

Use of trichloroacetic acid for management of oral lesions caused by human papillomavirus

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The human papillomavirus (HPV) has an affinity for squamous cells of stratified keratinized epithelium, thus affecting the lower genital, nasal, and oral tracts. In the oral cavity, HPV is associated with pathoses such as the verruca vulgaris (common wart), squamous cell papilloma, condyloma acuminatum (venereal wart), and focal epithelial hyperplasia (Heck disease). Among the treatments available for these lesions are cryotherapy, electrosurgery, surgical removal, laser therapy, and trichloroacetic acid (TCA). The objective of this research was to determine the behavior of HPV-associated oral pathoses treated with TCA. A prospective cohort study was performed in 20 patients who attended a dental consultation at 2 universities in Cartagena, Colombia. Among the patients, 65% were diagnosed as having focal epithelial hyperplasia, 20% as having verrucae vulgares, and 15% as having condylomata acuminata. Application of TCA to HPV-associated oral lesions proved to be a useful nonsurgical alternative treatment, as the resolution of the lesions was achieved atraumatically in a span of 45 days with 3 applications of 30-60 seconds each.

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The human papillomavirus (HPV), part of the Papillomaviridae family, is a nonencapsulated virus with an icosahedral structure and a double circular DNA chain.¹ HPV has an affinity for squamous cells of stratified keratinized epithelium, thus affecting the lower genital, nasal, and oral tracts.² More than 200 types of HPV have been isolated, and more than 40 infect the epithelium of the anogenital tract and mucosa.³ Serotypes commonly associated with oral lesions are HPV-13 and -32 in focal epithelial hyperplasia; HPV-6 and -11 in condylomata acuminata (also known as *venereal warts*); and HPV-2 and -4 in verrucae vulgares (also known as *common warts*).⁴

Focal epithelial hyperplasia (also known as *Heck disease*) is a benign proliferative pathosis of the oral mucosa that has an unpredictable chronic course and may show spontaneous remission.⁵ Although there are reports of affected adults, more than 90% of those who seek treatment are children and adolescents between 3 and 17 years of age.⁶ A greater proportion of patients are female.⁶ Clinically, focal epithelial hyperplasia presents as sessile, smooth, asymptomatic papules, which are generally located in the upper and lower labial mucosa, cheek mucosa, and tongue.⁷

Condylomata acuminata present as sessile-based verrucosities (warts) with a surface similar to cauliflower; in the oral cavity, they are usually located on the tip and dorsal surface of the tongue and the soft palate.⁸ The infection is transmitted sexually or via self-inoculation. Condylomata acuminata mainly affect adolescents and adults; however, more studies of affected adolescents between the ages of 11 and 17 years are reported every day.^{9,10}

Verrucae vulgares are exophytic papillary or benign tumors of the stratified epithelium.¹¹ Common warts affect children and adults. They may appear anywhere in the oral cavity but are most frequently located on the hard palate, soft palate, uvula, inner side of the lip, and lateral border of the tongue. The common wart must be differentiated from the condyloma acuminatum, which is larger and has a broader base.^{12,13}

Among the treatments available for the management of HPV lesions are cryotherapy, electrosurgery, surgical excision, laser, and trichloroacetic acid (TCA).¹⁴⁻¹⁶ The surgical approach to these lesions has been the most commonly used therapy; however, in the pediatric population—the segment that is the most affected by HPV-associated oral lesions—this therapy can cause trauma, anguish, and anxiety.¹⁷

A nonsurgical therapeutic alternative is the use of TCA, which was created in the 1830s and used in humans for the first time in 1926. Composed of carbon, chlorine, oxygen, and hydrogen, TCA works by producing denaturation, precipitation, and



Fig 1. Patient with a diagnosis of focal epithelial hyperplasia. Multiple sessile, asymptomatic papules are located along the entire extension of the upper labial mucosa.



Fig 2. Upper labial mucosa after TCA application. The mucosa has acquired a whitish appearance.



Fig 3. Results after a single application of TCA (follow-up at 15 days). Note the total resolution of the lesions.

destruction of lesions via chemical coagulation of the affected tissue. This caustic agent destroys warts by the chemical coagulation of proteins and direct destruction of viral DNA.¹⁸

TCA has been widely used for the treatment of HPV lesions in gynecology.¹³ However, the initiative to use it in oral lesions developed in Colombia as a result of a combined effort between the faculties of dentistry of the University of Cartagena and Rafael Núñez University Corporation. In 2010, Harris Ricardo et al reported the case of a pediatric patient in whom treatment with TCA achieved satisfactory resolution of lesions caused by focal epithelial hyperplasia.¹⁹ As a result of this success, it was decided that further research was needed in a larger population.

For research into using this therapy for oral lesions, the protocol for this and previous studies was based on gynecologic studies that treated HPV lesions with 80% TCA, taking into account the histologic similarity between the vaginal and oral mucosae.²⁰

Materials and methods

An analytical prospective cohort study was carried out to evaluate the behavior of TCA in the treatment of oral lesions in 20 patients who attended a dental consultation conducted at either the University of Cartagena or Rafael Núñez University Corporation, Cartagena, Colombia.

This study was carried out taking into account the provisions of Resolution No. 008430 of 1993 of the Ministry of Health and Social Protection of Colombia. An informed consent form was given to every patient (or guardian) to sign. They were told that patients were free to leave the investigation at any time, the confidentiality of the identification data would be respected, and the results of the investigation would be used only for academic and research purposes.

Those individuals who presented clinical and histopathologic features of HPV and who agreed to participate in the study were included (Fig 1). Patients who had a history of an allergic reaction to TCA and/or had consumed drugs that could influence the healing process were excluded.

The first step in the protocol for TCA application, which was performed by a single operator at each university, consisted of rinsing each oral lesion caused by HPV with copious amounts of water and drying the surface of the lesion. The second step consisted of applying TCA to each

lesion with a swab. The time of application of the acid varied between 30 and 60 seconds, depending on the size of the lesion and the patient's symptomatology during the application. The lesions became intensely white as a result of the chemical burn produced (Fig 2). In the third step, a mixture of water and sodium bicarbonate powder was applied to the lesion to neutralize the pH of the acid and remove residue that could affect adjacent tissues. This entire process was repeated every 15 days for any lesions that persisted. The final step in the protocol was to continue clinical follow-up of the patient until the lesions were resolved (Fig 3).

Among the study variables were the number of applications and the resolution time (in days) of the lesions treated. The analysis of the data counted on descriptive statistics for quantitative and qualitative variables.

Results

The study was performed in 20 patients, of whom 14 (70%) were female and 6 (30%) were male. Among the sample, 13 patients (65%) were diagnosed as having focal epithelial hyperplasia, 4 (20%) as having common warts, and 3 (15%) as having condylomata acuminata. The highest prevalence of focal epithelial hyperplasia lesions (10 of 13) occurred in a population with an age range of 0-10 years. This age group was equivalent to 50% of the sample. Of the other 10 patients, 6 (30%) were between the ages of 11 and 21 years, 3 (15%) were between the ages of 33 and 43 years, and 1 (5%) was between the ages of 44 and 54 years.

For 12 patients (60%), 1-3 TCA applications were required for the total resolution of diagnosed lesions; 7 patients (35%) required 4-6 TCA applications; and 1 patient (5%) required 7-9 TCA applications. The number of applications was directly proportional to the size and number of lesions in the patients; that is, the greater the size and number of lesions, the more applications were required.

The results showed that most patients (60%) needed 15-45 days to be totally lesion-free. The condylomata acuminata and the common warts required fewer TCA applications than focal epithelial hyperplasia lesions. While condylomata acuminata disappeared after 2 applications, lesions associated with Heck disease required 5-7 applications.

None of the treated patients had relapses during a 12-month period after the beginning of the treatment.

Discussion

Pérez Elizondo et al published an update on focal epithelial hyperplasia in Mexico and concluded that this disease is frequent in children and that there is a slightly higher incidence in female patients.⁶ Their results agreed with those of the present study, in which the most commonly affected population was pediatric female patients.

Trujillo et al carried out research work in a Cuban hospital regarding the efficacy of 80% TCA in treating condylomata acuminata.²¹ They found that 50% of their subjects suffered recurrences. This outcome differs from the results obtained in the present study, in which none of the patients experienced recurrence during 1 year of follow-up.

Harris Ricardo et al reported on 2 cases of papillomavirus-associated lesions in Cartagena, Colombia.²² In both patients, 80% TCA was used as therapy; treatment with TCA brought about the resolution of lesions at 2 months, after 6 applications. Those results differ from those of the present study, in which focal epithelial hyperplasia lesions resolved in 15-45 days.

It should be noted that the therapeutic effect of TCA depends on good operator handling because, if the application time is exceeded, chemical burns can occur on the tissues. The time of application of the acid varied between 30 and 60 seconds.

Conclusion

The application of 80% TCA caused the disappearance of HPV-associated lesions over a period ranging from 15 days to a maximum of 4 months. The application of TCA to HPV-associated oral lesions was an effective, atraumatic alternative treatment that was well tolerated by the patients. This therapy resulted in resolution of all the lesions without evidence of relapses.

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