

TREATMENT OF CONDYLOMATA ACUMINATA AND BOWENOID PAPULOSIS WITH CO₂ LASER AND IMIQUIMOD

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ABSTRACT

Some of the most common manifestation of Human Papilloma Virus (HPV) infection in venereology are Condylomata acuminata and Bowenoid Papulosis. These diseases are often difficult to diagnose by dermatologists, obstetricians, gynecologists and urologists. This article represents our entire clinical experience with the use of carbon dioxide (CO₂) laser in the treatment of 58 (40 male and 18 female) patients with Condylomata Acuminata after other treatments had failed. Successful eradication was accomplished in 53 patients with wide distribution of condylomatous lesions, with 88% per cent responding to a single laser treatment. In our experience there are no side effects, damage to the surrounding tissue is minimal and the lesions have not recurred. In 82.3% of the patients the treatment resulted in complete disappearance of the lesions, whereas in the other two to three percent treatments were required. The advantages of the laser treatment are discussed in this article.

Key words: Condylomata acuminata, Bowenoid papulosis, CO₂ laser vaporization, Immunotherapy, Imiquimod

INTRODUCTION

Genital warts are the result of human papilloma virus (HPV) infection and one of the most common sexually transmitted diseases, caused mainly by HPV types 6 and 11(3). They are usually asymptomatic and consist of papillomatous papules or nodules on the genitalia, perineum and anus. HPV infection accounts for an estimated 11% of the global cancer incidence in women. HPV-16 is the most prevalent type detected in cervical cancer and along with types 18,31,33 and 45 has been classified as a class I carcinogen. Genital warts are 2 main forms: Condylomata acuminata and Condylomata gigantea, known as tumor of Buschke-Lu¹wenstein. From 70 known types human papilloma virus (HPV) - Condylomata acuminata is caused by serotypes 6, 11, 16, 18, 26-32, 39-44, 53-55, 58, 59, 64, 67.

HPV infection is often the result of sexual intercourse in which the virus penetrates the epidermal basal cells. It activates the formation of proteins, which enhances cells proliferation, thickening of spinous layer and develops papillomatoses. The transmission of these infections occurs more frequently in sexually active individuals, with the use of oral contraceptives or in immunodeficiency states. Bowenoid papulosis (BP) of the genitalia, first described by Lloid and later by Wade, et al is a condition characterized by reddish, reddish-brown, brownish-violaceous discrete and confluent papules which resemble more seborrheic warts than condylomata acuminata.(25, 26) HPV serotypes 16, 18, 33, 34, 42, 55 have been identified in lesions of BP. In some cases the diagnosis of BP is difficult to establish, because it is rare and has a different clinical picture than that of Condylomata acuminata. Differential diagnosis of BP is made with Condylomata lata, Verruca seborrhoica, M. Bowen, Molluscum contagiosum, Lichen nitidus and neoplastic processes. Neoplastic lesions (e.g., verrucous carcinoma), inflammatory lesions (e.g., lichen nitidus), and normal physical findings (e.g., pearly penile papules) can mimic genital warts. The performance of physical examination using bright light and magnification aids in the diagnosis. Biopsy is recommended only when verrucous papules and plaques thought to be genital warts are not responsive to therapy, manifest with induration, are fixed to underlying structures, have ulcerations, grow suddenly or increase pigmentation, or change in appearance (1, 2, 3, 4, 5, 6). Acetic acid solutions (the acetowhite test) applied to warts to highlight them have a low positive predictive value for diagnosing genital warts. In men warts locate on sulcus coronarius, glans penis, prepuceum, the urethra and rarely on corpus penis and perianaly. In women it is most often localized in the, labia majora et minora, clitoris, introitus vaginae, perineum, urethra, cervix and more rarely – perianal. No etiological treatment exists for HPV infection. The objective is to undertake direct ablation of genital warts to break the chain of transmission and prevent malignant degeneration. Treatment includes physical destruction of

lesions, medical treatment and/or immunotherapy. The numerous medical, physical and destructive regimen used in the treatment of condylomata acuminata include topical therapy (cryotherapy, Podophyllin, 5-fluorouracil, Imiquimod, 6- interferon), electrocoagulation, surgical and CO2 lazer vaporization, sometimes combining two or more of these approaches (23,24). Our purpose is to report here our experience with treatment of different clinical cases of condylomata acuminata with CO-2 laser and Imiquimod. The topical immunostimulatory drug Imiquimod is imidazoquinolines and acts by stimulating *toll-like receptors* (TLR-7) thereby stimulating the innate immunity, i.e. giving a danger signal to the cells, which then start the production of pro-inflammatory cytokines like *IFN- δ* , *TNF- δ* , *IL-1,6,8* and 12 (22). Laser therapy is the most practical, innovative treatment modality to come along in the last 10 years. The CO 2 laser utilizes focuses infrared light energy to vaporize affected tissues. Carefully applied, CO-2 laser therapy directed at a field of treatment rather than a single spot, can yield cure rates of up to 95% for grossly visible lesions(9,14,19). Carbon dioxide laser is particularly useful for lesions which are recalcitrant to other types of therapy(17). It permits precise tissue ablation by spatial confinement of thermal damage and effective vaporization, which promotes rapid healing without scar formation in most cases. CO-2 laser therapy is a useful treatment modality, especially for extensive warts(16). HPV DNA may be released during laser vaporization of genital HPV infections; if appropriate evacuating equipment is used, contamination of the operator is unlikely(8, 9,13). The surgeon and assisting personnel must wear laser masks and use a vacuum ventilation system (10). Newer studies are either poorly designed or involve too small a sample size. Most studies require additional therapies (10,11,13).

PATIENTS AND METHODS

From 2010, to 2011, 40 male and 18 female patients within the age range of between fifteen and fifty-five years were treated. CO-2 laser treatment was done locally to these 58 patients, after infiltration of 1% lidocaine (Xylocaine). A Multi Function Fractional CO2 Laser System (Multixel), continuous wave mode, super dream pulse mode, with an optical spot size of 2.0 mm was used. The average power required varied from 3 to 6 watts for lesions measuring 0.2 to 0.8 mm in diameter. After the operation the patients were advised to treat the operative field twice a day for 15 days with Braunol (solution) and Braunovidon (ungv). The perianal postoperative wounds were treated additionally with an antibiotic spray. All patients were seen for an examination for a first time 15 days after the operation. After that the patients continue to use local antiseptic and epithelium creams for up to 30 days after the operation. All patients were receiving immunostimulant therapy for 2-3 months – Biozin – 2x1 tabs. daily for 30 days or Isoprinosine

3x2 tabs. for 30 days. During the period between 2009 and 2011 a group of 35 patients, consisting of men between the ages of 17 and 48 years, were treated with Imiquimod 5% - crume. Imiquimod was used to treat the lesion twice a week. The patients were advised to use Braunovidon ungv on the days when they were not applying Imiquimod 5% - crume. They were seen for a treatment evaluation after the first, second and third month since the beginning of the treatment.

RESULTS

1. *Patients treated with CO2 laser:* All patients were followed at three-month intervals for at least six months, and advised to return if any occurrence was noted. The first treatment evaluation was performed 15 days after the operation. Average follow-up ranged from two to thirty months. Out of the 58 new cases of condyomatous lesions, 55 patients (95%) responded to a single laser treatment. There were no recurrences in this group of patients 3 months after the operation. We have observed partial recurrence in 3 patients, which required repeated treatment with the CO2 laser. 2. *Patients treated with Imiquimod 5%- crume:* After the first month of local treatment with Imiquimod, we observed complete disappearance of the lesions in 22 patients. (62.86%) After the second month we observed complete recovery in another 5 patients with the total number of complete recovery reaching 27 patients (77.1%).

DISCUSIONS

The sexual nature of transmission is well known, but there is also evidence of vertical and transmission through non-genital contact. (1). Nowadays the association of certain types of HPV with cervical cancer and an increased risk of malignancy is well documented. Bowenoid papulosis is a pre-malignant condition affecting the ano-genital area, and has been associated with high risk HPV genotypes. This disease should be considered in patients presenting to a Sexual health clinic with an atypical appearance of ano-genital rash or warts. In atypical cases the diagnosis should be confirmed histologically. Treatment of genital warts and Bowenoid papulosis usually involves locally destructive or ablative therapies such as excisional surgery, electrocoagulation, cryotherapy, 5- fluorouracil and laser therapy. Ricart et al. reported successful clearance of 90% of the lesions using Imiquimod cream 5% once a day for 3 months. (6) A well tolerated and effective treatment, topical Imiquimod would appear to be a suitable alternative in cases of extensive or widespread ano-genital warts and Bowenoid Papulosis. It is difficult, if not impossible, to predict in which patients the treatment will be successful. (2, 7) Yan J, Chen S et al reported that imiquimod 5% cream and podophyllotoxin 0.5% solution have an identical beneficial effect on anogenital warts and are associated with identical and acceptable side effect. Both substances constitute

effective and safe treatments of untreated anogenital warts in immunocompetent individuals. (21) Carrozza et al. compared extensive genital warts in HIV-positive and HIV-negative patients. The clearance and recurrence rates were similar for both groups. (12,13) Local skin reactions such as erythema, erosion, excoriation, flaking and oedema are common after treatment with Imiquimod. Other local reactions such as induration, ulceration, scabbing, and vesicles have also been reported. Should an intolerable skin reaction occur, the cream should be removed by washing the area with mild soap and water. Treatment with imiquimod cream can be resumed after the skin reaction has moderated. (23, 24) The risk of severe local skin reactions may be increased when imiquimod is used at higher than recommended doses. However, in rare cases severe local reactions that have required treatment and/or caused temporary incapacitation have been observed in patients who have used imiquimod according to the instructions. Imiquimod cream should be washed from the skin before sexual activity. The combined treatment with Braunowidon ungu, which we used with our patients treated with Imiquimod, lessened the inflammatory reaction and enhanced the healing process. Imiquimod cream may weaken condoms and diaphragms, therefore concurrent use with imiquimod cream is not recommended. We recommend the treatment with Imiquimod as a method of choice for the flat type of Condylomata acuminata, in which laser treatment has a higher percentage of recurrences and postoperative complications and is much more difficult to perform. Local treatment with Imiquimod is a method of choice for patients who are scared of laser therapy and prefer to administer the treatment themselves despite the longer treatment period that is needed. The principal advantages of CO-2 laser therapy are precision (which results in sparing of normal tissue), probable elimination of the infective agent, and

relatively good cosmetic results. Carbon dioxide laser can be used to treat extensive and thick warts quickly and without the drawing of blood. The carbon dioxide laser is able to effect such wart clearance in part because of the deeper penetration than the one which generally occurs with cryotherapy. The CO₂ laser is best used at power settings of 3-10 Watts because it vaporizes tissue with a shallow depth of penetration at those settings. However, laser treatment is more complex and costly than electrosurgery or cryotherapy. (8, 9, 11, 12) A disadvantage of the lasers is that the risk of scarring, although small, is greater than with cryotherapy. CO-2 laser therapy is typically an office procedure. However, larger lesions and pediatric patients may require anesthesia and therefore can be done in the hospital under general anesthesia.

CONCLUSION

Our results show that treatment with CO-2 – laser vaporization was the best treatment for condyloma of the anus, vulva and penis. Imiquimod seems an acceptable therapeutic alternative in cases of widespread ano-genital warts, as well as flat type Condylomata acuminata located on the mucous membranes and the submucosa. Local treatment with Imiquimod is more effective in cases of condylomas which are recent in nature or are of the flat type. The treatment with Imiquimod is preferred by patients who want to do it themselves and are comfortable to wait for a long period of time to achieve results. It is difficult to predict in which patient the treatment will be successful. Immunosuppression is one of the major risk factors for treatment failure (7). It can be concluded that this definite treatment method has been clearly found superior so far. Treatment should be guided by the available resources, the experience of the health provider and the preference of the patient. (5)

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