997, and for dichotomous outcomes we will use the test proposed by Harbord 2006. If we detect asymmetry in any of these tests or by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2008). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect: i.e. where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. We will treat the random-effects summary as the average range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful, we will not combine trials.

If we use random-effects analyses, we will present the results as the average treatment effect with its 95% confidence interval, and the estimates of T^2 and I^2.

Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

We plan to carry out the following subgroup analyses:

1. previous caesarean section versus no previous caesarean section.

We will use the following outcomes in subgroup analysis:

- severe postpartum haemorrhage (blood loss more than 1500 ml);
- caesarean hysterectomy;
- maternal death.

For fixed-effect inverse variance meta-analyses we will assess differences between subgroups by interaction tests. For random-effects and fixed-effect meta-analyses using methods other than inverse variance, we will assess differences between subgroups by inspection of the subgroups' confidence intervals; non-overlapping confidence intervals indicate a statistically significant difference in treatment effect between the subgroups.

Sensitivity analysis

We will carry out sensitivity analyses for aspects of the review that might affect the results, for example, where there is risk of bias associated with the quality of some of the included trials. We will also perform sensitivity analysis to explore the effects of fixed-effect or random-effects analyses for outcomes with statistical heterogeneity.

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As part of the pre-publication editorial process, this protocol has been commented on by four peers (an editor and three referees who are external to the editorial team) and the Group's Statistical Adviser.

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CONTRIBUTIONS OF AUTHORS

Oybek Rustamov and Zarko Alfirevic prepared the protocol with assistance from Alana Mitchell. Rohit Arora and Iram Siddique commented on the protocol.

DECLARATIONS OF INTEREST

None known.