

Effect of 5-Aminolevulinic Acid Photodynamic Therapy Combined with Carbon dioxide Laser on Condyloma Acuminatum

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Xie *et al.*: Effect and Prognosis of Condyloma Acuminatum

By comparing 5-aminolevulinic acid photodynamic therapy combined with carbon dioxide laser and carbon dioxide laser therapy only, to explore the therapeutic effect of 5-aminolevulinic acid photodynamic therapy combined with carbon dioxide laser on perianal and anal canal condyloma acuminatum. A total of 74 patients with perianal and anal canal condyloma acuminatum who were admitted to our hospital from January 2021 to December 2021 were selected as the research objects. They were randomly assigned to the observation group and the control group, with 37 cases in each group. The observation group was treated with 5-aminolevulinic acid photodynamic therapy combined with carbon dioxide laser and the control group was treated with carbon dioxide laser therapy. Both groups were treated once a week for 3 w. The therapeutic effect, recurrence rate and adverse reactions were compared between the two groups. The cure rate of condyloma acuminatum in the observation group was 86.48 %, which was higher than 54.05 % in the control group, with statistical significance ($p < 0.05$). After follow-up, it was found that the recurrence rate of the observation group (13.51 %) was significantly lower than that of the control group (43.24 %), with statistical significance ($p < 0.05$). The incidence of superficial scar and perianal pain in the observation group was 27.03 % and 21.62 % respectively, which was not significantly different from 35.14 % and 29.73 % in the control group. 5-aminolevulinic acid photodynamic therapy combined with carbon dioxide laser in the treatment of perianal and anal canal condyloma acuminatum has the advantages of good curative effect and low recurrence rate, which is worthy of clinical promotion.

Key words: 5-aminolevulinic acid photodynamic therapy, carbon dioxide laser, perianal anal canal condyloma acuminatum, recurrence rate

Condyloma acuminatum is a disease mainly characterized by proliferative lesions of the genitals and anus. It is caused by Human Papillomavirus (HPV) infection and sexual contact is the main route of transmission. In men, it is more common in the foreskin, urethral opening, perianal and scrotum, in females it is more common in the labia minora, cervix and perianal, and the perianal canal is the most common site of disease^[1]. Condyloma acuminatum has the characteristics of long incubation period, high recurrence rate and strong infectivity. Traditional treatment methods such as Carbon dioxide (CO₂) laser and freezing are mainly to remove warts, but clinical practice shows that these methods have a high recurrence rate and poor treatment effect, likely to have adverse reactions such as infection and

bleeding^[2,3]. 5-Aminolevulinic Acid Photodynamic Therapy (ALA-PDT) is an emerging physical therapy method that uses photosensitizers to release cytotoxic substances and selectively destroy diseased tissues under the action of a specific light source. This treatment of condyloma acuminatum has the advantages of being safe, effective and low recurrence rate; at the same time, ALA-PDT is also suitable for the treatment of deep lesions and stenotic lesions that are difficult to reach by traditional methods^[4]. Thus, in this study, ALA-PDT combined with CO₂ laser was used to treat perianal condyloma acuminatum and its clinical efficacy, safety and prognosis were evaluated. A total of 74 patients with perianal condyloma acuminatum who were admitted to our hospital from January 2021 to December 2021 were selected as the

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research objects. The selected patients were included criteria; they had not received topical drug treatment and had taken drugs that affected the treatment results 2 w before admission; there are no contraindications for ALA-PDT and CO₂ laser; the patient gives informed consent and cooperates with the treatment. Exclusion criteria have breastfeeding or pregnant women; combined with autoimmune diseases, malignant tumors, etc.; poor compliance and combined with mental illness. Patients were randomly assigned to the observation group and the control group, 37 cases each. Among them, there were 22 males and 15 females in the observation group, aged 17-42 y, with an average age of (29.2±2.9) y; the course of disease was 0.5-8 mo, the average duration of the disease was (4.1±0.7) mo and the diameter of warts was 0.4-1.1 (0.5±0.3) cm. In the control group, there were 20 males and 17 females, aged 18-47 y, with an average age of (27.9±2.6) y; the course of the disease was 0.8-7 mo, the average duration of the disease was (3.3±0.6) mo and the diameter of the wart was 0.5-1.1 (0.4±0.2) cm. There was no statistically significant difference between the two groups in basic data such as age, gender and wart size (p>0.05). Thus, they were comparable. The control group was treated with CO₂ laser alone. After routine disinfection of the treatment site with 75 % ethanol, 2 % lidocaine was selected for local anesthesia and then a CO₂ laser treatment device (provided by Wuhan Huagong Laser Engineering Co. Ltd., model HCL-MC30) was used. Burn within 2 cm of the lesion and adjust the laser output power according to the size and depth of the wart. After the treatment, the mupirocin is wiped locally to avoid infection. The observation group was treated on the basis of CO₂ laser combined with ALA-PDT. Firstly, CO₂ laser treatment was used as in the control group and then Ayla (provided by Shanghai Fudan Zhangjiang Biomedical Co., Ltd., H20070027) was prepared with appropriate amount of water for injection. After forming a 20 % cream, spread it evenly on the 2 cm around the treatment site, cover it with plastic wrap for 4 h and then use the 635 semiconductor laser treatment device (provided by Wuhan Yage Photoelectric Technology Co., Ltd., model LED-II B). Irradiation was performed at a wavelength of 635 nm, and the total energy of irradiation reached 100 J/cm². Both groups were treated once a week for a total of 3 times. The recovery, recurrence and adverse reactions were compared between the two groups. The cure standard is; all the warts of the patient are detached and the acetic acid white test is negative, and there are

no new lesions within 12 w after treatment; the recurrence standard is; new warts appear at or around the skin lesions within 12 w after treatment. Statistical Package for the Social Sciences (SPSS) 22.0 was used to analyze and process the data. The count data were expressed in cases (%) and the Chi-square (χ^2) test was used for comparison between groups; the calculated data were calculated as $\bar{x}\pm s$, and the t test was used. p<0.05 indicated that the difference was statistically significant. After 12 w of follow-up, the cure rate of the observation group was 86.48 %, significantly higher than that of the control group (54.05 %) and the difference was statistically significant (p<0.05); at the same time, the recurrence rate of the observation group (13.51 %) was also significantly lower than that of the control group (43.24 %), the difference was statistically significant (p<0.05) are shown in Table 1. According to the statistics, there were 10 cases (27.03 %) of superficial wound scars and 8 cases (21.62 %) of perianal pain in the observation group, while 13 cases (35.14 %) of superficial wound scars and 11 cases (29.73 %) of perianal pain in the control group, the difference was not statistically significant (p>0.05) are shown in Table 2. Condyloma acuminatum is a common sexually transmitted disease, which spreads strongly among sexually active people; the incubation period of the disease is long, usually 1 mo to 8 mo and the onset occurs after an average incubation period of 3 mo^[5]. The disease is caused by HPV infection and the most common subtypes of that because condyloma acuminatum is HPV6/11. Condyloma acuminatum generally manifested as skin and mucous membrane vegetation's, with uneven surfaces, cockscomb, cauliflower-like or papillary protrusions and often appears in the perianal canal and external genitalia. Condyloma acuminatum appears in the perianal canal is more prone to large-scale infection because of its moisture and rich blood vessels. Meanwhile, the perianal canal is an easy-to-friction part of the body and genital warts are easily damaged after friction, which may cause ulcer and bleeding, even lead to cancer, increasing the difficulty of treatment^[6]. Studies have shown that genital warts not only affect the physical health of patients, but also have a certain negative impact on their mental health; genital warts are prone to occur in private parts of the body, causing patients to feel shame, depression, anxiety etc., resulting in poor quality of life. Female patients are more likely to have negative emotions than male patients, which also has a certain negative impact on

the recovery of the disease^[7]. At present, the traditional treatment methods for perianal genital warts mainly include cryotherapy, laser therapy and electro cauterization. The treatment effect on deep lesions or narrow lesions is not ideal; at the same time, genital warts include not only over warts, but also latent HPV infection foci and subclinical lesions. The above methods can remove over warts, but the elimination effect on HPV latent infection foci or subclinical lesions is not ideal^[8]. CO₂ laser therapy is currently widely used in the treatment of condyloma acuminatum. The perianal warts are carbonized and removed by laser. Although this method can remove warts visible to the naked eye, it is not suitable for the treatment of warts in narrow parts such as perianal folds. Thus, the recurrence rate is higher after using CO₂ laser therapy^[9,10]. ALA-PDT therapy is a popular therapy in recent years. In addition to treating genital warts, this method has a certain therapeutic effect on skin precancerous lesions, malignant tumors, acne and atrophic lichen sclerosis and it is not easy to cause drug resistance in the process of killing pathogenic microorganisms^[11,12]. ALA-PDT therapy is mainly based on the principle that photosensitizers produce destructive substances under the irradiation of specific wavelengths of light. 5-Aminolevulinic Acid (5-ALA) is a precursor for plants to synthesize chloroplasts and animals to synthesize heme. The endogenous substances in the body generally carry out negative feedback regulation on ALA synthetize through the content of chlorophyll or heme, so that the content of 5-ALA in the body is stable and cannot be accumulated in large quantities,

but a large amount of exogenous 5-ALA can be proliferated and exuberant. Absorbed by the cells and converted into protoporphyrin IX in the cells, the latter mainly exists in the mitochondria and produces free radicals and singlet oxygen and other cytotoxins under the irradiation of a certain wavelength (635 nm) of light, thereby causing damage of mitochondria and nucleic acid of diseased tissue cells to achieve therapeutic purposes; studies have shown that 5-ALA can be targeted to gather in tissue cells with high virus content, HPV infection and active replication, and normal tissues can be protected due to low penetration^[13]. However, due to the limited penetration of red light at 635 nm, it is difficult to remove hard or large warts, so combination therapy is generally used. The results of this study showed that the cure rate of the observation group was significantly higher than that of the control group ($p < 0.05$) and the recurrence rate of the observation group was lower than that of the control group ($p < 0.05$), which was statistically significant. At the same time, the study found that there was no significant difference in the incidence of shallow wound scars and perianal pain between the two groups ($p > 0.05$) and the incidence was low, indicating that ALA-PDT combined with CO₂ laser therapy is safe. In summary, the application of ALA-PDT combined with CO₂ laser in the treatment of condyloma acuminatum has the advantages of significant curative effect, high cure rate, low recurrence rate and good safety, which is worthy of clinical promotion.

TABLE 1: COMPARISON OF CURE RATE AND RECURRENCE RATE BETWEEN THE TWO GROUPS [n (%)]

Group	Case	Cure	Recurrence
Observation	37	32 (86.48)	5 (13.51)
Control	37	20 (54.05)	16 (43.24)
χ^2		9.315	8.045
p		0.002	0.005

TABLE 2: COMPARISON OF ADVERSE REACTIONS BETWEEN THE TWO GROUPS [n (%)]

Group	Case	Superficial wound scars	Perianal pain
Observation	37	10 (27.03)	8 (21.62)
Control	37	13 (35.14)	11 (29.73)
χ^2		0.568	0.637
p		0.451	0.425

Author's contributions:

Xiaolei Xie and Huajie Zhong have contributed equally to this work.

Conflict of interests:

The authors declared no conflict of interests.

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