

Dimethylether Treatment for Condyloma Acuminata in Women

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■**Abstract:** *Objective.* Our aim was to test a new cryosurgical wart treatment, dimethylether (Histofreezer®), for clinical efficacy in newly diagnosed cases of genital warts. *Methods.* All patients of the gynecology clinic of a teaching hospital who were at least 12 years of age and who had between one and eight external genital warts were eligible. Treatment occurred at the initial visit and at follow-up visits at 2, 4, 6, and 8 weeks. If all warts were gone at any particular visit, the patient had completed the study and was not required to return. *Results.* In 14 of 15 patients [93%; 95% confidence interval (CI), 81- 100%], all warts resolved within the 8-week study period. This included 39 of 44 warts (89%; 95% CI 80-98%). Most warts [35 of 44 (80%)] resolved within 4 weeks. One patient with five warts failed treatment. No known complications were seen. *Conclusion.* Dimethylether (Histofreezer®) is an effective cryosurgical treatment for genital warts.■

Key Words: condyloma, cryosurgery

OBJECTIVE

Genital warts are common. Traditional treatments for genital warts include trichloroacetic acid, podophyllin, cryotherapy, surgical excision, and laser vaporization [1].

It was the objective of this prospective study to test a new cryosurgical wart treatment, dimethylether (Histofreezer®, Koninklijke Utermohlen, NV, Utrecht, The Netherlands), for clinical efficacy in a group of women in whom genital warts were newly diagnosed.

MATERIALS AND METHODS

In a single-arm, prospective trial, all patients consecutively seen in the Obstetrics and Gynecology clinic of St. Luke's Hospital, Bethlehem, PA, who were at least 12 years of age, and who had between one and eight previously untreated external genital warts with a maximum diameter of less than 1.5 cm were eligible. The study was approved by the institutional review board of the hospital. Written informed consent was obtained.

On a patient's entry into the study, the patient's age and number, size, and type of wart were recorded. Follow-up visits at 2, 4, 6, and 8 weeks were performed. If all warts resolved at any particular visit, the patient completed the study and was not required to return. A map of the warts' locations was made at the first and last visits. An incentive fee of \$50.00 was paid to participants at completion of the study.

Directions for the use of the Histofreezer® (Fig. 1) canister were as follows:

1. Fit the applicator tip to the aerosol canister.
2. Remove the cap and depress the actuator until the gas condenses in the applicator tip, forming several droplets.
3. Wait for 10 sec.

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4. Apply the applicator tip to the lesion for 40 sec.
5. Do not touch the test site for at least 2 minutes after application.
6. The 5-mm applicator tip will maintain the treatment temperature at -57°C for 120 sec. This is long enough for three 40-sec applications.

Scoring was conducted at each visit in accordance with the following scale: *pass*, condyloma no longer visible; *fail*, condyloma still visible. Cryotherapy problems, such as depigmentation of the treatment site, blistering of skin, and scarring, were assessed.

Previous studies [2-10] show resolution rates for warts ranging from 22% to 88% for trichloroacetic acid, podophyllin, or conventional cryotherapy, and from these we adopted 70% as the typical resolution rate ($p = .70$). Using the wart resolution response rate of 70%, we determined that 40 warts would require treatment to achieve statistical significance assuming $\alpha = 0.05$ and a power of 0.80 [11].

This was a pilot study of Histofreezer[®] and does not include a randomization or control group. We included as the experimental unit resolution rate and CI for both lesions ($n = 40$) and patients ($n = 15$). The clearance rate, the proportion of passes, and the 95% CIs for the proportion were determined using a binomial distribution.

RESULTS

Eighteen patients were enrolled in the study. However, three patients did not complete the 8-week study and were lost to follow-up. This analysis of results is based on the 15 patients who completed the study. Their average age was 22.2 years. In 14 of 15 (93 %; 95 % CI 81-100%) patients, all warts passed within the 8 weeks. The one non-responding patient with five

warts completed the 8 weeks of study. Considering individual warts to be the unit of study, 39 of 44 warts resolved (89%; 95% CI 80-98%), most [35 (80%)] within 4 weeks.

Figure 2 shows the number of warts at initial visit and the number remaining at 2, 4, 6, and 8 weeks of follow-up. No complications such as depigmentation, blistering, or scarring were seen in these 15 patients.

DISCUSSION

Dimethylether was developed by a family practitioner as a less painful and destructive alternative to liquid nitrogen. It has been used in Europe for 7 years to treat many types of warts. In the United States, it is indicated for treating common plantar and genital warts. The dimethylether, applied from a small hand-held canister, freezes skin at -57°C vs. -65°C for CO_2 , -89°C for N_2O , and -196°C for liquid nitrogen. The epidermis is frozen and separates from the basement membrane, with subsequent growth of healthy skin in approximately 2 weeks.

In this small, prospective study, we have demonstrated the effectiveness of Histofreezer[®] for treatment of female condyloma. Trichloroacetic acid and podophyllin show resolution rates of 22 to 77% [2-10] and standard cryotherapy at 63 to 88% [3]. Our Histofreezer[®] method appears to be comparable to the published response rates of those three standard methods.

The Histofreezer[®] has many advantages. It is easy to use and could be employed by nurse practitioners and physician's assistants. One 125-cc unit costs \$185.00.



Figure 1. Histofreezer[®] unit.

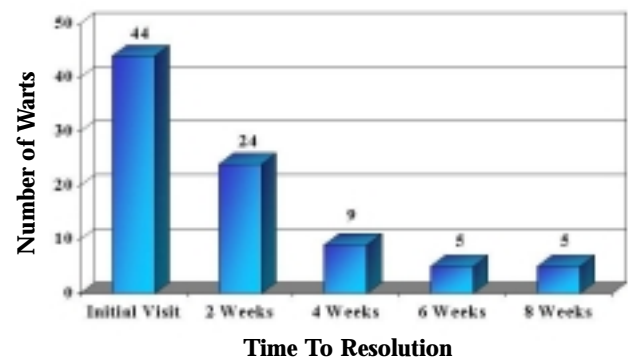


Figure 2. Number of warts at initial visit and warts remaining at follow-up.

This unit would supply about 40 charges at a cost of \$4.62 per charge. Each charge can treat two or three small warts. It is a disposable product, and no capital investment is required. The product has a 4-year shelf life, and cryogen evaporation is not an issue. With the disposable application tip, there is no chance of cross-contamination of the wart virus between patients. Treatment with the Histofreezer® does not require a local anesthetic. The small, 125-cc canister stores in any cabinet and is easily held during treatment.

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REFERENCES

1. Tying SK, Friedman-Kien AE, Kent HL, et al. Alpha interferon in the management of genital warts. *Female Patient* 1993; 18:33-9.
2. Godley MJ, Gradbeer CS, Gellan M. Cryotherapy compared with trichloroacetic acid in treating genital warts. *Genitourin Med* 1987; 63:390-2.
3. Kraus SJ, Stone KM. Management of genital infection caused by human papillomavirus. *Rev Infect Dis* 1990; 12(suppl 6):S620-32.
4. Simmons PD. Podophyllin 10% and 25% in the treatment of genital warts. *Br J Vener Dis* 1981; 57:208-9.
5. Bashi SA. Cryotherapy versus podophyllin in the treatment of genital warts. *Int J Dermatol* 1985; 24:535-6.
6. Jensen SL. Comparison of podophyllin application with simple surgical excision in clearance and recurrence of perianal condylomata acuminata. *Lancet* 1985; 2:1146-8.
7. Stone K, Becker T, Hadgu A, Kraus S. Treatment of external genital warts: A randomized clinical trial comparing podophyllin, cryotherapy, and electrodesiccation. *Genitorurin Med* 1990; 66:16-9.
8. Lassus A, Haukka K, Forsstrom S. Podophyllotoxin for treatment of genital warts in males: A comparison with conventional podophyllin therapy. *Eur J Sex Transm Dis* 1984; 2:31-3.
9. von Krogh G. Topical treatment of penile condylomata acuminata with podophyllin, podophyllotoxin and colchicine. *Acta Dermatol Venereol (Stockh)* 1978;58:163-8.
10. von Krogh G. Penile condylomata acuminata: An experimental model for evaluation of topical self-treatment with 0.5%-1.0% ethanolic preparations of podophyllotoxin for three days. *Sex Transm Dis* 1981; 8:179-86.
11. Daniel W. *Biostatistics: A Foundation for Analysis in the Health Sciences*, 2nd ed. New York: Wiley, 1978; 131-3.