Local steroid production (intracrinology) in endometriosis - inter & intra patient variability

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Compounds targeting the 17β-HSD type 1 enzyme are close to the first human trials.To best design future human trials it is important to characterise the intra & inter patient variability of 17β-HSD-1 and other enzymes involved...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON55550

Source
ToetsingOnline

Brief title
Steroid hormones in endometriosis / ENDRIN

Condition

- Other condition
- Female reproductive tract infections and inflammations

Synonym
endometriosis

Health condition

endometriosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: endometriosis, estrogens, intracrinology

Outcome measures

Primary outcome

Clinical data (via a case report form) and epidemiological data (via a questionnaire) and urine will be collected prospectively. Blood samples will be taken before treatment. During surgery endometrial, endometriosis and peritoneal biopsies will be collected. Serum and tissue will be analysed for the steroid profile (LCMS). Biopsies will be assessed for the levels of the enzymes involved in the local estrogen generation

Secondary outcome

not applicable

Study description

Background summary

Endometriosis is characterised by the presence of endometrial tissue outside the uterine cavity. This condition affects 10% of women of reproductive age and is associated with a number of distressing symptoms such as dysmenorrhoea, dyspareunia, pelvic pain and sub-fertility, with important economic impacts on the society.
In a recent study, we showed the endometriotic tissue (ectopic) is capable of producing local higher levels of 17β-estradiol than the endometrium located inside the uterus (eutopic) because of high level of the enzyme 17β-hydroxysteroid-dehydrogenase type 1 (17β-HSD-1) that converts the low-potent estrone into the high-potent 17β-estradiol. In addition to our findings, also

others showed that 17β-HSD-1 can be a potential drug target for endometriosis.

Study objective

Compounds targeting the 17β-HSD type 1 enzyme are close to the first human trials.
To best design future human trials it is important to characterise the intra & inter patient variability of 17β-HSD-1 and other enzymes involved in the local generation of estrogens (e.g. intracrinology).

1) Chart the intracrine metabolism in women with endometriosis, e.g.: determine the steroid content in endometriosis lesions and in the serum; assess the levels of the intracrine enzymes (mRNA and protein) in endometriosis lesions.
2) Chart the intracrine metabolism (as described in Objective 1) in lesions from distinct location in the same patient.
3) Chart the intracrine metabolism (as described in Objective 1) in the normal endometrium of patients with endometriosis and controls.

As secondary objectives, intracrine features will be correlated with additional clinical and radiology characteristics (obtained through standard care) and metabolite profile (such as steroids, inflammatory mediators) in urine and peritoneal fluid. Three hundreds (300) patients and 100 control subjects will be recruited for a total of 400 study subjects.

Study design

Prospective cross-sectional multicentre observational case / control study.
Serum and biopsies of ectopic and eutopic endometrium from women diagnosed with endometriosis (300) and controls (100) will be analysed to assess steroid levels (LCMS), enzyme levels (mRNA, Immunohistochemistry and enzyme activity - HPLC) in relation with patient characteristics. Subjects will also fill a life-style and personal data (including pain symptoms) questionnaire

Study burden and risks

Some burden is expected for the endometrial and peritoneal control sampling. These procedures will be however performed under anaesthesia for the intervention indicated as standard care. The risks associated are low and the discomfort for the subject is negligible.
The burden for subjects enrolled for the remaining intervention is minimal, being a blood sampling (10 ml) and peritoneal fluid (performed under anaesthesia for the intervention indicated as standard care) and urine sampling. Biopsies from ectopic tissue of patients will be obtained from rest-surgical material, which does not implicate any intervention/burden for the patient. The expected benefits are the further drug development for

endometriosis patients. Thus the balance benefits / burdens is positive.

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

Cases:
- Being older than 18 year
- Diagnosis of endometriosis (laparoscopically confirmed)
- Being scheduled for elective laparoscopic (or laparotomy) surgery for endometriosis
- Not taking hormonal medications in the previous three months
- Subjects must have signed an approved informed consent, Controls:
- Being older than 18 year
- Being premenopausal

- Having no prior diagnosis of endometriosis
- Not taking hormonal medications in the previous three months
- Being scheduled for any gynaecological surgery like for tubal ligation, for a benign uterine disease, for diagnosis, for laparoscopic hysterectomy and bilateral adnexectomy
- Subjects must have signed an approved informed consent

Exclusion criteria

Cases:
- Being younger than 18 year
- Diagnosis of atypical hyperplasia, other types of cancer
- Previous diagnosis of endometrial carcinoma
- Being under hormonal medication during the three months preceding the sampling
- Pregnancy
- Inability to approve the informed consent form, Controls:
- Being younger than 18 year
- Being diagnosed with a benign ovarian diseases
- Being diagnosed with any malignancy
- Previous diagnosis of endometriosis
- Being under hormonal medication during the three months preceding the sampling
- Pregnancy
- Inability to approve the informed consent form

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-07-2019

Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	28-02-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-06-2021
Application type:	Amendment
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

ID: 20678
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	Nederlands Trialregister (NTR) 29520
CCMO	NL65333.068.18
OMON	NL-OMON20678