Magnetic Resonance Imaging to diagnose endometriosis using Ablavar ® as contrast agent - a feasibility study

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Primary Objective: test the feasibility of Dynamic-CE-MRI using Ablavar ® as contrast agent to detect peritoneal endometriosis in women.Secondary Objective(s): # To assess the image quality of Ablavar ®-enhanced MRI in comparison to unenhanced MRI...

Ethical review	Approved WMO
Status	Pending
Health condition type	Menstrual cycle and uterine bleeding disorders
Study type	Interventional

Summary

ID

NL-OMON39343

Source
ToetsingOnline

Brief title
Ablavar ® in endometriosis diagnosis

Condition

- Menstrual cycle and uterine bleeding disorders

Synonym
endometriosis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ablavar, diagnosis, endometriosis, magnetic resonance imaging

Outcome measures

Primary outcome

The MR images will be scored by two independent radiologists with experience in gynaecological imaging and MR abdominal imaging, independently and blinded to each other*s results. Each radiologist prospectively record any sites suspected for peritoneal endometriotic lesions. Conventional T1 and T2 images will be studied for signal intensity abnormalities characterised as focal hyper intensities or cavities and morphologic abnormalities (e.g. regular and irregular stellate margins) . The high-spatial resolution contrast-enhanced MR images will be visually analysed by the two afore mentioned radiologists who will trace regional hyper intensities related to the increased uptake and delayed washout of the contrast medium in hyper vascularised regions of the pelvis.

Secondary outcome

non applicable

Study description

Background summary

Endometriosis is characterised by the presence of functional endometrial tissue outside the uterine cavity. It affects 10-15% of women during pre-menopause and has a big social and professional impact because of its association with dyspareunia, dysmenorrhea, pelvic pain and subfertility. In addition, the health costs for endometriosis are as high as $22 billion per year in the US. Clinically, endometriosis can be peritoneal, ovarian (endometrioma) or

adenomyotic nodules, also called deep invasive lesions, which can infiltrate different organs in the peritoneal cavity (rectum, bladder, uterus). The majority of affected patients have stage one disease, i.e. peritoneal.
The diagnosis of endometriosis is currently based on symptoms. However, because of the large overlap with other gynaecologic, gastro-intestinal and urogenital disturbances, the correct diagnosis is often made 8-11 years after the patient has reported the first complaints.
Although endometriomas can be diagnosed by ultrasound and deep invasive lesions by careful physical examination and MRI, superficial peritoneal endometriosis cannot be easily diagnosed either at physical examination, or by using ultrasound or MRI. The gold standard for the detection of peritoneal disease remains laparoscopy.
Therefore, the development of a non-invasive diagnostic test is a recognised priority in endometriosis research and is needed to: (i) allow an early diagnosis, without an invasive procedure like laparoscopy, especially in young women; (ii) avoid costs and risks of laparoscopic examination; (iii) select which patients need further invasive evaluation; (iv) allow adequate pre-operative planning, which is essential for treatment success; (v) distinguish recurrent disease from post-operative fibrosis, which presents similar symptoms as endometriosis.
Endometriosis is characterised by vigorous angiogenesis, and we have recently demonstrated in a pre-clinical study that endometriosis-associated angiogenesis can be visualised by CE-MRI. Contrarily to the most commonly used gadolinium, which has shown already little accuracy and a sensitivity lower than 40% in diagnosing peritoneal endometriosis, we have devised a small-animal-study in which endometriotic lesions were surgically induced in mice and could be visualised by CE-MRI using gadovosveset-trsodium (currently marketed under the name Ablavar ® by Lantheus Medical Imaging). Specifically, distinct dynamics of contrast inwash and outwash in endometriosis compared to the surrounding tissues (abdominal wall) was observed and could be used to establish a diagnostic protocol. Gadovosveset-trsodium is used for angiography in animal models and in human and it has a high tolerability and a safe profile in humans.

The feasibility of Ablavar ® to detect peritoneal endometriosis in human should be tested

Study objective

Primary Objective: test the feasibility of Dynamic-CE-MRI using Ablavar ® as contrast agent to detect peritoneal endometriosis in women.

Secondary Objective(s): # To assess the image quality of Ablavar ®-enhanced MRI in comparison to unenhanced MRI;
To assess the confidence level of diagnosis of Ablavar ®-enhanced MRI in comparison to laparoscopy (reference standard).

Study design

The study is conducted as an open-label, single group feasibility clinical trial. No control group will be included. The diagnostic results of CE-MRI will be compared to the diagnosis performed with laparoscopy and histology (standard reference).
Duration of the study: from January to March 2013.
Setting: 1. Physical examination. Women presenting at the Maastricht University Medical Centre for symptoms of recurrent endometriosis will be examined by the gynaecologist. For the present feasibility study, five women with a palpable superficial nodule at physical examination and prescribed with a laparoscopic diagnosis/treatment will be asked to participate to the study and eventually enrolled.
2. Hospitalisation for laparoscopy. Prior to laparoscopy, a conventional T1 and T2 weighted MRI (routine procedure at our centre) and Ablavar ®-enhanced MRI will be performed on patients. Digitalised images of the peritoneal cavity will be made during laparoscopy.
3. Digitalised images of the peritoneal cavity will be scored for the presence of endometriosis, to be able to relate the laparoscopic presence of endometriosis to the MRI findings by two radiologists.

Intervention

Subjects will get an extra MRI sing a contrast agent (Ablavar).

Study burden and risks

The present study includes MRI and the application of the intravascular contrast agent Ablavar ®. There are very few risks associated with MRI scans. The changing radiofrequencies and magnetic fields can theoretically produce heat, but this is not known to be associated with relevant side effects. The risk of the injection of MR contrast agents is considered to be low. According to the Summary of Product Characteristics of Ablavar ®, the most common adverse drug reactions were pruritus, paresthesia, headache, nausea, vasodilation, burning sensations and dysgeusia. Most of the undesirable effects were mild to moderate in intensity. Rare serious adverse events were observed in clinical trials (coronary artery disease, hyperglycemia, gangrene, chest pain, and anaphylactoid reaction; see paragraph 5.4).
This study aims at the elaboration of a potentially useful non-invasive MRI tool to diagnose endometriosis, and it is the promise of this study that the results will help to establish a non-invasive diagnostic test.
In light of the relatively low rate of side effects and the promise of developing a safe and non-invasive imaging method for patients with endometriosis, the benefit-risk ratio for this study is regarded as favourable. Patients in whom a theoretical risk of Ablavar ®-enhanced MRI cannot be a priori excluded are not allowed to enter this study (pregnant

women, patients with metal implants, etc.).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Older that 18 years;
Suspect of peritoneal endometriosis, palpable nodule at physical examination;
Patient planned for MRI and laparoscopic treatment of the disease;
Pre menopausal;
Using contraception during the time of the study;
Willing and able to undergo all study procedures;
written informed consent.

Exclusion criteria

Pregnancy / breast feeding;
Post menopausal status or under GnRH analogue treatment;
Patients presenting with a contraindication to MRI such as pacemaker, aneurysm clip, severe claustrophobia or ferromagnetic implants;
Impaired kidney function (estimated Glomerular Filtration Rate, eGFR < 60) or acute kidney injury;
History of severe allergic reaction or allergic reaction to MR contrast media;
Allergy (hypersensitivity) to any of the ingredients of Ablavar ®;
Being unable to give informed consent in person.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2013
Enrollment:	5
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Lantheus Medical Imaging
Generic name:	Ablavar

Ethics review

Approved WMO Date:	19-10-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	03-04-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-002991-15-NL
CCMO	NL41273.068.12
Other	NTR TC 3738 (trialregister.nl)