



LEEP/Cone combined with photodynamic therapy for successful treatment of high-grade squamous intraepithelial lesion



Dear Sir,

Three young married female patients were admitted to the hospital for a high-grade squamous intraepithelial lesion according to pathological examinations of the cervix. HPV test of the cervix showed that HPV16, HPV18 and HPV53 were positive. All three inpatients were treated with loop electrosurgical excision procedure (LEEP). HPV and TCT test were taken after three months. HPV tests were still positive, the same as before, and the TCT showed atypical squamous epithelium. Furthermore, cervical pathology hinted low-grade squamous intraepithelial lesions. Photodynamic therapy with 5-aminolevulinic acid was applied because patients desired to become pregnant in the future. The vagina and cervix were cleaned with sterile saline, then, freshly prepared 20% ALA thermo gel (Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd.) soaked on a thin cotton swab was applied to the cervical mucosa and the adjacent normal ectocervix for 3 h. Light irradiation of 100 J/cm² was applied to both the ecto- and endocervical canal using a cylindrical optical fiber coupled to a 633 nm ± 10 nm diode laser (LED-IIC; Wuhan Yage Photo-Electronic Co. Ltd, Wuhan, China). The treatment was performed a total of 3 times, once every week. Sexual activity was prohibited during treatment. TCT showed no abnormalities and HPV test were negative after 3 months. No recurrence was observed at 6 months, 9 months, 15 months, and 21 months. One of the patients successfully delivered a child after 3 years.

Cervical intraepithelial neoplasia (CIN) is becoming more and more common in young people. Cervical human papilloma virus (HPV) infection is detected in more than 99.7% of cases of cervical cancer and is implicated as the main risk factor for CIN [1]. Conventional methods for the treatment of CIN and cervical HPV infection such as diathermocoagulation, cryotherapy, laser evaporation, and laser or electrosurgical excision are too invasive. These invasive treatment methods may cause adverse reactions, such as hemorrhages, endometriosis or even affect the patient's future pregnancies [2]. LEEP is a traditional treatment of high-grade squamous intraepithelial lesion, HR-HPV cannot be completely removed in some patients, which is a potential high risk factor for CIN recurrence [3]. Studies of PDT on the treatment of CIN included randomized control trials, case-control study and case series. Photosensitizers mainly included 5-aminolevulinic acid and hexaminolevulinic acid. It has been reported that photodynamic therapy is efficacy and safety in patients with CIN I, CIN II and CIN III [4–6]. Though studies showed that PDT with 5-aminolevulinic acid is well tolerated but has minimal activity in the treatment of CIN II and CIN III [7], a newly systematic review and meta-analysis of randomized clinical trials showed PDT that targets CIN actually improves the complete response rate (CRR). Moreover, it is seen to have an obvious anti-viral efficacy [8]. Another systemic review revealed that PDT is a safe and tolerable treatment for CIN; the CRR of PDT on CIN ranged from 0% to 100%, and the HPV eradication rate (HER) ranged from 53.4% to 80.0%

[9]. Studies also found that persistent HPV infection after treatment of CIN was an independent risk factor for recurrence, so the clearance of HPV was important. In our study, after LEEP treatment, the HR-HPV is still positive with low-grade squamous intraepithelial lesions. Photodynamic therapy with 5-aminolevulinic acid was applied and achieved satisfactory results. Studies revealed that HPV-infected cells can selectively absorb ALA after exposure, thus causing the accumulation of protoporphyrin IX inside the infected cells. After irradiation, reactive singlet oxygen selectively destroys the cells and stops viral replication through oxygen-dependent cytotoxic reactions, viral nucleic acid strand breaking, or base site disappearance [10].

In our study, these three young patients who desired to preserve fertility, used photodynamic therapy with 5-aminolevulinic acid after LEEP/Cone, HPV reinfection and recurrence of CIN was not observed after 21 months follow up.

These cases indicated that LEEP/Cone combined with photodynamic therapy with 5-aminolevulinic acid is an alternative approach for the treatment of cervical intraepithelial neoplasia, especially those of child-bearing age. Eventhough the amount of evidence is low, owing to the small number of patients in our study, more patients and a longer follow up shall be included in our future study.

Conflicting interest (If present, give more details)

None.

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