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Anticoagulant therapy for deep vein thrombosis (DVT) in pregnancy

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Abstract

Background—Thromboembolic complications are much higher in pregnancy due to procoagulant changes. Heparin does not cross the placenta and the use of unfractionated heparin (UFH) is the current established practice in prophylaxis and treatment for thromboembolism in pregnancy.

Objectives—To compare the effectiveness of anticoagulant therapies for the treatment of deep vein thrombosis in pregnancy. The anticoagulant drugs included are UFH, low molecular weight heparin (LMWH) and warfarin.

Search methods—We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (March 2010) and reference lists of retrieved studies.

Selection criteria—Randomised controlled trials comparing any combination of warfarin, UFH, LMWH and placebo in pregnant women.

Data collection and analysis—We used methods described in the Cochrane Handbooks for Systemic Reviews of Interventions for assessing the eligibility of studies identified by the search strategy. A minimum of two review authors independently assessed each study.

Main results—We did not identify any eligible studies for inclusion in the review.

We identified three potential studies; after assessing eligibility, we excluded all three as they did not meet the prespecified inclusion criteria. One study compared LMWH and UFH in pregnant

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CONTRIBUTIONS OF AUTHORS

The five review authors were involved in the planning and development of the protocol. One review author (Che Anuar Che Yaakob) drafted the protocol, incorporating suggestions from other review authors. CACY, NAZNL, and JJH jointly wrote the data input and text of the review, with input from the other authors.

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DECLARATIONS OF INTEREST

None known.

women with previous thromboembolic events and, for most of these women, anticoagulants were used as thromboprophylaxis. There were only three women who had a thromboembolic event during the current pregnancy and it was unclear whether the anticoagulant was used as therapy or prophylaxis. We excluded one study because it included only women undergoing caesarean birth. The third study was not a randomised trial.

Authors' conclusions—There is no evidence from randomised controlled trials on the effectiveness of anticoagulation for deep vein thrombosis in pregnancy. Further studies are required.

Medical Subject Headings (MeSH)

Anticoagulants [*therapeutic use]; Heparin [therapeutic use]; Heparin, Low-Molecular-Weight [therapeutic use]; Pregnancy Complications, Hematologic [*drug therapy]; Venous Thrombosis [*drug therapy]; Warfarin [therapeutic use]

MeSH check words

Female; Humans; Pregnancy

BACKGROUND

Deep vein thrombosis in pregnancy

Deep vein thrombosis (DVT) is a serious problem in the antenatal and postpartum period of pregnancy. Thromboembolic complications are the leading cause of both maternal and fetal morbidity and mortality (Greer 2002). The incidence of venous thromboembolism during normal pregnancy is six-fold higher than in the general female population of childbearing age (Holmes 2005).

Pathophysiology

During normal pregnancy there are substantial changes in the haemostatic system, many of which are procoagulant and are thought to be in preparation for the haemostatic challenge of delivery. Normal haemostasis requires a balance between coagulation and fibrinolysis to maintain the integrity of the vasculature. The complex physiological changes evident during pregnancy appear to ensure a constant coagulation-fibrinolysis balance. The balance is maintained, at least partly, by an increase in fibrinolytic activity, but decreases in other factors such as factor XI, and monocyte tissue factor expression may also serve to counter balance procoagulation changes.

Anticoagulant therapy

Anticoagulant therapy is the standard treatment for DVT but is mostly used in non-pregnant patients (RCOG 2007). In pregnancy, unfractionated heparin (UFH) and low molecular weight heparin (LMWH) are commonly used. Warfarin therapy is generally avoided in pregnancy because of its fetal toxicity.

LMWH has been shown to be as safe and effective as UFH for the treatment of acute venous thrombosis and non life-threatening pulmonary embolism (Gouin-Thibault 2005). LMWH

are anticoagulants of choice when rapid anticoagulant effect is required. LMWH has several advantages over UFH, including a longer plasma half life, higher bioavailability and a predictable dose response, which enable once or twice-daily dosing, and a more convenient route of administration (Turpie 2002).

The main adverse effect of UFH and LMWH is bleeding. The non-haemorrhagic adverse effects of UFH include heparin-induced thrombocytopenia (HIT) and osteoporosis which is less with LMWH. HIT is a life-threatening condition that is associated with the development of antibodies, which activates platelets and the coagulation system in the presence of UFH or LMWH (Dager 2003).

The safety of LMWH administration for the mother and fetus has not been well established. Enoxaparin has been shown not to cross the placenta and therefore, appears safe for the fetus (Dimitrakakis 2000). It is uncertain whether weight adjusted dosage regimens without laboratory monitoring can be used in pregnant women (Gouin-Thibault 2005).

Diagnosis

Therapy is usually initiated following a clinical diagnosis of venous thrombosis. Therapy is continued while awaiting diagnostic tests such as Doppler ultrasound (compression or duplex scanning) or X-ray venography which is the gold standard. D-Dimer, a screening test for DVT with high negative predictive value is used in the non-pregnant patient. Its use in pregnancy is still controversial.

Mode of administration of anticoagulant

The mode of administration influences the effectiveness of anticoagulant therapy. UFH is administered intravenously at initiation to achieve rapid therapeutic anticoagulation. For convenience, UFH is subsequently administered subcutaneously. Intravenous administration has a more rapid onset and is therapeutically more reliable than subcutaneous administration. However, intravenous administration is difficult to maintain on a long-term basis.

Subcutaneous injection of LMWH leads to less pain due to smaller injection volume. However, the patient may still suffer from bruises.

Warfarin therapy is easier to administer but it is usually avoided in pregnancy due to its embryopathy effect.

Monitoring of anticoagulant therapy

Patients receiving anticoagulant therapy are monitored to observe therapeutic efficacy as well as side effects. Haemorrhagic complications are clinically assessed. Patients receiving UFH, LMWH and warfarin are routinely monitored with APTT, anti-Xa activity and INR respectively. Platelet count is occasionally assessed especially on patients receiving UFH and LMWH. Patient knowledge of proper injection technique, prevention and recognition of complications are re-emphasised during follow up.

OBJECTIVES

The objective of this review is to compare the effectiveness of anticoagulant therapies for the treatment of deep vein thrombosis in pregnancy. The anticoagulant drugs included are unfractionated heparin, low molecular weight heparin and warfarin.

METHODS

Criteria for considering studies for this review

Types of studies—Randomised or quasi-randomised controlled trials.

Types of participants—Pregnant women with deep vein thrombosis diagnosed clinically or by radioiogy imaging.

Types of interventions

1. Warfarin versus placebo.
2. UFH versus placebo.
3. LMWH versus placebo.
4. UFH versus LMWH.

Types of outcome measures

Primary outcomes

1. Propagation or resolution of thrombosis (measured on imaging).
2. Combined outcome of serious side effects (pulmonary embolism, stroke or death).
3. Pulmonary embolism.
4. Mortality.
5. Stroke and intracerebral haemorrhage.

Secondary outcomes

1. Recurrent DVT.
2. Leg ulceration.
3. Convenience of dosing (staff and participant).
4. Thrombocytopenia.
5. Osteoporosis.
6. Haemorrhage.
7. Duration of hospital stay.
8. Fetal outcome (warfarin embryopathy), fetal intrauterine death, neonatal outcome, neurodevelopmental outcome in children.

Search methods for identification of studies

Electronic searches—We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group's Trials Register (March 2010).

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.

Searching other resources—We searched the reference lists of retrieved studies.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies—Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved disagreement through discussion and consultation with a third author.

In this version of the review we did not identify any studies eligible for inclusion, and so in the following sections we set out the methods we will use in future updates if relevant papers are subsequently identified.

Data extraction and management—We have designed a form to extract data. For eligible studies, two review authors (CACY and NAZNL) planned to extract the data using the agreed form and to resolve discrepancies through discussion or by consulting a third author (JJH). We planned to enter data into Review Manager software (RevMan 2008) and check them for accuracy.

Assessment of risk of bias in included studies—Two review authors (CACY and NAZNL) planned to independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008) and resolve any disagreement by discussion or by involving a third assessor (JJH).

(1) Sequence generation (checking for possible selection bias): We planned to 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 planned to 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 planned to 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 planned to 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 planned to 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 planned to judge studies at low risk of bias if they were blinded, or if we judged that the lack of blinding could not have affected the results. We planned to assess blinding separately for different outcomes or classes of outcomes.

We planned to 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 planned to describe for each included study, and for each outcome or class of outcomes, the completeness of data, including attrition and exclusions from the analysis, and to state whether attrition and exclusions are 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 are balanced across groups or related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we intend to re-include missing data in the analyses. We planned to assess methods as:

- adequate (e.g. where there is no missing data or low levels (less than 10%) and where reasons for missing data are balanced across groups);
- inadequate (e.g. where there are high levels of missing data (more than 10%));
- unclear (e.g. where there is insufficient reporting of attrition or exclusions to permit a judgement to be made).

(5) Selective reporting bias: We planned to describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We planned to assess the methods as:

- adequate (where it was clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review are reported);
- inadequate (where not all the study's pre-specified outcomes are reported; one or more reported primary outcomes are 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 planned to describe for each included study any important concerns we have about other possible sources of bias.

We planned to assess whether each study is free of other problems that could put it at risk of bias:

- yes;
- no;
- unclear.

(7) Overall risk of bias: We planned to make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2008). With reference to (1) to (6) above, we then planned to assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. If more than one study is included we intend to 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 planned to present results as summary risk ratio with 95% confidence intervals.

Continuous data—If there are any continuous data, we intended to use the mean difference if outcomes were measured in the same way between trials and the standardised mean difference to combine trials measuring the same outcome, but using different methods.

Dealing with missing data

For included studies, we intended to note levels of attrition. We intended to 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 intended that analyses would be carried out, as far as possible, on an intention-to-treat basis, i.e. we would attempt to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial would be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We planned to use the I^2 statistic to examine heterogeneity among the trials in each analysis and if we identified substantial heterogeneity we intended to explore it by pre-specified subgroup analysis.

Data synthesis

We intended to enter data and, if we pooled results from several trials, to carry out statistical analysis, both using the Review Manager software (RevMan 2008) using a fixed-effect inverse variance meta-analysis for combining data where trials examined the same intervention, and the trials' populations and methods were judged sufficiently similar. Where we suspected clinical or methodological heterogeneity between studies sufficient to suggest that treatment effects may differ between trials, we intended to use random-effects meta-analysis.

If we identified substantial heterogeneity in a fixed-effect meta-analysis, we planned to note this and to repeat the analysis using a random-effects method.

Subgroup analysis and investigation of heterogeneity

We planned the following subgroup analyses.

1. Stage of pregnancy at diagnosis, i.e. first trimester, second trimester, third trimester.

Sensitivity analysis

We intended to carry out sensitivity analysis to explore the effect of trial quality assessed by concealment of allocation; we intended to exclude studies with clearly inadequate allocation concealment.

RESULTS

Description of studies

See: Characteristics of excluded studies.

We found three potential studies. One study comparing LMWH and UFH included a total of 105 women (Pettilä 1999) with previous thromboembolic events; for most of these women, anticoagulants were used as thromboprophylaxis. There were only three women who had a

thromboembolic event during this current pregnancy and it was unclear whether the anticoagulant was used as therapy or prophylaxis. We therefore excluded this study. We excluded one study (Burrows 2001) comparing LMWH and placebo because it included only women undergoing caesarean birth. The third study (Rodie 2002) was a prospective observational study and we excluded it for this reason. We have provided further details of the excluded studies in the Characteristics of excluded studies table.

Risk of bias in included studies

We found no randomised trials suitable for inclusion in the review.

Effects of interventions

We found no randomised trials suitable for inclusion in the review.

DISCUSSION

There is no evidence from randomised controlled trials on the effectiveness of anticoagulation for deep vein thrombosis in pregnancy. There is also very little evidence from non-random studies. In a prospective uncontrolled observational study, Rodie 2002 reported on the administration of 1mg/kg of the LMWH enoxaprin to 33 women (29 during pregnancy) with thromboembolic events. Since no haemorrhagic events occurred, further studies comparing LMWH with UFH need to be carried out.

There are two other Cochrane Reviews comparing LMWH and UFH in other clinical settings (Akl 2008; Van Dongen 2004). Akl 2008 compared LMWH and UFH in patients with cancer and venous thromboembolism and found reduced mortality in the LMWH group. However, there was inconclusive evidence about venous thromboembolism, and bleeding was not reported. Van Dongen 2004 compared LMWH and UFH in hospitalised patients with confirmed venous thromboembolism (DVT or PE), and found LMWH was more effective in reducing thrombotic complications and thrombus size, as well as fewer major haemorrhages in the LMWH group. Overall, these two reviews provide evidence that LMWH is superior to UFH in the treatment of venous thromboembolism outside of the context of pregnancy. A further Cochrane Review (Gates 2002) examines prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. Although there were sixteen studies that qualified for inclusion in the Gates 2002 review, the authors conclude that there is insufficient evidence to make recommendations for thromboprophylaxis in this setting.

In conclusion there is no evidence from randomised controlled trials about the efficacy of LMWH for the treatment of DVT in pregnancy.

AUTHORS' CONCLUSIONS

Implications for practice

This systematic review is unable to draw any conclusions on the effectiveness of LMWH compared to UFH for treating thromboembolic disease in pregnancy. The effectiveness of LMWH compared with UFH has been established elsewhere but at present we cannot

recommend its use during pregnancy. Further trials are needed. At this stage we are unable to recommend the adoption of LMWH as a standard clinical practice during pregnancy.

Implications for research

Further studies are required to compare LMWH and UFH in patients with deep vein thrombosis during pregnancy. Where possible, blinding of outcome assessors should be practised.

The use of warfarin (compared to LMWH) also needs to be evaluated to confirm or deny reports of warfarin's toxicity when used during pregnancy.

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As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

SOURCES OF SUPPORT

Internal sources

- Universiti Sains Malaysia, Malaysia.
- Penang Medical College, Malaysia.

External sources

- SEA-ORCHID Project, Malaysia.

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DATA AND ANALYSES

This review has no analyses.

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 6, 2010

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Burrows 2001	RCT of LMWH compared to placebo in women undergoing caesarean birth. Does not meet inclusion criteria for this review
Pettilä 1999	Trial of thromboprophylaxis and not therapy. RCT of LMWH compared to UFH thromboprophylaxis in women with a previous DVT. 3 of the 107 women had a thromboembolic episode during the current pregnancy and the remaining women had previous episodes of DVT
Rodie 2002	This was not a RCT. This prospective observational study reported on the administration of LMWH to 33 women (29 during pregnancy) with thromboembolic events

DVT: deep vein thrombosis

LMWH: low molecular weight heparin

RCT: randomised controlled trial

References to studies excluded from this review

- Burrows 2001 {published data only} . Burrows RF, Gan ET, Gallus AS, Wallace EW, Burrows EA. A randomised double-blind placebo controlled trial of low molecular weight heparin as prophylaxis in preventing venous thrombotic events after caesarean section: a pilot study. *British Journal of Obstetrics and Gynaecology*. 2001; 108:835–9. [PubMed: 11510709]
- Pettilä 1999 {published data only} . Pettila V, Kaaja R, Leinonen P, Ekblad U, Kataja M, Ikhala E. Thromboprophylaxis with low molecular weight heparin (Dalteparin) in pregnancy. *Thrombosis Research*. 1999; 96:275–82. [PubMed: 10593430]
- Pettila V, Leinonen P, Markkola A, Hiilesmaa V, Kaaja R. Postpartum bone mineral density in women treated for thromboprophylaxis with unfractionated heparin or LMW heparin. *Thrombosis and Haemostasis*. 2002; 87(2):182–6. [PubMed: 11858475]
- Rodie 2002 {published data only} . Rodie VA, Thomson AJ, Stewart FM, Quinn AJ, Walker ID, Greer IA. Low molecular weight heparin for the treatment of venous thromboembolism in pregnancy: a case series. *BJOG: an international journal of obstetrics and gynaecology*. 2002; 109:1020–24. [PubMed: 12269676]

Additional references

- Akl 2008 . Akl EA, Rohilla S, Barba M, Sperati F, Terrenato I, Muti P, et al. Anticoagulation for the initial treatment of venous thromboembolism in patients with cancer. *Cochrane Database of Systematic Reviews*. 2008; (Issue 1) [DOI: 10.1002/14651858.CD006466].
- Dager 2003 . Dager WE, White RH. Pharmacotherapy of heparin-induced thrombocytopenia. *Expert Opinion on Pharmacotherapy*. 2003; 4(6):919–40. [PubMed: 12783589]
- Dimitrakakis 2000 . Dimitrakaki C, Papageorgio P, Papageorgiou I, Antzaklis A, Sakarelou N, Michalas S. Absence of transplacental passage of the low molecular weight heparin enoxaparin. *Haemostasis*. 2000; 30:243–8. [PubMed: 11251331]
- Gates 2002 . Gates S, Brocklehurst P, Davis LJ. Prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. *Cochrane Database of Systematic Reviews*. 2002; (Issue 2) [DOI: 10.1002/14651858.CD001689].
- Gouin-Thibault 2005 . Gouin-Thibault I, Pautus E, Siguret V. Safety profile of different low-molecular weight heparins used at therapeutic dose. *Drug Safety*. 2005; 28(4):333–49. [PubMed: 15783242]
- Greer 2002 . Greer IA. Exploring the role of low-molecular-weight heparins in pregnancy. *Seminars in Thrombosis and Hemostasis*. 2002; 28(Suppl 3):25–31. [PubMed: 12232820]

- Higgins 2008 . Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [updated September 2008]. The Cochrane Collaboration. 2008 Available from www.cochrane-handbook.org.
- Holmes 2005 . Holmes VA, Wallance JMW. Haemostasis in normal pregnancy: a balancing act? Biochemical Society Transactions. 2005; 33(Pt 2):428–32. [PubMed: 15787621]
- RCOG 2007 . Royal College of Obstetricians and Gynaecologists. Green-top Guideline no. 27. RCOG; London: 2007. Thromboembolic disease in pregnancy and the puerperium: acute management.
- RevMan 2008 . The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.0. The Nordic Cochrane Centre, The Cochrane Collaboration; Copenhagen: 2008.
- Turpie 2002 . Turpie AGG, Mason JA. Review of enoxaparin and its clinical applications in venous and arterial thromboembolism. Expert Opinion on Pharmacology. 2002; 3(5):575–98.
- Van Dongen 2004 . Van Dongen CJ, Van den Belt AGM, Prins MH, Lensing AWA. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for venous thromboembolism. Cochrane Database of Systematic Reviews. 2004; (Issue 4) [DOI: 10.1002/14651858.CD001100.pub2].

* *Indicates the major publication for the study*

PLAIN LANGUAGE SUMMARY

Anticoagulation therapy for serious blood clots during pregnancy

Pregnant women are more susceptible than non-pregnant women to forming blood clots in their veins (venous thrombosis). When these clots occur in the deep leg veins, the clot can break up and fragments (emboli) move to the lungs where they may block the blood flow to the lungs (pulmonary embolism). This can have serious consequences.

Anticoagulants are used to treat clots and are given to pregnant women with increased susceptibility to clotting. These medications thin the blood to reduce the risk of the further thrombosis and reduce the risk of pulmonary embolism. An important complication of treatment is haemorrhage. During pregnancy heparin is the most common anticoagulant used, either the older unfractionated heparin (UFH) or the newer low molecular weight heparin (LMWH). Neither of these cross the placenta, and both have been shown to be safe during pregnancy, whereas there are concerns that warfarin may affect the fetus. LMWH has been shown to be more effective than UFH outside pregnancy.

In this review we planned to compare these two types of heparin in pregnancy for their ability to reduce clotting and their safety. We could not find any randomised controlled trials for inclusion in the review.

This means that we do not have any evidence from randomised controlled trials on the effectiveness of anticoagulation for deep vein thrombosis in pregnancy, and the effectiveness of LMWH compared to UFH. There is a need for further studies in this area.