Efficacy and safety of photodynamic therapy for cervical and vaginal intraepithelial neoplasia:A multicenter prospective cohort study

Study protocal

2023.1

Program design

[Design of the study methodology]

The aim of this project is to study the efficacy and safety of photodynamic therapy (20% 5-aminolivulonic acid +630nm red light) in the treatment of cervical and vaginal intraepithelial neoplasia in women in real-world applications.

[Eligibility, exclusion and withdrawal criteria]

Inclusion Criteria:

- cervical/vaginal high-grade squamous intraepithelial lesions (HSILs) confirmed by colposcopy and pathological biopsy (CIN2 /CIN3 and/or VaIN2/ VaIN3) or persistent CIN1/VaIN1 lasting for more than one year with a strong willingness to treat;

-colposcopy was adequate, and analysable colposcopy images were retained;

- endocervical curettage (ECC) did not suggest higher-grade lesions.

Exclusion Criteria:

-coexistence or suspicion of cancer;

-porphyria or suspected allergies to red and blue light;

-severe medical comorbidities;

Withdrawal Criteria:

- The subject requested to withdraw from the clinical trial;
- Those who experienced serious adverse events during the trial;
- Those whose conditions have progressed during the trial and are not suitable to continue with this research protocol;
- The researcher or/and sponsor consider that the patient does not meet the experimental requirements and is not suitable to continue participating in this study.

[Study duration and follow-up]

The specific implementation steps are as follows:

After enrollment, the subjects signed the informed consent form and made an appointment for the first treatment time. No treatment was given 3 days before and after menstruation.

For the first treatment, after the patient ate, the bladder was emptied, the lithotomy position of the bladder was taken, the cervix was exposed with a endoscope, the vaginal secretions of the cervix were wiped with a dry gauze ball, 20% aminolevulonic acid photosensitizer (5-ALA) was applied to the lesion site, a cotton condom was stuffed into the vagina, and the patient was instructed to sit still and wait for 3-4 hours. Avoid activities during this period, reduce walking and urination. Four hours later, the patient lay on the examination bed again and was irradiated with red light at 630-635nm. After the treatment is completed, observe for half an hour. If there is no discomfort, you can leave the hospital. Before leaving, an adverse reaction record card will be issued. Make an appointment for treatment 7 days later. If it falls during menstruation, it will be postponed by one week.

For the 2nd and 3rd treatments, the parameters and energy density are the same as those of the first one. The treatment interval is 7 days. If it falls during the menstrual period, it will be postponed by one week.

One month after the end of the third treatment, colposcopy was performed. If the suspected lesion worsened, a biopsy was taken. If no abnormalities are found under colposcopy, a single-point biopsy is taken at the most severe site of the original lesion. If the biopsy indicates that the lesion persists, continue the treatment for three times. TCT+HPV was reexamined 6 months after the start of the first treatment. If the lesion worsens, the patient will be referred for surgical resection (conization of the cervix or local mucosal resection of the vaginal wall) in accordance with the diagnosis and treatment norms.

Data management

1. Data Entry

Data collection will be obtained by team staff via the Case Report Form (CRF). As a part of the clinical data management system, the case report form for data collection is jointly negotiated and prepared by the project leader and the clinical epidemiology Research Center, and the experts are invited to discuss and modify it for use. The data collation process includes automated validation procedures and manual validation to ensure the completeness and accuracy of the data entered into the case report form. When the data does not match, the data can be queried, and the team staff can verify and modify the entered data.

2. Contents and methods of data verification and management

According to the data entered in the case report form, medical supervision is conducted regularly to ensure the accuracy of data entry, and medical problems are discussed separately.

3. Data Archiving

After data entry and verification are completed as required, the case report form shall be filed and stored in numbered order, and be filled with a retrieval catalogue for reference. Electronic data files, including databases, inspection programs, analysis programs, analysis results, coding and explanatory files, should be classified and stored in different disks or recording media with multiple backups, properly stored to prevent damage. All original files shall be kept for the period specified accordingly.

Statistical analysis

Based on the assessment of traditional Chinese medicine practitioners in prospective clinical trials combined with the treatment intentions of patients, various control groups were formed. Appropriate clinical research methods were selected for statistical analysis.