OPEN ACCESS Freely available online

Journal of Clinical & Experimental Dermatology Research

Research Article

Sequential Therapy of Common and Plantar Warts with Salicylic Acid after Cryotherapy versus Cryotherapy Alone: A Case-Control Study in 42 Subjects

Federico Diotallevi[1], Massimo Milani[2*], Anna Maria Offidani[1]

[1]Department of Clinical and Molecular Sciences, Dermatological Clinic, Polytechnic University of Marche, Ancona, Italy; [2]Medical Department, Cantabria Labs Difa Cooper, Via Milano 160, Caronno Pertusella, Italy

ABSTRACT

Background: Common Wart (CW; Verruca vulgaris) is a benign cutaneous virus infection caused by human papilloma virus commonly located in the palmar and plantar regions. Warts, especially located at pressure points, could be painful, but in general they are asymptomatic. Treatment is not always necessary but when multiple lesions, pain, immunosuppression and discomfort are present therapeutic intervention could be mandatory. Chemical or physical destructions are commonly used for the treatment of CW. Cryotherapy with liquid nitrogen is a common clinician-administered treatment. The most relevant drawbacks of this procedure are the pain associated with treatment, the need of several sessions and the recurrence of new lesion. Salicylic Acid (SA) applied under tape occlusion is a convenient, effective and safe therapy of CW, even if no effective as cryotherapy. So far, there are few data regarding the efficacy and safety of the sequential treatment of CW with cryotherapy followed by a 10-day treatment course with SA.

Study Design: We evaluated in a case-control study the clinical efficacy of cryotherapy alone and cryotherapy with SA in adult immunocompetent subjects with common or plantar warts.

Subjects and Methods: We evaluated a total of forty-two men and women, mean age 33 ± 13 years, with CW located in the palm (30% of the lesions) and plantar (70%) regions. Twenty subjects (mean CW lesion number: 2.2 ± 0.7) represented the cases group and twenty-two the control group. The cases subjects were treated with a cryotherapy session and after 3 days topical SA patch was applied for additional 10 consecutive days. The control group, after the initial cryotherapy session, was followed clinically to evaluate the need of new cryotherapy procedures. After the last cryotherapy, all subjects underwent to a follow up evaluation of three months.

Results: In the case group the sequential therapy was very effective with disappearance of the treated lesion. After the first cryotherapy session and the sequential SA treatment, the additional cryotherapy treatments were on average, mean ± SD, 1.4 ± 0.6 (range 1-3). In the control group, in order to obtain a complete cure of CW, the additional cryotherapy treatments were 3.4 ± 0.7 (range 1-5). This difference was statistically significant (p=0.0001) in favour of the cases vs. control subjects. Only two subjects (both in the control group) suffered from recurrences in the follow up.

Conclusion: In subjects with CW, the sequential therapy with cryotherapy and topical salicylic acid is an effective strategy able to reduce significantly the need of additional cryotherapy procedures therefore reducing the procedure-associated discomfort. Furthermore, this sequential therapeutic strategy could offer additional benefits in term of cost-saving.

Key Words: Common warts; Cryotherapy; Salicylic acid; Case-control study

Correspondence to: Massimo Milani, Medical Department, Cantabria Labs Difa Cooper, Via Milano 160, Caronno Pertusella, Italy, Tel/Fax: 029659031; E-mail: massimo.milani@difacooper.com

Received: 25-Aug-2022, Manuscript No. JCEDR-22-18995; **Editor assigned:** 29-Aug-2022, PreQC No. JCEDR-22-18995 (PQ); **Reviewed:** 12-Sep-2022, QC No. JCEDR-22-18995; **Revised:** 19-Sep-2022, Manuscript No. JCEDR-22-18995 (R); **Published:** 29-Sep-2022, DOI: 10.35841/2329-9509.22.13.617.

Citation: Diotallevi F, Milani M, Offidani AM (2022) Sequential Therapy of Common and Plantar Warts with Salicylic Acid after Cryotherapy versus Cryotherapy Alone: A Case-Control Study in 42 Subjects. J Clin Exp Dermatol Res. 13: 617.

INTRODUCTION

Common Wart (CW; Verruca vulgaris) is a benign cutaneous virus infection caused by Human Papilloma Virus (HPV) commonly located in the palm and plantar regions [1]. HPV could infect skin by direct and indirect contacts and the risk of transmission is increased when there is a macerated skin [2]. CW is very common in children and young adults [3]. Epidemiological data report that between 10 and 30% of school children present cutaneous warts [4]. Immunosuppression is also a relevant risk factor [5]. CW is much delimitated skin growth firm and rough hyperkeratotic papules or nodules and could be considered as self-limiting papilloma [6]. Warts, especially located at pressure points, could be painful, but in general they are asymptomatic [7]. Treatment is not always necessary but when multiple lesions, pain, discomfort, functional impairment, or immunosuppression are present a specific therapeutic intervention could be mandatory [8]. Chemical or physical destructions are commonly used for the treatment of CW [9]. Cryotherapy with liquid nitrogen is a common clinician-administered treatment [10]. The most relevant drawbacks of this procedure are the pain associated with treatment, the need of multiple sessions for complete resolution and the recurrence of new lesions [11]. Salicylic Acid (SA) applied under tape occlusion is a convenient, effective, and safe therapy of CW, even if no effective as cryotherapy [12]. So far, there are few data regarding the efficacy and safety of the sequential treatment of CW with cryotherapy followed by a 10-day treatment course with SA. This approach, at least theoretically, could increase the efficacy of the treatment strategy with a reduction of the number of cryotherapies needed to eliminate CW lesions.

Study design

We evaluated in a case-control study the clinical efficacy of cryotherapy alone in comparison with cryotherapy with sequential SA treatment in adult immunocompetent subjects with palm-plantar warts. The study was conducted according to Good Clinical practices procedures [13].

MATERIALS AND METHODS

We evaluated a total of forty-two men and women, mean age 33± 13 years, with CW located in the palmar (30% of the lesions) and plantar (70%) regions. Twenty subjects (mean CW lesions 2.2 ± 0.7) represented the cases group and twenty-two the control group (mean CW lesions 1.2 ± 0.5). The cases were treated with a cryotherapy session and after 3 days topical SA 15% patch (one application/day) was applied for additional 10 consecutive days. The control group, after the initial cryotherapy session, was followed clinically to evaluate the need of new cryotherapy procedures. Additional cryotherapy sessions were programmed every two weeks until all warts were completely gone. After the last cryotherapy, all subjects underwent to a follow up evaluation of three months. Cryotherapy session was performed as follow: a wad of cotton wool saturated with liquid nitrogen was applied on and around the wart until a frozen halo appeared (i.e. 15 sec). The SA application, (15% SA patches, Transversal™, Difa Cooper Italy) starting 3 days after the cryotherapy treatment, was made every day for 10 consecutive days. The wart lesion would be considered cured when no longer visible and palpable.

Statistical analysis

Statistical analysis was performed using GraphPad statistical software ver. 13.0 (La Jolla, CA, USA). Continuous variables were expressed as mean ± Standard Deviation (SD). The Mann-Whitney tests were used for the analysis of the primary outcome of the study. We calculated the 95% Confidence intervals of the difference in the variables evaluated. According to the nature of a pilot study no sample size calculation was performed.

RESULTS

This case-control trial was performed in a University Dermatologic Clinic (Ancona Hospital) between September 2021 and May 2022. Table 1 shows the subjects characteristics of cases and controls. In the case group the sequential therapy was very effective with disappearance of all the treated lesions. After the first cryotherapy session and the sequential SA treatment, additional cryotherapy treatments were on average, mean ± SD, 1.4 ± 0.6 (range 1-3). In the control group the additional cryotherapy treatments were 3.4±0.7 (range 1-5). This difference was statistically significant (p=0.0001) (minus 2.2 sessions in comparison with controls; 95% CI of the difference: from 1.6 to 2.4) in favour of the cases vs. control subjects (Figure 1). Only two subjects (both in the control group) suffered from recurrences in the follow up.

	Number	Sex M/W	Age	Risk factors	Duration of warts in months Mean ± SD	Number of lesions before Cryotherapy, Mean ± SD	Localization of Warts
Cases	20	9/11	33	Yes in 7 subjects (35%)	5±7	2.2±0.7	Hand: 20 lesions Foot: 24 lesions
Controls	22	11/11	33	Yes in 7 subjects (32%)	4±8	1.2±0.5	Hand: 7 lesions Foot: 20 lesions

Table 1: Subjects' characteristics at baseline.

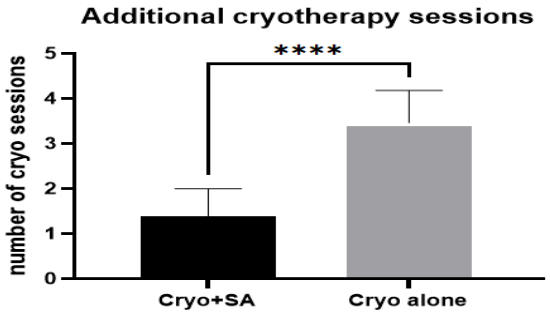

Figure 1: Number of cryotherapy sessions needed after the initial cryotherapy treatment in cases (Cryo+SA) and in controls (Cryo alone). **Note:** ****: p=0.0001, Mann Whitney Test.

DISCUSSION

In this case-control study we found that the sequential strategy using cryotherapy followed by 10-day topical salicylic acid treatment is an effective therapeutic approach for palm-plantar CW. The sequential use of SA after cryotherapy significantly reduces the need of additional cryotherapy sessions. This offers a dual advantage: the reduction of procedure-associated discomfort and pain for the patient and a direct and indirect cost saving effect. The usual treatment of CW is cryotherapy with liquid nitrogen [14]. Topical application of salicylic acid is an alternative approach with less procedure-associated pain and discomfort. Some trials suggest that cryotherapy is more effective than SA [15], however other evidence comparing these two therapeutic strategies showed no differences in effectiveness [16,17]. A common problem with both treatments is the recurrency of CW lesions [18]. In addition, cryotherapy is considered an expensive option for the treatment of warts in primary care [19]. Several cryotherapy treatments are usually required increasing the cost of the CW treatment [20]. A session of cryotherapy has an average cost of 120 €. A sequential approach (using a course of SA topical application after an initial cryotherapy session) could increase the clinical effectiveness of the cryotherapy regimen. So far, there are few data regarding the efficacy and safety of the sequential treatment approach of CW with cryotherapy followed by SA application. The main limitation is that the present study is a case-control trial. Future controlled randomized studies are warranted to better evaluate the clinical efficacy of this sequential therapy approach for this very common skin disorder.

CONCLUSION

Treatment with a single treatment strategy of common wart is often unsatisfactory. Complete clearance rates of warts lesions after cryotherapy alone are in fact around 15%. The use of topical salicylic acid offers a clearance of 14%. Therefore, there is room for improvement in increasing the rate of complete clearances of warts lesions. Our study suggests that in subjects with CW, the sequential therapy with cryotherapy and topical salicylic acid is a high effective strategy able to significantly reduce the need of additional cryotherapy procedures therefore reducing the procedure-associated discomfort. Furthermore, this sequential therapeutic strategy could offer additional benefit in term of cost-saving in the therapeutic approach of common warts. In fact, using the sequential therapy approach suggested by our study a significant reduction of direct and indirect costs is obtained.

Declaration of funding

This was an independent non-sponsored trial.

Declaration of financial/other relationships

MM is an employee of Cantabria Lab, Difa Cooper. The other authors (FD and AMO) report no conflicts of interest.

Contribution statement

FD conducted the trial performing visits and clinical evaluations. MM was involved in study protocol design. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Acknowledgment

None reported.

REFERENCES

1. Jabłonska S, Majewski S, Obalek S, Orth G. Cutaneous warts. Clin Dermatol. 1997;15(3): 309-319.
2. Jenson AB, Sommer S, Payling-Wright C, Pass F, Link Jr CC, Lancaster WD. Human papillomavirus. Frequency and distribution in plantar and common warts. Lab Invest. 1982;47(5): 491-497.
3. Kilkenny M, Marks R. The descriptive epidemiology of warts in the community. Aust J Dermatol. 1996;37(2): 80-86.
4. Kasim K, Amer S, Mosaad M, Abdel-Wahed A, Allam H. Some epidemiologic aspects of common warts in rural primary school children. Int Sch Res Notices. 2013;2013(1300): 1-6.
5. Tyring SK. Human papillomavirus infections: epidemiology, pathogenesis, and host immune response. J Am Acad Dermatol. 2000;43(1): S18-S26.
6. Jablonska S, Orth G, Obalek S, Croissant O. Cutaneous warts Clinical, histologic, and virologic correlations. Clin Dermatol. 1985;3(4): 71-82.
7. Witchey DJ, Witchey NB, Roth-Kauffman MM, Kauffman MK. Plantar warts: epidemiology, pathophysiology, and clinical management. Int J Osteopath Med. 2018;118(2): 92-105.
8. Dall'Oglio F, D'Amico V, Nasca MR, Micali G. Treatment of cutaneous warts. Am J Clin Dermatol. 2012;13(2): 73-96.
9. Khozeimeh F, Alizadehsani R, Roshanzamir M, Khosravi A, Layegh P, Nahavandi S. An expert system for selecting wart treatment method. Comput Biol Med. 2017;81: 167-175.
10. Ahmed I, Agarwal S, Ilchyshyn A, Charles-Holmes S, Berth-Jones J. Liquid nitrogen cryotherapy of common warts: cryo-spray vs. cotton wool bud. Br J Dermatol. 2001;144(5): 1006-1009.
11. Bourke JF, Berth-Jones J, Hutchinson PE. Cryotherapy of common viral warts at intervals of 1, 2 and 3 weeks. Br J Dermatol. 1995;132(3): 433-436.

12. Sterling JC, Handfield-Jones S, Hudson PM. Guidelines for the management of cutaneous warts. Br J Dermatol. 2001;144(1): 4-11.
13. Vijayananthan A, Nawawi O. The importance of Good Clinical Practice guidelines and its role in clinical trials. Biomed Imaging Interv J. 2008;4(1).
14. Verbov J. How to manage warts. Arch Dis Child. 1999;80(1): 97-99.
15. Bruggink SC, Gussekloo J, Berger MY, Zaaijer K, Assendelft WJ, de Waal MW, et al. Cryotherapy with liquid nitrogen versus topical salicylic acid application for cutaneous warts in primary care: randomized controlled trial. Can Med Assoc J. 2010;182(15): 1624-1630.
16. Bacelieri R, Johnson SM. Cutaneous warts: An evidence-based approach to therapy. Am Fam Physician. 2005;72(4): 647-652.
17. Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, Stamuli E, et al. Cryotherapy versus salicylic acid for the treatment of plantar warts (verrucae): a randomised controlled trial. Br Med J. 2011;342.
18. Youn SH, Kwon IH, Park EJ, Kim KH, Kim KJ. A two-week interval is better than a three-week interval for reducing the recurrence rate of hand-foot viral warts after cryotherapy: A retrospective review of 560 hand-foot viral warts patients. Ann Dermatol. 2011;23(1): 53-60.
19. Bruggink SC, Assendelft WJ. Cryotherapy for plantar warts more costly but no more effective than salicylic acid self-treatment. BMJ Evid Based Med Title. 2012;17(5): 156-157.
20. Stamuli E, Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, et al. Cost-effectiveness of cryotherapy versus salicylic acid for the treatment of plantar warts: economic evaluation alongside a randomised controlled trial (EVerT trial). J Foot Ankle Res. 2012;5(1): 1-10.