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Comparison of cervical screening using visual inspection with acetic acid (VIA) with Swede score using Gynocular in detecting cervical intraepithelial Neoplasia (CIN) lesions

Submission date 23/04/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 15/05/2014	**Overall study status** Completed	
Last Edited 15/05/2014	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Colposcopic evaluations and biopsies are important diagnostic steps and standard management for abnormal pap smears in developed countries. Conventional colposcopes are expensive, heavy and large microscopes. Colposcopy may also be used as a primary cervical screening tool in low-resource settings in combination with the Swede score (a scoring system for colposcopy). The Gynocular® is a portable, easy to use, pocket-size battery-driven colposcope that was developed to provide gold-standard examinations in low and high resource settings; The aim of this study is to compare screening with Swede score using the Gynocular with screening with the current method.

Who can participate?
Adult female patients undergoing cervical screening.

What does the study involve?
Participants will be randomly allocated to one of two groups: Swede score using the Gynocular colposcopes or standard screening method.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
The National Cancer Institute, Al-Azhar University Faculty of Medicine, Cairo (Egypt)

When is the study starting and how long is it expected to run for?
May 2014 to May 2017

Who is funding the study?
H&M (Sweden) and Gynius (Germany)

Who is the main contact?
Prof Ahmed Sekotory M Ahmed

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Protocol serial number
402GynocularEGYPT

Study information

Scientific Title
Comparison of cervical SCREENing using visual inspection with acetic acid (VIA), to Swede score using GYNOCULAR in detecting cervical intraepithelial Neoplasia (CIN) lesions: a multicentre prospective randomized clinical trial

Acronym
GYNOCULARSCREEN

Study objectives
Cervical screening with the Swede score method using the Gynocular is superior to VIA method at detecting CIN2 or higher-grade cervical lesions and selecting patients for immediate treatment.
Primary study aims:
1. To compare the efficacy of opportunistic screening using Gynocular and Swede scoring system, to visual inspection using acetic acid (VIA) in detecting women with cervical intraepithelial neoplasia (≥CIN2) verified by histological assessment of punch biopsies.
2. To investigate the feasability of immediate on-site outpatient treatment using cold coagulation based on a cut-off Swede score under Gynocular inspection, or VIA positivity.
3. To assess the prevalence of HPV virus infection in the study cohort and the proportion and typing of high-risk HPV positive patients.

Secondary study aims:
1. To assess patient acceptance of the one-stop assessment and treatment based on the Swede score using Gynocular.

2. To examine the cost of opportunistic screening by direct event-costing, cost-effectiveness, and cost-benefit analysis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Faculty of Medicine, Alazhar University, IRB ref number 402

Primary study design
Interventional

Study design
Multi-centre prospective randomized non-blind clinical trial

Study type(s)
Screening

Health condition(s) or problem(s) studied
Cervical cancer

Interventions
Examination procedure
All consented patients will be placed in a standardized lithotomy position on a gynecological couch and a self-holding speculum will be inserted in the vagina. A Pap smear and cervical brush for HPV (high risk) DNA detection will be taken from the cervix in all recruited patients prior to cervical examination by either method. Cervical scoring (VIA: pos/neg; Swede score: 0-10), smears, and biopsies from each group will be respectively recorded in a designated examination sheet according to clinical routine and listed in the study database protocol together with all results when available. The Histopathology staff will be blinded as to the method via which biopsies were obtained. Histopathology samples will be re-evaluated by an expert pathologist at the end of the study. Cytology will be sampled according to locally used method and will be inerpreted at the local laboratory. HPV-testing will be carried out on separate cervical smear (cellular) samples by a central laboratory at Al-Azhar University virology labs. The results of Pap smears and HPV DNA testing will only be revealed at the completion of the study.

Treatment modality, timing and outcome will similarly be doumented and recorded. All treated patients will be followed up in 3-6 month with Gynocular and smear test; then on 6 monthly basis for a total of two years using cervical cytology only to detect any recurrent cervical dyskaryosis.

Examination methods:

1. VIA Method:
1.1. For women randomized to VIA, a trained doctor will first obtain a cervical smear for cytology, and HPV DNA testing. The cervix is then swabbed with 3-5% acetic acid for 1 minute and inspected with a desk lamp under the naked eye. Sharp, distinct, well defined, dense acetowhite areas on the cervix, with or without raised margins, close to the squamocolumnar junction (SCJ) in the transformation zone are considered to be VIA positive.
1.2. Two cervical punch biopsies or more are taken from VIA positive areas. In case of normal findings, two punch biopsies will be taken from the squamous columnar junction at 6 and 12 o

clock positions.
1.3. Immediate treatment on-site is based on the VIA positive test with cold coagulation under local anaesthesia. However, patients not suitable for cold coagulation or with biopsies revealing microinvasive cervical disease or worse will receive the appropriate
diagnostic workup and management protocol.
1.4. The indication for treatment under general anaesthesia would be the same as in routine practice. If excision treatment is to be carried out under general anaesthesia, Gynocular device would be the first choice.
1.5. The results of the pap smears, and biopsies will be recorded in the study database and acted upon accordingly. HPV DNA testing will be carried out and revealed at the end of the study and will similarly be documented in the secure study database for correlation and statistical analysis.
1.6. Cytological Follow up every 6 month for 2 years, will be carried out for those who received treatment for confirmed CIN, to detect any recurrent cervical dyskaryosis.

2. Swede scoring using Gynocular Method:
2.1. For women randomized to Swede score, a trained doctor will first obtain a cervical smear for cytology, and HPV DNA testing. Each of five Swede Colposcopic score variables will be assessed using the Gynocular device (acetowhiteness, margins plus surface, vessel pattern, lesion size and iodine staining) will be given a score of 0, 1 or 2 points13.
2.2. At least two biopsies will be taken from the worst looking areas. In case of a normal examination, two biopsies will be taken at the squamous columnar junction at 6 and 12 oclock positions.
2.3. Women with Swede score 6 and above will undergo immediate treatment with cold coagulation under visualisation with the Gynocular and local anaesthesia. However, patients not suitable for cold coagulation or with biopsies revealing microinvasive cervical disease or worse will receive the appropriate diagnostic workup and management protocol.
2.4. The indication for treatment under general anaesthesia would be the same as in routine practice. If excision treatment is to be carried out under general anaesthesia, Gynocular device would be the first choice.
2.5. The results of the pap smears and biopsies will be recorded in the study database when available and acted upon accordingly. HPV DNA testing will be carried out and revealed at the end of the study and will similarly be documented in the secure study database for correlation and statistical analysis.
2.6. Cytological follow up every 6 month for 2 years will be carried out for those who received treatment for confirmed CIN, to detect any recurrent cervical dyskaryosis.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
CIN 1, CIN2, CIN3, Invasive cancer, HPV, PAP smear, histopatology of punch biopsy

1. To compare the efficacy of opportunistic screening using Gynocular and Swede scoring system, to visual inspection using acetic acid (VIA) in detecting women with cervical intraepithelial neoplasia (≥CIN2) verified by histological assessment of punch biopsies.
2. To investigate the feasability of immediate on-site outpatient treatment using cold

coagulation based on a cut-off Swede score under Gynocular inspection, or VIA positivity.
3. To assess the prevalence of HPV virus infection in the study cohort and the proportion and typing of high-risk HPV positive patients

Key secondary outcome(s)
1. Receiver Operator Characteristic Curve (ROC) will be used to determine the diagnostic performance at different cut-off values of the Swede score with respect to high-grade CIN lesions.
2. Descriptive statistics will reflect the frequencies, proportion of high-risk HPV virus and various grades of CIN lesions in the study cohort in both arms.
3. To assess patient acceptance of the one-stop assessment and treatment based on the Swede score using Gynocular at the time of first examination
4. To examine the cost of opportunistic screening by direct event-costing, cost-effectiveness, and cost-benefit analysis comparing the different costs of the 2 study groups. This will be done when the study is completed.

Completion date
15/05/2017

Eligibility

Key inclusion criteria
1. Age between 25-65
2. No current significant vaginal bleeding
3. No current clinical signs of pelvic infection
4. No current clinical signs of acute cervicitis
5. More than one week since any last pelvic gynecological examination
6. Able to understand written and/or oral information
7. Mentally capable of providing informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. Not fulfilling any of the inclusion criteria
2. Gross cervical lesions suggestive of invasion (cancer)
3. Pregnancy
4. Less than 3 months since last delivery or miscarriage
5. Lesions involving > 75% (subjective) of the cervix are excludd from same day outpatient treatment
6. Lesions with endocervical involvement > 2mm are excluded from cold coagulation

7. Bleeding disorders
8. Sensitivity to any of the drugs/materials used

Date of first enrolment
15/05/2014

Date of final enrolment
15/05/2017

Locations

Countries of recruitment
Egypt

Study participating centre
The National Cancer Institute
Cairo
Egypt
11787

Sponsor information

Organisation
H&M Conscious Foundation (Sweden)

ROR
https://ror.org/00yrbts90

Funder(s)

Funder type
Industry

Funder Name
H&M (Hennes & Mauritz) AB (Sweden)

Funder Name
Gynius AB (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration