Evaluating the Visual Appearance of Cervical Lesions in Relation its Histological Diagnosis, Human Papillomavirus Genotype and Other Viral Parameters: a Prospective Cohort Study

Published: 18-05-2010
Last updated: 02-05-2024

Primary objectives:- Evaluate colposcopic visual appearance of cervical lesions in relation to its histological substrate, HPV genotype(s) and molecular parameters.- Study cervical disease on the lesion level using HPV genotyping and other viral...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cervix disorders (excl infections and inflammations)
Study type	Observational invasive

Summary

ID

NL-OMON41350

Source
ToetsingOnline

Brief title
EVAH study

Condition

- Cervix disorders (excl infections and inflammations)

Synonym
Cervical Intraepithelial Neoplasia, Cervical lesions

Research involving
Human

Sponsors and support

Primary sponsor: DDL Diagnostic Laboratory
Source(s) of monetary or material Support: DDL Diagnostic Laboratory;Wetenschappelijke Activiteiten Commissie Reinier de Graaf Groep

Intervention

Keyword: CIN, Colposcopy, HPV, Laser Capture Microdissection

Outcome measures

Primary outcome

Primary study parameters are:

- Digitalized colposcopic imaging results

- Histological examination data (CIN classification of lesions)

- HPV results from LCM isolated lesions

- HPV results from entire LEEP/ biopsies

Secondary outcome

Secondary study parameters are:

- HPV results from cervico-vaginal self samples

- HPV results from physician-taken cervical scrapes

Study description

Background summary

Persistent infection with high-risk human papillomavirus (HR-HPV) types is necessary for the development of cervical cancer. One of the most important tools to reduce the incidence of this disease is the early diagnosis and treatment of its precursor lesions, e.g. by cervical cytology.
In women with abnormal cytology, colposcopic evaluation is used to obtain cervical biopsies for histological confirmation. However, the sensitivity of this approach is limited. DNA techniques for detecting HR-HPV have shown to be effective in the clinical management of patients with cervical disease. The

main contribution of these techniques is their high sensitivity and negative predictive value. Nonetheless, this increase in sensitivity is accompanied by a notable reduction in specificity; therefore a considerable number of transient infections are detected, which have only minimal chance of progression, but nevertheless require a thorough survey. Consequently, other specific markers than the presence of HR-HPV, such as HPV genotype or molecular transformation markers are needed to identify patients at significant risk of progression and improve their management.
To date, 20*40% of HPV-positive women are reported to be infected with multiple HPV types. Detailed understanding of the natural history and dynamics of HPV infection, and the pathogenic effect of infection with multiple types is crucial to monitor the impact of the recently introduced HPV-vaccination on the risk of infection with individual HPV types.

In case abnormal cytology is diagnosed in a woman, she is referred for colposcopy. Digitalized colposcopic imaging has been developed in the last decade and comprises the recording of high quality digital photographs for several purposes. Compared to conventional colposcopy it provides greater objectivity to evaluate colposcopic images and to quantify the findings. Furthermore it provides the opportunity of monitoring progression or regression of the observed lesions. Digital colposcopy with a system to annotate the lesions of interest, gives the opportunity to study the correlation between the characteristics of colposcopic image, histological diagnosis, HPV genotype(s) and molecular transformation markers.

Recently the Laser Capture Microdissection (LCM) method has been applied to cervical biopsy specimens. This technique allows molecular assessment of selected cell populations, e.g. HPV status, that are histologically or pathologically distinct although topographically close. LCM can give more insight in the pathogenesis of cervical premalignant lesions.

Study objective

Primary objectives:
- Evaluate colposcopic visual appearance of cervical lesions in relation to its histological substrate, HPV genotype(s) and molecular parameters.
- Study cervical disease on the lesion level using HPV genotyping and other viral parameters.

Secondary objectives:
- Determine the incremental benefit of taking multiple biopsies to detect CIN.
- Compare visual assessment and biopsy placement between expert colposcopists.
- Set standards of documenting colposcopic impression and biopsy placement to initiate a world-wide database of cervical images with clinical outcomes.
- Determine the predictive value of HPV self-sampling in the management and follow-up of women with CIN.

- Study the clinical value of HPV self-sampling compared to physician obtained HPV testing

Study design

This study is designed as a prospective multicenter observational cohort study.

Study burden and risks

Risks and burden are linked to protocol procedures, such as cervical sampling and colposcopy. Although these are routine procedures, carried out by medically qualified personnel, they may cause side effects or discomfort to the woman. However, it is expected that these procedures will generally be well tolerated. The only extra burden involves the self-sampling of cervical-vaginal cells using a user-friendly self-sampling device. Self-sampling poses no threats to the physical well-being of a woman.

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

-An abnormal cytological test result
-18 years of age or older
-Written informed consent prior to enrolment
-Sufficient knowledge of the Dutch language
-The intention to comply with the requirements of the protocol

Exclusion criteria

-History of surgery on the cervix
-Previous pelvic radiotherapy
-Pregnancy or pregnant in the last 3 months
-Actually breast-feeding or breast-feeding in the last 3 months
-Diagnosis of cervix carcinoma

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-07-2010
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	18-05-2010
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-02-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-10-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL31335.098.10