Systemic and local estrogen metabolism in healthy women compared to endometrial cancer patients

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON25168

Source
NTR

Brief title
TEC study

Health condition

endometrial cancer
estrogen metabolism
estrone
17beta-estradiol
17beta-hydroxysteroid dehydrogenase
steroid sulfatase
steroid sulfotransferase
aromatase
serum hormone levels
endometrial tissue

Sponsors and support

Primary sponsor: Maxima Medisch Centrum, Veldhoven
Source(s) of monetary or material Support: Maxima Medisch Centrum, Veldhoven
KWF grant

Intervention

Outcome measures

Primary outcome

The primary outcome will be the difference between premenopausal, postmenopausal and endometrial cancer patients in the local tissue enzyme mRNA levels analysed by rt-PCR and described as fold change compared to housekeeping genes. Enzyme activity levels analysed by LCMS for HSD17B1, HSD17B2, STS, SULT1E1, ARO will be described in pmol/mg/hour. Systemic serum steroid levels (see for specification section 5.3 study procedures).will be measured and described in ng/ml or pg/ml.

Secondary outcome

Secondary objectives are; differences in BMI, presence of diabetes, presence of hypertension, hormone use, parity, and history of other malignancies.

Study description

Background summary

Rationale: Endometrial cancer is the most common gynaecological malignancy in the western world with over 320.00 new patients a year worldwide (1). Although good 5 year survival ranging between 74% to 91%, 20-30% will develop recurrence or are diagnosed at high stage (1). For those patients besides chemotherapy and/or hormonal therapy (which is only successful in 30% of the cases) no other options are available.

It is well known that exposure to estrogens increases the risk of the development of endometrial cancer. However, little is known about the complete estrogen metabolism, i.e. the way estrogens are supplied to endometrial cancer, which can occur via the circulation, or through the local generation of steroids.
Objective: To investigate the complete estrogen metabolism in pre- and postmenopausal healthy women compared with endometrial cancer patients.

Our secondary objective is the detection of possible serum and/or endometrium specific risk factors in the development of endometrial cancer, patients' prognosis in relation to specific serum and/or endometrium markers, novel interesting biomarkers for future therapeutic target.

Study design: We aim to conduct a prospective pilot cohort study investigating the estrogen metabolism in blood serum and endometrial (cancer) tissue.

Study population: Pre- and postmenopausal healthy women and endometrial cancer patients who underwent hysterectomy in our hospital can be included. An endometrial tissue sample and blood sample will be taken to investigate or objective.

Main study parameters/endpoints:

The main parameters are: the levels of enzymes involved in the local estrogen synthesis (HSD17B1, HSD17B2, STS, SULT1E1, ARO) in endometrial tissue and the systemic serum steroid levels. Premenopausal, postmenopausal women and endometrial cancer patients will be compared.

Study objective

This study is a pilot study to obtain an idea of the complete estrogen metabolism in pre- and post menopausal healthy women, compared to endometrial cancer patients. The complete estrogen metabolism is defined as the serum steroid levels and the local estrogen metabolism in endometrial (cancer) tissue. This will result in an overview of patients' specific estrogen metabolism; furthermore, the level of each individual serum steroid and endometrial tissue enzyme levels per group will be compared to indicate if there are any differences

Study design

Endpoint all inclusions01-11-2017, after all inclusions the analyses will be preformed.

Intervention

Endometrial tissue analysis

mRNA analyses will be preformed using real-time PCR.
RNA will be isolated with Trizol reagent and assesses spectrophotmetrically for quantity and purity and c DNA will be synthesized. Primers for PCR amplification for HSD17B1, HSD17B2, STS, SULTE1 and Aromatase are commercially available and will be used.

Enzyme activity levels will be measured using our recently developed method by Liquid chromatography–mass spectrometry (LCMS).

Method; frozen samples will be homogenized with a blender in a radioimmunoprecipitation assay buffer, debris will be removed by centrifugation and protein concentration will be determined. The activity of enzymes will be determined using a LCMS-based method.

The following mRNA and enzyme activity levels of the proteins controlling the local estrogen metabolism will be assessed;

- 17beta-hydroxysteroid dehydrogenase type 1 (HSD17B1)

- 17beta-hydroxysteroid dehydrogenase type 2 (HSD17B2)

- Steroid sulphatase (STS)

- Estrogen sulphotransferase (SULT1E1)

- Aromatase (ARO)

Blood analysis

Blood analyses will be assessed in collaboration with prof. Auriola of the Eastern University Finland (34).
The most recently developed Multiplex steroid analyse protocol allows the identification and quantification of the following steroids; estradiol, cortisol, cortisone, estriol, aldosterone, 17OH-pregnenolone, 11deoxycortisol, estrone, DHEA, testosterone, 17OH-progesterone, androstrome, etiocholanolone, dht, androstenedione, pregnenolone, 21OH-progestreone, progesterone.

Additional steroids will be analysed at the laboratory at the Maastricht University Medical Center (MUMC) by LCMS.

- Adiol

- Estrone sulphate (E1S)

In case of specific new research questions or interest on the analyses of other parameters and metabolites, separate METC protocol or appropriate amendments will by applied.

Contacts

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Eligibility criteria

Inclusion criteria

Patients with;

- Hysterectomy needs to be preformed because of endometrial cancer or benign indication (like prolapse, menorrhagia, uterus myomatosis)

- Menopausal status is known

- Blood collection need to be allowed

- Informed consent is given

- No history of malignancies in the previous 5 years

- Minimum age: 18 years

Exclusion criteria

Patients with;

- Neoadjuvant treatment defined as chemotherapy and/or radiotherapy

- Aged under 18 years

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-05-2016
Enrollment:	90
Type:	Anticipated

Ethics review

Positive opinion Date:	20-03-2016
Application type:	First submission

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
NTR-new	NL5007
NTR-old	NTR5780
CCMO	NL55799.015.15

Study results