Depth of Necrosis in Normal Cervical Epithelium After 85% Trichloroacetic Acid (TCA) Application

STATISTICAL ANALYSIS PLAN (SAP)

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- ClinicalTrials.gov identifier : NCT04911075
- Unique Protocol ID : 21020134
- Version Date : 15/02/2021

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1. Introduction

The therapeutic effectiveness of cervical precancerous lesions will be determined by the ability to reach beyond the depth of a high-grade lesion. The primary objective of this study is to estimate depth of cervical epithelial ablation based on the cervical epithelium damage (necrosis), both squamous (ectocervix), transformation zone, and columnar (endocervix) epithelium after application of 85% trichloroacetic acid (TCA) solution.

2. Study Design

2.1 Description

This is an open label, interventional study. Participants are subject who will undergo an elective total hysterectomy procedure for indications of gynecological organ abnormalities, whether benign, pre-cancerous, or malignant other than cervical pathology. Patients will receive a single administration of 85% TCA solution 24 hours before surgery, performed by one clinician at a medical ward. The 85% TCA will be applied topically onto the ectocervix and the endocervical canal with a cotton swab. After surgery, cervical tissue biopsy specimen will be sent for pathological examination to identify the depth of cervical tissue necrosis.

2.2 Number of Subjects

$$\mathbf{N} = \left\{\frac{(\boldsymbol{Z\alpha})\boldsymbol{x}\ \boldsymbol{SD}}{\boldsymbol{d}}\right\}^{\mathbf{2}}$$

Note: Zα; α = 5% (1,96); SD (0,64) – refference; d absolut error 5% (0,21)

Fourty patients will be enrolled in this study.

2.3 Number of Study Centers

The study will be performed at one investigational site (Cipto Mangunkusomu National General Hospital)

2.4 Duration of Study

Estimated study completion date for the study will be until October 2021.

3. Outcomes

3.1 Primary Outcome

Depth of Cervical Epithelial Ablation

Based on damage to the cervical epithelium, both squamous (ectocervix), transformation zone, and columnar (endocervix) epithelium. Destruction of base membrane and stromal tissue will also be evaluated. Microscopic evaluation using a micrometer on a 10 times magnification eyepiece. The deepest ablative destruction in epithelial, base membrane, and stromal tissue will be recorded and stated in millimetres.

3.2 Secondary Outcome

Pain Scores

Measured immediately after application of the 85 percent TCA solution with Visual Analogue Scale (VAS) score. Higher score means worse outcome. Minimum score is 0 (No Pain) and maximum score is 10 (worst pain).

4. Eligibility Criteria

All patients must participate in the consent process. During the consent process, the person obtaining consent must inform the patient of all elements of informed consent. No protocol specific procedures, including screening procedures, are to be performed until the patient has signed and dated an institutional review board (IRB)- approved informed consent form. The study begins with the signing and dating of the informed consent form. Patients must also meet the inclusion and exclusion criteria to be enrolled in the study. This eligibility checklist is used to determine patient eligibility and filed with signature in the patient research form.

4.1 Inclusion Criteria

1. Normal cervix without significant changes and must be tested negative for Visual Inspection Acetic-Acid (VIA) test (no acetowhite lesions are found)
2. Participants are willing to participate voluntarily in this research by signing a consent form.

4.2 Exclusion Criteria

1. Patients who finally have undergone sub-total or supra-vaginal hysterectomy.
2. Any abnormalities found in postoperative cervical histopathology results.

5. Statistical Analysis

Descriptive statistics will be employed to analyze the data. Summary statistics for continuous variables will include the mean, standard deviation, proportion and range (minimum/maximum). Statistical analysis will be perfomed by using IBM SPSS® 26 software.