

Efficacy and safety of 85% phenol and 4% croton oil solution in the treatment of anogenital penile warts: a proof-of-concept study

Eficácia e segurança de solução de fenol 85% e óleo de cróton 4% no tratamento das verrugas anogenitais do pênis: um estudo tipo prova de conceito

DOI: <http://www.dx.doi.org/10.5935/scd1984-8773.2025170334>

ABSTRACT

INTRODUCTION: An 85% phenol and 4% croton oil solution (SFC) has cytotoxic effect on the epithelium; however, it has not been evaluated in the treatment of anogenital warts (AGW).

OBJECTIVE: To evaluate the effectiveness of SFC in the treatment of penile AGW in immunocompetent patients.

METHODS: Open, uncontrolled clinical trial (proof-of-concept), involving patients with penile AGW treated with SFC and reevaluated after 28 days.

RESULTS: We evaluated 16 treatments in 9 participants. SFC promoted total clearance of the lesions in 25% (95% CI 2-48%) of treatments.

CONCLUSIONS: Although well tolerated, SFC caused insufficient rates of total clearance.

Keywords: Condylomata Acuminata; Phenol; Papillomavirus Infections; Sexually Transmitted Diseases.

RESUMO

INTRODUÇÃO: solução de fenol 85% e óleo de cróton 4% (SFC) tem efeito citotóxico para o epitélio, porém não foi avaliada no tratamento das VAGs.

OBJETIVO: avaliar a eficácia da SFC no tratamento de VAGs penianas em imunocompetentes.

MÉTODOS: ensaio clínico aberto, não controlado (prova de conceito), envolvendo portadores de VAGs tratados com SFC e reavaliados após 28 dias.

RESULTADOS: foram avaliados 16 tratamentos em nove participantes. A SFC promoveu o clareamento total das lesões em 25% (IC95%: 2-48%) dos tratamentos.

CONCLUSÕES: apesar de bem tolerada, a SFC apresentou taxas insuficientes de clareamento total.

Palavras-chaves: Condiloma Acuminado; Fenol; Infecções por Papillomavirus.

Letters to the editor

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Financial support: None.

Conflicts of interest: None.

Submitted on: 18/12/2023

Approved on: 08/01/2023

How to cite this article:

Efficacy and safety of 85% phenol and 4% croton oil solution in the treatment of anogenital penile warts: a proof-of-concept study. Belli MC, Miot HA, Garbers LE, Martimiano BD. Surg Cosmetic Dermatol.2025;17:e20250334.

Dear editor,

Anogenital warts (AGWs) are epithelial proliferations caused by the human papillomavirus (HPV). It is the most common sexually transmitted infection (STI) in the world, with an estimated incidence rate varying between 160 and 289 new cases per 100,000 people per year.¹

HPV types 6 and 11 are found in 90% of genital condylomas and are considered to be of low oncogenic risk. Different kinds of treatment have been described for AGWs, although no consensus has been reached on an absolute therapy, as they all imply recurrence and the need for multiple sessions. Topical treatment with phenol and croton oil solutions has demonstrated a cytotoxic and immunogenic effect on precancerous skin lesions, suggesting that it may be effective in the treatment of viral infections.² The search for strategies to increase the therapeutic efficacy of AGWs is valuable and implies reduced costs for the health system.

The indications for use of this solution consist of its ability to perform deep peels, and its cytotoxic, immunogenic and viricidal effect, with excellent cost/benefit ratios.³ However, there is still a need for studies demonstrating the histological and clinical findings of this deep peel on AGWs and its effectiveness when compared to other approaches currently used.

This study aimed to investigate the efficacy and safety of 85% phenol and 4% croton oil in the treatment of penile STIs in immunocompetent men.

This open, non-controlled, proof-of-concept clinical trial was conducted between August 2022 and May 2023, involving 16 treatment in nine men seen at an STI outpatient clinic at the *Unesp Hospital das Clínicas da Faculdade de Medicina de Botucatu (HCFMB)*.

The patients eligible for the study were immunocompetent, adult men who had STIs on the penis, diagnosed by physical examination or acetoscopy performed by a qualified dermatologist. A session of application of 85% phenol and 4% croton oil solution was conducted until the lesions were completely frosted. The AGWs were photographed before and after application of the solution and reassessed after 28 days. After this time, the result presented by each patient was classified as total lesion clearance or therapeutic failure. Some patients who presented lesions at the reassessment were included in the study again.

The primary outcome of the study was total lesion clearance on Day 28. The secondary outcomes were a lower lesion count and analysis of pain during application, which was assessed using the visual analog scale (VAS 0 to 10). The data were analyzed according to the protocol (per protocol), and cases that missed the follow-up on Day 28 were excluded. A p-value <0.05 was considered significant.

The rate of total clearance and lower lesion count was compared with the results of clinical trials conducted on the same population using treatment with 90% trichloroacetic acid and cryotherapy with liquid nitrogen (historical control).^{4,5}

The sample for the pilot study phase was initially made up of 17 treatment on 10 consecutive participants, of whom it was hoped to find a total clearance rate of more than 30% after one session (proof-of-concept).

During the treatment, one participant was excluded from the study for not attending the follow-up on Day 28 after the first session. The study therefore ended with 16 treatment and nine participants.

Figure 1 shows the number of lesions on the day of application and the lesion count on Day 28. Figure 2 shows the quantification of pain, assessed using the VAS. There were no serious adverse effects and the treatment was well tolerated.

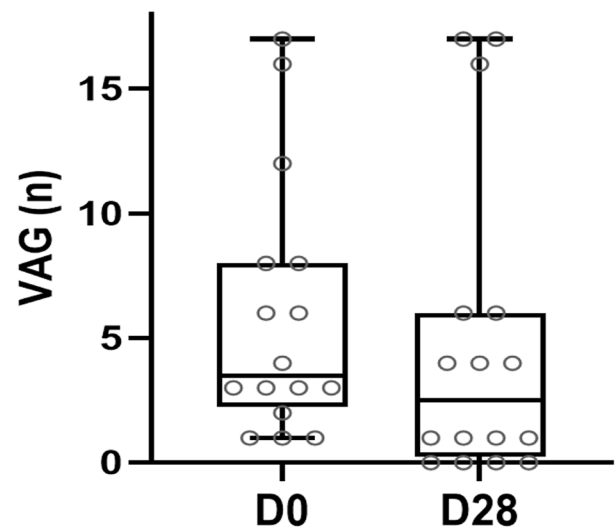


FIGURE 1: Count of penile anogenital warts before and after 28 days of treatment with 85% phenol and 4% croton oil solution (p=0.167)

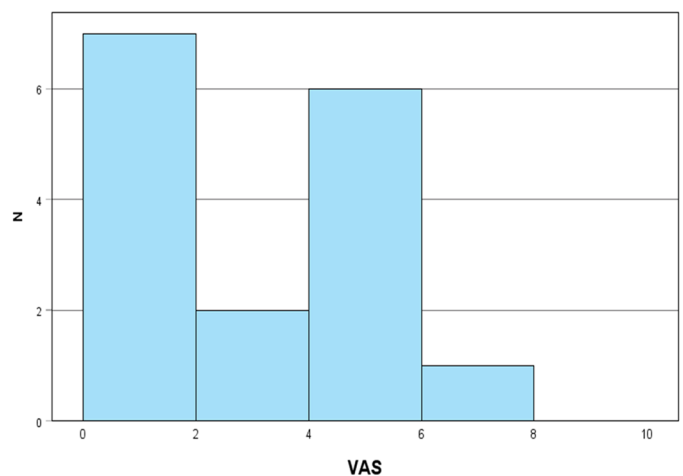


FIGURE 2: Histogram of pain scores during application, as per the VAS

Total lesion clearance occurred in 25% (95% CI: 2–48%) of cases per session, which was historically lower than treatment with liquid nitrogen in the same population (historical control).

In this feasibility study, total clearance of penile AGWs treated with 85% phenol and 4% croton oil solution occurred in 25% of treatment.

In studies with the same methodology and population, penile AGWs clearance after one session occurred in 23% (95%CI: 9–34%) of patients treated with trichloroacetic acid; 46% (95%CI: 31–59%) with liquid nitrogen; and 26% (95%CI: 11–37%) with the combination of nitrogen and trichloroacetic acid.^{4,5}

The study has limitations because it is a single-center study, has not quantitatively assessed immunity, has not determined the subtype of the HPV virus in each patient, requires a clinical diagnosis of the lesions, and one individual was lost to follow-up. However, these elements have not prevented the evaluation of the performance of lesion clearance.

Although well tolerated and effective, the 85% phenol and 4% croton oil solution showed total clearance rates below 30%. ●

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Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; critical literature review; critical review of the manuscript.

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