Testing for HPV and TSLC1 silencing as marker for the risk assessment of cervical cancer

Published: 13-10-2006
Last updated: 20-05-2024

The main objective is to determine whether testing for TSLC1 methylation in hrHPV positive women with abnormal cytology better predicts underlying high-grade cervical lesions necessitating ablative treatment.

Ethical review	Approved WMO
Status	Pending
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON29859

Source
ToetsingOnline

Brief title
HPV and TSLC1 testing in cervical specimens

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC

Synonym
high-grade cervical intraepithelial neoplasia; high-grade premalignant cervical lesions

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Kanker Bestrijding (KWF)

Intervention

Keyword: cervical cancer, cervical specimen, DNA testing

Outcome measures

Primary outcome

The main study parameter is the frequency of CIN3 in two study populations,

i.e. women who test positive for hrHPV and TSLC1 compared with women who test

negative for either or both hrHPV and TSLC1.

Secondary outcome

As one of the secondary parameters it will be assessed whether the CIN3 lesions

are advanced lesions. This will be evaluated by measuring the size of the

lesions using colposcopic imaging and the status of molecular markers for

advanced CIN3 (a.o. elevated hTERT mRNA expression levels) in the lesions.

Study description

Background summary

Infection with high-risk human papillomavirus (hr-HPV) is necessary for the development of cervical cancer, but additional (epi)genetic processes drive the progression of a hr-HPV-induced premalignant cervical intraepithelial neoplasia (CIN, graded 1 to 3) to invasive cancer
Despite the population based cervical screening program still 750 women are diagnosed with cervical cancer patients in The Netherlands each year. This can in part be explained by a considerable degree of false-negativity of the cytology, which is used for cervical screening.
In our previous studies we have shown that additional testing for hrHPV results in a major improvement of the screening program, particularly due to a reduction in false negative scrapes. Recently, we also showed that the specificity of the detection of women at higest risk of invasive cancer can be improved by testing for silencing of the TSLC1 gene, a gene which was also shown to be functionally involved in cervical carcinogenesis(Steenbergen et al., J.Nat.Cancer Inst. 2004).
We hypothesize that testing of cervical scrapes or other cervical specimens for

hrHPV and TSLC1 silencing improves the detection of women that are at highest risk to develop invasive cervical cancers. This will lead to an improved clinical management of women who are referred to the outpatient clinic for abnormal cytology and reduce the overtreatment of women who are not at immediate risk to develop invasive cervical cancer.

Study objective

The main objective is to determine whether testing for TSLC1 methylation in hrHPV positive women with abnormal cytology better predicts underlying high-grade cervical lesions necessitating ablative treatment.

Study design

open, prospective, intervention study

Intervention

Participating women will receive a user-friendly self-sampling package by regular mail in order to collect a cervico-vaginal specimen. These specimens will be send to the Vumc and tested for the presence of hr-HPV DNA and TSLC1 methylation.
When visiting the gynaecologist women will be examined by colposcopy as part of the routine procedures.
Women who test positive for both hr-HPV and TSLC1 methylation will be directly treated by large loop excision of the transformation zone (LLETZ) following colposcopic examination, as is the regular procedure.
Women who test negative for either or both hrHPV and TSLC1 methylation will not be treated directly but colposcopy-directed biopsies will be taken first for histomorphological analysis. In this group of women the treatment/follow-up strategy will be based on the colposcopic and histological outcome; i.e. women with high gradeCIN lesions will be treated and those with less severe lesions will undergo follow-up cytology and colposcopy at 6 months.

All procedures at the gynaecologist will be in accordance with current treatment guidelines in the Netherlands.

Study burden and risks

The burden for participants is nearly equal to the burden of the regular visit to the gynaecologist. The extra risks are negligible. The only extra burden involves the self-sampling of cervical-vaginal cells using a user-friendly self-sampling device.

No blood samples will be taken and no questionnaires or diaries have to be

filled in.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1081 HV Amsterdam
Nederland
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1081 HV Amsterdam
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Female
-Age 20-70
-Previous two Pap smears read as bordeline/mild dyskaryosis (Pap2/3a1) or previous single Pap smear read as moderate dyskaryosis or worse (*Pap3a2)
-Intact cervix (no history of treatment involving damage to the transformation zone of the cervix)
- Sufficient knowledge of the Dutch language.
- Able to understand the content of the study (according to the gynecologist).
- Signed informed consent form.

Exclusion criteria

-Pap smear read as Pap 5 (suspect for invasive cancer)
-Cancer at other sites
-Withdrawal of permission by the patient
-History of surgery on the cervix
-Pregnancy or pregnant in the last 3 months.
-Breast-feeding, or breast-feeding in the last 3 months.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	82
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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
CCMO	NL13108.029.06