Complete Summary

GUIDELINE TITLE

The management of gestational trophoblastic neoplasia.

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). The management of gestational trophoblastic neoplasia. London (UK): Royal College of Obstetricians and Gyneacologists (RCOG); 2004 Feb. 7 p. (Guideline; no. 38). [16 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Gestational trophoblastic neoplasia (GTN) (hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumour)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Obstetrics and Gynecology
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide guidance on the management of women with gestational trophoblastic neoplasia in the United Kingdom

TARGET POPULATION

Women with gestational trophoblastic neoplasia (GTN) (hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumour)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Ultrasound scanning
2. Estimation of human chorionic gonadotrophin (hCG) levels

Management

1. Evacuation of molar pregnancies
    - Surgical evacuation (suction curettage)
    - Medical termination (oxytocic infusions, prostaglandin analogues)
2. Histological examination of products of conception
3. Consultation with screening centre (for women with persistent symptoms following evacuation)
4. Pregnancy test (for women with persistent abnormal vaginal bleeding)
5. Urgent referral in cases where indicated
6. Management of placental site trophoblastic tumour
    - Consultation with appropriate registration centre
    - Surgery
    - Multi-agent chemotherapy
7. Future pregnancy management
8. Contraception and hormone replacement therapy

MAJOR OUTCOMES CONSIDERED

- Cure rates
- Chemotherapy rates
- Viable twin pregnancy birth rate
- Complications associated with viable twin pregnancy
- Complications associated with evacuation of molar pregnancy
- Side effects of pharmacological agents
- Risk of further molar pregnancy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Cochrane Database and Medline were searched, using the terms "molar pregnancy," "hydatidiform mole," "gestational trophoblastic disease," "gestational neoplasms," and "choriocarcimona," between the years 1966 and 2003.

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-analysis 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

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 (NHS) 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-conducted 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 experience 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 (RCOG) website for further peer 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 Gestational Trophoblastic Neoplasia

C - Early complete molar pregnancies are commonly associated with the ultrasound diagnosis of delayed miscarriage or anembryonic pregnancy. Complete moles may be associated with suggestive ultrasonographic changes in the placenta. However, ultrasound has limited value in detecting partial molar pregnancies. In twin pregnancies with a viable fetus and a molar pregnancy, the pregnancy should be allowed to proceed.

The ultrasound features of a complete mole are reliable but the ultrasound diagnosis of a partial molar pregnancy is more complex. The finding of multiple soft markers, including both cystic spaces in the placenta and a ratio of transverse to anterior-posterior dimension of the gestation sac of greater than 1.5 is required for the reliable diagnosis of a partial molar pregnancy. Estimation of human chorionic gonadotrophin (hCG) levels may be of value in diagnosing molar pregnancies. When there is diagnostic doubt about the possibility of a combined molar pregnancy with a viable fetus, then ultrasound examination should be repeated before intervention. In the situation of a twin pregnancy, where there is one viable fetus and the other pregnancy is molar, the pregnancy should be allowed to proceed if the mother wishes, following appropriate counselling. [Evidence level III]

Evacuation of Molar Pregnancies

C - Surgical evacuation of molar pregnancies is advisable. Routine repeat evacuation after the diagnosis of a molar pregnancy is not warranted.

Suction curettage is the method of choice of evacuation for complete molar pregnancies. Because of the lack of fetal parts, a suction catheter, up to a maximum of 12 mm, is usually sufficient to evacuate all complete molar pregnancies. Medical termination of complete molar pregnancies, including cervical preparation prior to suction evacuation, should be avoided where possible. There is theoretical concern over the routine use of potent oxytocic agents because of the potential to embolise and disseminate trophoblastic tissue through the venous system. This is known to occur in normal pregnancy, especially when uterine activity is increased (e.g., with accidental haemorrhage). The contraction of the myometrium may force tissue into the venous spaces at the site of the placental bed. The dissemination of this tissue may lead to the profound deterioration in the woman, with embolic and metastatic disease occurring in the lung. [Evidence level III/IV]

While it is recognised that significant haemorrhage may occur as a consequence of evacuating a large uterine cavity, it is recommended, where possible, that oxytocic infusions are only commenced once evacuation has been completed. If the woman is experiencing significant haemorrhage prior to evacuation and some

degree of control is required, then use of these agents will be necessary according to the clinical condition. Oxytocic infusions have been in common use for this purpose. It is suggested that prostaglandin analogues should be reserved for cases where oxytocin is ineffective. Because evacuation of a large molar pregnancy is a rare event, advice and help from an experienced colleague should be sought where appropriate. In partial molar pregnancies where the size of the fetal parts deters the use of suction curettage, medical termination can be used. These women may be at an increased risk of requiring treatment for persistent trophoblastic neoplasia, although the proportion of women with partial molar pregnancies needing chemotherapy is low (0.5%).[Evidence level III/IV]

Data from the management of molar pregnancies with mifepristone are limited. Evacuation of complete molar pregnancies with this agent should be avoided at present since it increases the sensitivity of the uterus to prostaglandins. [Evidence level III/IV]

Histological Examination of Products of Conception

C - All products of conception obtained after evacuation (medical or surgical) should undergo histological examination. Products of conception from therapeutic terminations of pregnancy should be examined if there is no evidence of fetal tissue.

In view of the difficulty in making a diagnosis of a molar pregnancy before evacuation, the histological assessment of material obtained from the medical or surgical management of incomplete miscarriage is recommended in order to exclude trophoblastic neoplasia. Ploidy status may help in distinguishing partial from complete moles. Because persistent trophoblastic neoplasia may develop after any pregnancy, it is recommended that all products of conception obtained after repeat evacuation should undergo histological examination. [Evidence level IV]

The Management of Women with Gynaecological Symptoms After Evacuation of a Molar Pregnancy

C - In cases where there are persisting symptoms, such as vaginal bleeding, after initial evacuation, consultation with the screening centre should be sought before surgical intervention.

There is no clinical indication for the routine use of a second uterine evacuation in the management of molar pregnancies. Uterine evacuation may be recommended, in selected cases, by the screening centre as part of the management of persistent trophoblastic neoplasia. [Evidence level IV]

Persistent Gestational Trophoblastic Neoplasia (GTN) after a Nonmolar Pregnancy

C - Women with persistent abnormal vaginal bleeding after a nonmolar pregnancy should undergo a pregnancy test to exclude persistent GTN. Persistent GTN should be considered in any woman developing acute respiratory or neurological symptoms after any pregnancy.

The prognosis for women with GTN after nonmolar pregnancies may be worse (21% mortality after a live birth, 6% after a nonmolar miscarriage) and in part due to the delay in diagnosis (0.5-58.0 months). Urgent referral of such cases should occur. [Evidence level III/IV]

Placental Site Trophoblastic Tumour

C - Advice on the management of these rare tumours should be sought from the appropriate registration centre.

Placental site trophoblastic tumour is now recognised as a variant of GTN. Surgery and multi-agent chemotherapy play major roles in the clinical management of this tumour. [Evidence level III]

Future Pregnancy

C - Women should be advised not to conceive until the hCG level has been normal for six months.

After the conclusion of any further pregnancy, at any gestation, further urine or blood samples for hCG estimation are requested to exclude disease recurrence. Women who undergo chemotherapy are advised not to conceive for one year after completion of treatment. [Evidence level III]

Contraception and Hormone Replacement Therapy

C - The combined oral contraceptive pill and hormone replacement therapy are safe to use after hCG levels have reverted to normal.

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-conducted clinical studies but no randomised clinical trials on the topic of recommendations (evidence levels IIa, IIb, III)

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Levels of Evidence

Ia: Evidence obtained from meta-analysis 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

Appropriate diagnosis and treatment of gestational trophoblastic neoplasia

POTENTIAL HARMS

- In the situation of a twin pregnancy, where there is one viable fetus and the other pregnancy is molar, the pregnancy should be allowed to proceed if the mother wishes, following appropriate counselling. The probability of achieving a viable baby is 40% and there is a risk of complications such as pulmonary embolism and pre-eclampsia.
- There is theoretical concern over the routine use of potent oxytocic agents because of the potential to embolise and disseminate trophoblastic tissue through the venous system.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Clinical 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 Royal College of Obstetricians & Gynaecologists (RCOG) Green-top Guidelines*.

- 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 is 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

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). The management of gestational trophoblastic neoplasia. London (UK): Royal College of Obstetricians and Gyneacologists (RCOG); 2004 Feb. 7 p. (Guideline; no. 38). [16 references]

ADAPTATION

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

DATE RELEASED

2004 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

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Deirdre J Murphy, MRCOG (Chair); Lizzy Dijeh (Secretary); Ms Toni Belfield, Consumers' Representative; Professor P R Braude, FRCOG, Chairman, Scientific Advisory Committee; Mrs C Dhillon, Head of Clinical Governance and Standards Dept.; Dr Martin Dougherty, A. Director NCC-WCH; Miss L M M Duley, FRCOG, Chairman, Patient Information Subgroup; Mr Alan S Evans, FRCOG; Dr Mehmet R Gazvani, MRCOG; Dr Rhona G Hughes, FRCOG; Mr Anthony J Kelly MRCOG; Dr Gwyneth Lewis, FRCOG, Department of Health; Dr Mary A C Macintosh, MRCOG, CEMACH; Dr Tahir A Mahmood, FRCOG; Mrs Caroline E Overton, MRCOG, Reproductive medicine; Dr David Parkin, FRCOG; Oncology; Ms Wendy Riches, NICE; Mr Mark C Slack, MRCOG, Urogynaecology; Mr Stephen A Walkinshaw, FRCOG, Maternal and Fetal Medicine; Dr Eleni Mavrides, Trainees Representative

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.

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:

- Guidance for the development of RCOG green-top guidelines. Clinical Governance Advice No 1. 2000 Jan. 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 Outcomes are provided in section 14 of the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

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