Complete Summary

GUIDELINE TITLE

Thromboembolic disease in pregnancy and the puerperium: acute management.

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). Thromboembolic disease in pregnancy and the puerperium: acute management. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2007 Feb. 17 p. (Green-top guideline; no. 28). [99 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Royal College of Obstetricians and Gynaecologists (RCOG). Thromboembolic disease in pregnancy and the puerperium: acute management. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2001 Feb.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism during pregnancy and in the puerperium

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide information, based on clinical evidence, where available, regarding the immediate investigation and management of women in whom venous thromboembolism is suspected during pregnancy or the puerperium

TARGET POPULATION

Women with suspected venous thromboembolism during pregnancy or the puerperium

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Compression duplex ultrasound
2. Chest x-ray
3. Ventilation-perfusion lung scan
4. Computed tomography pulmonary angiogram

Note: D-dimer testing was considered but not recommended.

Management/Treatment

1. Anticoagulant therapy
    - Low-molecular-weight heparin (LMWH)
    - Intravenous unfractionated heparin in massive pulmonary thromboembolism with cardiovascular compromise
    - Maintenance therapy (LMWH, or heparinoid, danaparoid sodium, or fondaparinux)
2. Postnatal anticoagulation therapy
3. Prevention of post-thrombotic leg syndrome (graduated elastic compression stockings)

Note: Oral anticoagulants were considered but not recommended for anticoagulant therapy during pregnancy.

MAJOR OUTCOMES CONSIDERED

- Incidence of venous thromboembolism (VTE)
- VTE recurrence rate
- Maternal mortality and morbidity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A search of Medline and PubMed (electronic databases) 1966–2005 was performed to identify all relevant randomised controlled trials, systematic reviews, and meta-analyses. The databases were searched using the relevant Medical Subject Heading (MeSH) terms including all subheadings. The principle terms used were: "venous thromboembolism," "deep venous thrombosis," "pulmonary thromboembolism," and "pregnancy."

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analyses of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The recommendations were graded according to the level of evidence upon which they were based. The grading scheme used was based on a scheme formulated by the Clinical Outcomes Group of the National Health Service Executive.

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

Grade B - Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following discussion in the Guidelines and Audit Committee, each green-top guideline is formally peer reviewed. At the same time the draft guideline is published on the Royal College of Obstetricians and Gynaecologists Web site for further peer review discussion before final publication.

The names of author(s) and nominated peer reviewers are included in the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

Levels of evidence (**Ia-IV**) and grading of recommendations (**A-C**) are defined at the end of the "Major Recommendations" field.

Diagnosis of Acute Venous Thromboembolism (VTE)

How Is Acute VTE Diagnosed in Pregnancy?

C - Any woman with signs and symptoms suggestive of VTE should have objective testing performed expeditiously and treatment with low-molecular-weight heparin (LMWH) (see section "Initial anticoagulant treatment of VTE in pregnancy" below) until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated.

What Investigations Are Needed for the Diagnosis of an Acute DVT?

C - Compression duplex ultrasound should be undertaken where there is clinical suspicion of deep venous thrombosis (DVT). If ultrasound is negative and there is a low level of clinical suspicion, anticoagulant treatment can be discontinued.

Compression duplex ultrasound is the primary diagnostic test for DVT. If ultrasound confirms the diagnosis of DVT, anticoagulant treatment should be continued. If ultrasound is negative and a high level of clinical suspicion exists, the woman should remain anticoagulated and ultrasound repeated in 1 week or an alternative diagnostic test employed. If repeat testing is negative, anticoagulant treatment should be discontinued. (Evidence level IV)

When iliac vein thrombosis is suspected (back pain and swelling of the entire limb), magnetic resonance venography or conventional contrast venography may be considered. (Evidence level IV)

What Investigations Are Needed for the Diagnosis of an Acute Pulmonary Thromboembolism (PTE)?

C - Where there is clinical suspicion of acute PTE a chest x-ray should be performed. Compression duplex Doppler should be performed where this is normal. If both tests are negative with persistent clinical suspicion of acute PTE, a ventilation–perfusion (V/Q) lung scan or a computed tomography pulmonary angiogram (CTPA) should be performed.

C - Alternative or repeat testing should be carried out where V/Q scan or CTPA and duplex Doppler are normal but the clinical suspicion of PTE is high. Anticoagulant treatment should be continued until PTE is definitively excluded.

B - Women with suspected PTE should be advised that V/Q scanning carries a slightly increased risk of childhood cancer compared with CTPA (1/280,000 versus less than 1/1,000,000) but carries a lower risk of maternal breast cancer (lifetime risk increased by up to 13.6% with CTPA, background risk of 1/200 for study population).

Chest x-ray may identify other pulmonary disease such as pneumonia, Pneumothorax, or lobar collapse. Whilst the x-ray is normal in over 50% of pregnant women with objectively proven PTE, abnormal features caused by PTE include atelectasis, effusion, focal opacities, regional oligaemia, or pulmonary oedema. The radiation dose to the fetus from a chest x-ray performed at any stage of pregnancy is negligible. If the x-ray is abnormal with a high clinical suspicion of PTE, CTPA should be performed. (Evidence level IV)

If the x-ray is normal, bilateral Doppler ultrasound leg studies should be performed. Although the use of lower-limb Doppler ultrasound in the investigation of PTE has not been validated in pregnancy, there have been several studies investigating its role in nonpregnant women with suspected PTE. A diagnosis of DVT may indirectly confirm a diagnosis of PTE and, since anticoagulant therapy is the same for both conditions, further investigation may not be necessary.This would limit the radiation doses given to the mother and her fetus. (Evidence level IV)

Should D-dimer Testing Be Performed Prior to Objective Diagnosis?

C - D-dimer testing should not be performed to diagnose acute VTE in pregnancy

Baseline Blood Investigations

The use of anticoagulant therapy can be influenced by renal and hepatic function and blood should be taken to confirm that these are normal before starting treatment.

Initial Anticoagulant Treatment of VTE in Pregnancy

What is the Initial Treatment of VTE in Pregnancy?

C - In clinically suspected DVT or PTE, treatment with LMWH should be given until the diagnosis is excluded by objective testing, unless treatment is strongly contraindicated.

What Is the Therapeutic Dose of LMWH in Pregnancy?

See Table 1 in the original guideline document for calculation of initial doses of drugs by early pregnancy weight.

Should Blood Tests Be Performed to Monitor LMWH Therapy in Pregnancy?

If the diagnosis of VTE is confirmed (DVT or PTE), treatment should be continued. Experience indicates that satisfactory anti-Xa levels (peak anti-Xa activity, 3 hours post-injection, of 0.5–1.2 units/mL) are obtained using a weight-based regimen and monitoring of anti-Xa is not routinely required in women with VTE on therapeutic doses of LMWH, particularly as there are concerns over the accuracy of anti-Xa monitoring. There may be a case for monitoring levels at extremes of body weight (less than 50 kg and 90 kg or more) and women with other complicating factors, including renal disease and recurrent VTE.

Guideline documents recommend that routine platelet count monitoring is not required in obstetric women who have received only LMWH as there have been no cases of heparin-induced thrombocytopenic thrombosis in pregnancies managed with LMWH. If unfractionated heparin is employed, or if the obstetric patient is receiving LMWH after first receiving unfractionated heparin, or if she has received unfractionated heparin in the past, the platelet count should ideally be monitored every 2 to 3 days from day 4 to day 14 or until heparin is stopped, whichever occurs first.

How Should Massive Life-Threatening PTE in Pregnancy be Managed?

B - Intravenous unfractionated heparin is the preferred treatment in massive PTE with cardiovascular compromise.

In massive life-threatening PTE with haemodynamic compromise there is a case for considering thrombolytic therapy, as anticoagulant therapy will not reduce the

obstruction of the pulmonary circulation. After thrombolytic therapy has been given, an infusion of unfractionated heparin can be given but the loading dose should be omitted.

If the woman is not suitable for thrombolysis or is moribund, a discussion with the cardiothoracic surgeons with a view to urgent thoracotomy should be undertaken.

Additional Therapies

What Additional Therapies Should Be Employed in the Management of VTE in Pregnancy?

Pain and swelling in the affected leg are debilitating symptoms of DVT. Short-term studies in patients with proximal DVT showed that pain and swelling improved faster in mobile patients wearing compression hosiery than in those resting in bed without any compression. This approach can also prevent the development of post-thrombotic syndrome.

There is evidence that the use of an inferior vena caval filter prior to labour or delivery reduces the risk of PTE. However, when VTE occurs in the antepartum period, delivery should be delayed, if possible, to allow maximum time for anticoagulation rather than putting in a filter.

Maintenance Therapy of VTE

What Is the Maintenance Treatment of DVT or PTE?

B - Treatment with therapeutic doses of subcutaneous LMWH should be employed during the remainder of the pregnancy.

C - Pregnant women who develop heparin-induced thrombocytopenia or have heparin allergy and require continuing anticoagulant therapy should be managed with the heparinoid, danaparoid sodium or fondaparinux, under specialist advice.

Can Oral anticoagulants Be Used During Pregnancy for the Maintenance Treatment of VTE?

C - Because of their adverse effects on the fetus, oral anticoagulants should not be used for antenatal VTE treatment.

Anticoagulant Therapy During Labour and Delivery

Should Anticoagulant Therapy Be Altered During Labour and Delivery?

In order to avoid an unwanted anticoagulant effect during delivery, LMWH should be stopped as soon as a woman is in established labour or thinks she is in labour. For elective delivery, LMWH should be stopped 24 hours before induction of labour or caesarean section. Bleeding complications appear to be very uncommon with LMWH.

Postnatal Anticoagulation

How Should Anticoagulation Be Managed Postnatally?

C - Therapeutic anticoagulant therapy should be continued for the duration of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total.

Prevention of Post-thrombotic Leg Syndrome

What Measures Can Be Employed to Prevent the Development of Post-Thrombotic Syndrome?

A - Graduated elastic compression stockings should be worn on the affected leg for 2 years after the acute event, if swelling persists, to reduce the risk of post-thrombotic syndrome.

Postnatal Clinic Review

At the postnatal review, an assessment should be made of post-thrombotic venous damage, thrombophilia tests should be reviewed and arrangements made to repeat them if necessary. Advice should be given on the need for thromboprophylaxis in any future pregnancy and at other times of increased risk. Hormonal contraception should be discussed.

Definitions:

Grading of Recommendations

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)

Grade B - Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Levels of Evidence

Ia: Evidence obtained from meta-analyses of randomised controlled trials

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IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis, appropriate management, and effective prevention of venous thromboembolism in pregnancy and the puerperium.

POTENTIAL HARMS

- There is a slightly increased risk of childhood cancer with ventilation–perfusion (V/Q) scanning compared with computed tomography pulmonary angiogram (CTPA) (1/280,000 versus less than 1/1,000,000) but V/Q carries a lower risk of maternal breast cancer (lifetime risk increased by up to 13.6% with CTPA, background risk of 1/200 for study population).
- Adverse effects of anticoagulants on mother and fetus
- Heparin-induced thrombocytopenia

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines are "systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions." Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: Guidance for the Development of RCOG Green-top Guidelines (See the "Availability of Companion Documents" field in this summary.)
- These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local

ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). Thromboembolic disease in pregnancy and the puerperium: acute management. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2007 Feb. 17 p. (Green-top guideline; no. 28). [99 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Apr (revised 2007 Feb)

GUIDELINE DEVELOPER(S)

Royal College of Obstetricians and Gynaecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

Royal College of Obstetricians and Gynaecologists

GUIDELINE COMMITTEE

Guidelines and Audit Committee of the Royal College of Obstetricians and Gynaecologists

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: Professor IA Greer, FRCOG, Glasgow and Dr AJ Thomson, MRCOG, Paisley

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Guideline authors are required to complete a "declaration of interests" form.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Royal College of Obstetricians and Gynaecologists (RCOG). Thromboembolic disease in pregnancy and the puerperium: acute management. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2001 Feb.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.

Print copies: Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Bookshop, 27 Sussex Place, Regent's Park, London NW1 4RG; Telephone: +44 020 7772 6276; Fax, +44 020 7772 5991; e-mail: bookshop@rcog.org.uk. A listing and order form are available from the RCOG Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Development of RCOG green-top guidelines: policies and processes. Clinical Governance Advice No 1a. 2006 Nov. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.
- Development of RCOG green-top guidelines: producing a scope. Clinical Governance Advice No 1b. 2006 Nov. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.

- Development of RCOG green-top guidelines: producing a clinical practice guideline. Clinical Governance Advice No 1c. 2006 Nov. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.
- Searching for evidence. Clinical Governance Advice No 3. 2001 Oct. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.

Additionally, auditable standards can be found in section 13 of the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on November 30, 2007. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection.

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DISCLAIMER

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Readers with questions regarding guideline content are directed to contact the guideline developer.

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