A single-blind study of podophyllotoxin cream 0.5% and podophyllotoxin solution 0.5% in male patients with genital warts

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Abstract

Objective—To evaluate the efficacy-safety ratio of a new topical podophyllotoxin cream 0.5% compared with podophyllotoxin solution 0.5% (Condyline) in male patients with genital warts.

Methods—In an observer-blinded controlled study a total of 136 and 133 wart lesions were treated with podophyllotoxin cream 0.5% and podophyllotoxin solution 0.5%, respectively. The preparations were applied twice daily for 3 days, repeated with 4 days intervals for a minimum of two and a maximum of four treatment cycles.

Results—At the conclusion of the study (8 weeks after completion of therapy) a significant reduction in mean wart area was observed in both the cream group (87.7, SD 8.4 to 20.6, SD 2.7) and in the solution group (92.3, SD 7.5 to 21.5, SD 2.8) ($p < 0.01$). At the same time all treated warts had completely cleared in 63% of patients in both study groups. Mild to moderate side effects occurred to the same extent in both podophyllotoxin cream and podophyllotoxin solution recipients.

Conclusion—We conclude that podophyllotoxin 0.5% administered in a cream formulation does not give additional clinical benefits when compared with podophyllotoxin solution 0.5% in male patients with external genital warts.

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Keywords: Genital warts; podophyllotoxin

Introduction

Purified ethanolic solutions of 0.5% podophyllotoxin have in recent years been available for self-treatment of external genital warts in both male¹⁻³ and female patients.^{4,5} The 0.5% cream formulation of podophyllotoxin was developed in order to make application more convenient with an efficacy-safety profile comparable to that of podophyllotoxin solution 0.5%. The use of a solution and applicator is convenient in the self-treatment of warts that are visible to the patient. When warts are inaccessible, or patients find it difficult or inconvenient to use a solution and applicator, then an alternative pharmaceutical preparation such as a cream could be preferred.

This study was designed to evaluate the comparative efficacy and safety of patient-

applied podophyllotoxin cream 0.5% versus podophyllotoxin solution 0.5% in the treatment of external genital warts in male patients.

Patients and methods

The study was conducted and approved by the appropriate institutional review boards in three dermatovenereological centres in Copenhagen, Bispebjerg Hospital, Rigshospitalet and Gentofte Hospital which enrolled 14, 12 and 10 patients, respectively. After informed consent was obtained the patients were randomly and observer-blind assigned to one of two study groups. One group of patients received podophyllotoxin in an alcoholic solution 0.5% (Condyline) twice daily for three days repeated with four days interval for a minimum of two and a maximum of four treatment cycles. Patients in the other group were treated with a cream formulation containing podophyllotoxin 0.5% applied as described above. The cream was administered by fingertip application.

Patients who had been given a diagnosis of condyloma acuminatum were enrolled if they were in general good health and if they had not received topical or systemic antiviral or anti-wart therapy within the last four weeks.

Clinical efficacy was determined by quantitative assessment of the treated warts. The two larger perpendicular dimensions of the warts were measured and the wart area was defined as the product of those two measurements. Clearing of warts were defined as the disappearance of all treated warts in a patient.

Safety was assessed by questioning and examining patients for local reactions indicating intolerance of the treatment. Adverse reactions including tenderness, burning, pain, erythema, erosions and oedema were noticed and if present described as mild, moderate or severe.

The distributions of the demographic and efficacy and safety data on the two treatment groups were compared with the use of analyses of variance, the Wilcoxon test, Fisher's exact test and the chi square test.

Results

Clinical efficacy

The demographic data of included patients are shown in table 1. The majority of treated wart lesions were penile and the mean wart area was comparable in the two treatment groups. Application of podophyllotoxin solution 0.5% was associated with a rapid and significant

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Table 1 Demographic data on patients

Characteristic	Study group	
	Podophyllotoxin solution 0.5%	Podophyllotoxin cream 0.5%
Mean age (year)	24	22
Previous therapy (%)	30	28
Duration of warts (months)	2.5	3.5
Median number of warts per patient	7	8
Mean (SD) wart area (mm ²)	92.3 (7.5)	87.7 (8.4)
Location of warts (no)		
Penile	122	126
Perianal	5	7
Urethral	4	3

Table 2 Reduction in wart area during treatment of condyloma acuminatum with podophyllotoxin cream 0.5% and podophyllotoxin solution 0.5% in male patients. P values (*, †) indicates significant reduction from baseline. No significant difference was found between treatment groups

Week of study	Podophyllotoxin cream 0.5%		Podophyllotoxin solution 0.5%	
	Total no of lesions	Mean (SD) wart area	Total no of lesions	Mean (SD) wart area
0	136	87.7 (8.4)	133	92.3 (7.5)
1	122	76.0 (5.6)	85	59.7 (6.7)*
2	102	66.4 (8.7)	72	47.0 (4.8)*
3	80	52.2 (7.2)*	38	25.2 (3.2)†
5	51	33.6 (4.2)*	12	9.2 (0.8)†
6	44	29.2 (3.2)†	5	4.5 (0.5)†
12	32	20.6 (2.7)†	29	21.5 (2.8)†

*p < 0.05; †p < 0.01.

reduction in number and size of treated lesions, whereas the effect of podophyllotoxin 0.5% cream was somewhat protracted (table 2). A total of 95% of patients treated with podophyllotoxin 0.5% solution were free of warts two weeks after completion of therapy, but only 63% remained clear at the final control-visit (week 12). In comparison 63% of patients treated with podophyllotoxin 0.5% cream were wart free two weeks after stopping therapy. However, the final cure rate of 63% in cream recipients was identical to that obtained in solution recipients. No difference could be detected in the overall efficacy of the two formulations of podophyllotoxin (table 2). The number of applications of either podophyllotoxin cream or solution was not significantly different in the two treatment groups.

Evaluation of safety

Local adverse reactions graded mild to moderate were noticed in 35% of podophyllotoxin solution recipients compared with 40% of podophyllotoxin cream recipients (none significant). Separate analyses of tenderness, burning, pain, erythema, erosions and oedema did not show differences between the two treatment groups. Only one patient treated with podophyllotoxin cream 0.5% did not complete the trial for reasons not associated with therapy.

Discussion

The final cure rate obtained with the two podophyllotoxin preparations is well within the range seen in previous published studies.¹⁻⁵ In this trial an advantage of podophyllotoxin cream 0.5% over a well-known ethanolic solution of podophyllotoxin 0.5% could not be documented. Neither the clinical efficacy nor safety aspects were in favour of podophyllotoxin cream 0.5%. It is possible that a cream formulation of podophyllotoxin may be easier to apply and therefore improve the compliance in female patients with external genital warts. A drawback of a cream formulation, however, may be a greater rate of adverse reactions, due to spreading of the cream over a larger area, as reported in a recently published study in female patients.⁶

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