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Reducing blood loss in laparoscopic and open myomectomy: a prospective randomised controlled trial comparing the benefit of triple tourniquets against gonadotropin releasing hormone (GnRH) analogues

Submission date 30/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/09/2005	**Overall study status** Completed	
Last Edited 13/09/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N0256159688

Study information

Scientific Title

Study objectives
Please note that as of 15/09/2008 this trial has been extensively updated. All updates can be found in the relevant field under the above update date. Please also note that the anticipated start and end dates of this trial have also changed. The previous anticipated trial dates are as follows:
Anticipated start date: 01/09/2004
Anticipated end date: 30/09/2006
Finally, please note that the contact details below have changed since the initial assignation of an ISRCTN. The previous contact for this trial was Dr Lynne Chapman at the Royal Free Hampstead NHS Trust.

Current hypothesis as of 15/09/2008:
Fibroids are common benign tumours of the smooth muscle of the uterus. Historically, an open myomectomy or a hysterectomy has been the mainstay of treatment for symptomatic fibroids. Intra-operative haemorrhage is the most feared complication of myomectomy, necessitating blood transfusion or worse, hysterectomy. Several interventions to reduce intra-operative blood loss at myomectomy have been described, including gonadotropin releasing hormone (GnRH) analogues and intra-operative application of triple tourniquets to occlude the uterine blood supply.

GnRH analogues have been used for a long time to shrink fibroids and reduce blood loss. However, these agents are expensive, they need to be taken for several months prior to surgery in order to exert a noticeable effect, they cause unwanted oestrogen deficient symptoms, and because of their tissue effects, they tend to prolong the surgery.

The use of tourniquets to reduce intra-operative blood loss at open myomectomy is well established. A recent randomised controlled trial from our unit confirmed that triple tourniquets applied to the uterine and ovarian vessels significantly reduced operative blood loss, the need for blood transfusion and peri-operative morbidity at open myomectomy compared with controls. We propose to conduct a randomised controlled trial to compare the efficacy of gonadotropin-releasing hormone (GnRH) analogues and triple tourniquets in reducing intra-operative bleeding compared at open and laparoscopic myomectomy.

Initial hypothesis:
Does the application of surgical tourniquets around the major blood supply to the uterus reduce bleeding, thereby need the blood transfusion compared with traditional GnRH analogues?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added 15/09/2008:
Ethics approval received from the Royal Free Hospital & Medical School Local Research and Ethics Committee on the 26th October 2004 (ref: 04/Q0501/94)

Primary study design
Interventional

Study design
Randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fibroids

Interventions
Current interventions as of 15/09/2008:
Patients with symptomatic fibroids requiring open myomectomy will be randomised to treatment with either GnRH analogues pre-operatively for 3 months or intra-operative triple tourniquets.

Pre-randomisation assessment:
Each patient will be identified after history, clinical examination and diagnosis are confirmed by means of imaging techniques. Baseline haemoglobin and follicular stimulating hormone (FSH) will also be estimated.

Treatment:
1. GnRH analogues group: pre-operatively treatment (typically using Nafarelin nasal spray 200 µg twice daily [b.d.] or Zoladex 3.6 mg by intramuscular injection every 28 days) will be administered during the 3 months period prior to surgery.
2. Tourniquet group: these patients will have a tourniquet tied around the infundibulo-pelvic ligaments (thus occluding the ovarian vessels on each side) and a number 1 vicryl suture tied around the cervix to occlude the uterine vessels. The tourniquets around the infundibulo-pelvic ligaments will be removed as soon as the uterus has been repaired following the myomectomy, but the suture around the uterine arteries will be left in situ to be gradually absorbed.

Intra-operative assessment:
Operative blood loss will be measured by weighing all swabs and measuring blood collected by suction.

Post-operative follow-up:
In the immediate post-operative period the amount of blood collected in the pelvic drain will be recorded; the drain will stay in situ for a minimum of 48 hours, and will be removed once the drainage is less than 100 ml in 24 hours. Temperature will be monitored in the usual way every 4 - 6 hours. Haemoglobin (Hb) will be measured on day 2; blood transfusion will be given if Hb is less than 8 g/dl or if it is clinically indicated for other reasons. Prior to discharge from hospital patients will undergo doppler studies of uterine blood flow.

Patients will be reviewed at six weeks, three months and six months after surgery. Symptomatic response to the surgery will be documented together with any complications encountered (including menopausal symptoms). Serum FSH levels will also be checked. Patients undergoing laparoscopic myomectomy will be randomised in the operating theatre to one of two groups

(with or without triple tourniquets). Pre-operative assessment, intra-operative assessment and technique of applying the tourniquets as well as the post-operative care will be exactly as in the case of open myomectomy (as above).

Initial interventions:
Each patient will be identified. History clinical examination and pelvic. Control group: These patients will be having a standard laparoscopic or open myomectomy (depending on size of fibroids) having several GnRH analogues for 3 months first.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Gonadotropin releasing hormone (GnRH) analogues

Primary outcome(s)
Current primary outcome measures as of 15/09/2008:
Intra-operative blood loss, assessed by the standard method of meticulous measurement of blood loss during surgery, measured at conclusion of surgery.

Initial primary outcome measures:
1. Post-operative blood loss + FPC need for blood transfusion
2. Febrile mortality
3. Ovarian function
4. Uterine blood flow
5. General health
6. Menstrual blood loss

Key secondary outcome(s)
Added as of 15/09/2008:
1. Post-operative blood loss, assessed by amount collected in surgical drains and by post-operative changes in haemoglobin, measured after removing the drain, i.e. on average this will be at day 2 post-operatively
2. Intra- and post-operative blood transfusion rates. Blood transfusion rate is measured (if it is required) intra-operatively plus (if required) post-operatively.
3. Intra- and post-operative morbidity: immediate post-operative morbidity measured within the first week after surgery. Late morbidity (complications) measured at post- operative check-up at 6 weeks, then 3 months and then 6 months.
4. Ovarian function, assessed by serial serum FSH concentrations: measured pre-operatively and again at follow-up at 6 weeks, then 3 months and then 6 months

Completion date
01/11/2009

Eligibility

Key inclusion criteria

Current inclusion criteria as of 15/09/2008:
Inclusion criteria for open myomectomy:
1. Symptomatic multiple fibroids (more than three fibroids)
2. Uterine size less than 24 weeks gestation equivalent

Inclusion criteria for laparoscopic myomectomy:
1. Uterine size up to 16 - 18 weeks gestation equivalent
2. No more than three fibroids, with maximum diameter of 15 cm 3. Mostly intramural fibroids

Initial inclusion criteria:
Patients will be referred from the GP to our fibroid clinic and have symptomatic fibroids. They will have chosen to have a myomectomy and agreed to be in the study.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
Added as of 15/09/2008:
Exclusion criteria for open myomectomy:
1. Large uterus more than 24 weeks gestation equivalent
2. Women with a bleeding disorder
3. Women on anticoagulants
4. Treatment with GnRH analogues within the previous six months
5. Women with a haemoglobin level of less than 10.5 g/dl

Exclusion criteria for laparoscopic myomectomy:
1. Uterine size of more than 16 - 18 weeks gestation equivalent
2. Women with a bleeding disorder
3. Women on anticoagulants
4. Women with a haemoglobin level of less than 10.5 g/dl
5. Mostly subserous fibroids

Date of first enrolment
01/11/2004

Date of final enrolment
01/11/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Sponsor information

Organisation
Department of Health

Funder(s)

Funder type
Government

Funder Name
The Royal Free Hampstead NHS Trust (UK)

Funder Name
NHS R&D Support Funding

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	01/04/2009	Yes	No