

# New Alternative Combination Therapy for Recalcitrant Common Warts: The Efficacy of Imiquimod 5% Cream and Duct Tape Combination Therapy

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Dear Editor:

Although verruca vulgaris (a common wart) is highly prevalent, but its treatment method is still not accepted by both patients and doctors<sup>1</sup>. Current modalities depend on the ablation of warts (cryotherapy, laser vaporization, electrodesiccation, salicylic acid, silver nitrate and trichloroacetic acid) or the interruption of cell division (podofilox, intralesional or systemic interferon, intralesional bleomycin and 5-fluorouracil)<sup>2,3</sup>. All contemporary therapies are connected to significant pain, tissue destruction and common recurrence<sup>2,3</sup>. No accessible drug therapy is known to successfully eradicate viral infection or replication.

Until now, imiquimod, 1-(2-methylpropyl)-1Himidazo[4,5-c]quinolin-4-amine has been used as a topical immune response to effectively treat external anogenital warts<sup>4</sup>. Because cell mediated immunity is the primary mechanism accountable for the regression of warts<sup>5</sup>, we accessed imiquimod as a promising therapy for these frequent viral diseases. In addition, several reports<sup>6,7</sup> have recommended that occlusion with adhesive tape could also be an efficacious therapy for the treatment of warts. Given that duct tape therapy is economical and painless, we decided to use this method.

The aim of this study was to estimate the safety, tolerance and effectiveness of combination therapy with imiquimod and duct tape for the treatment of the common verruca that have been resistant to prior treatment options.

This was a phase II, open-label, clinical study. Approval of the Institutional Review Board (Approved No. AS10101) was obtained prior to the initiation of the study, and

written consent was obtained from all patients prior to enrollment. Inclusion criteria were the following: (1) ability to understand and provide informed consent; (2) age greater than 18 years; (3) having at least 1 common wart with a diameter of 2 to 15 mm; and (4) lesions recalcitrant to prior reiterated medical and/or destructive treatment and patient denial to go through painful treatment. Fifty patients were enrolled in the study. Ten patients, 5 from the petrolatum group and 5 from the imiquimod 5% cream group, were not available for follow-up and thus were not included in the analysis.

Patients obtained either petrolatum or imiquimod 5% cream. Imiquimod 5% cream or petrolatum was instructed to be self-applied, and then the wart was occluded with duct tape (Silver Duct Tape; 3M, St. Paul, MN, USA) by the patient once daily for 5 days per week. Patients were requested to apply either petrolatum or imiquimod 5% cream to the lesions in an amount that could be rubbed into the skin. In addition, a supply of standard duct tape was provided. The tape was left off in the daytime and reapplied the following night. The therapy proceeded for a maximum of 16 weeks or until resolution of the wart. Patients were asked to revisit the hospital every 2 weeks, so the doctor could remeasure the wart and document the results on the data sheet. Statistical analysis of response to treatment was performed using Fisher's exact test, with  $p \leq 0.05$  being considered significant.

Of 40 patients who completed the study, 20 were in the petrolatum arm, and 20 were in the imiquimod 5% cream arm. There were no significant differences in the mean

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**Fig. 1.** Common warts before (A) and after (B) treatment with imiquimod 5% cream and duct tape occlusion therapy: complete response.

**Table 1.** Treatment outcome of imiquimod 5% cream and duct tape occlusion therapy and petrolatum and duct tape occlusion therapy ( $p=0.05$ )

Response	Treatment group	
	Imiquimod 5% cream & duct tape occlusion (n=20)	Petrolatum & duct tape occlusion (n=20)
Complete response	8 (40)	0 (0)
Partial response	6 (30)	4 (20)
No response	6 (30)	16 (80)

Values are presented as number (%).

age or sex of the patients or in baseline size or location of the warts between the two groups. We found that imiquimod 5% cream and duct tape occlusion therapy was appreciably more effective than petrolatum and duct tape occlusion therapy. Eight (40%) of 20 patients in the imiquimod 5% cream and duct tape occlusion arm had complete resolution of their warts (Fig. 1) vs. 0 (0%) of 20 patients in the petrolatum and duct tape occlusion therapy arm ( $p=0.05$ ). In addition, 6 patients (30%) enrolled in the imiquimod arm vs. 4 patients (20%) enrolled in the petrolatum arm had partial resolution (>50% size reduction) of their warts (Table 1). No recurrence of warts occurred during a follow-up period of 16 weeks. Although no major complications were noted in either group, the main adverse effects were erythema and itching sensation at the site.

In our study, we found that imiquimod 5% cream and duct tape occlusion therapy was more effective than petrolatum and duct tape occlusion therapy for the treatment of common warts. The mechanism of action of imiquimod in humans has not been exactly recognized, but several reports imply that it stimulates the cellular

immune system, including the use of specific cytokines<sup>4,8</sup>. Through induction of interferon-alpha, imiquimod could improve antigen presentation by increasing the expression of major histocompatibility complex class I. Together with induced interleukin (IL)-12 p40, imiquimod augments the development of a Th1 type immune response. Other cytokines that are induced by imiquimod such as tumor necrosis factor-alpha, IL-1 and IL-6 may contribute to wart regression by increasing T-cell trafficking to the epidermis, enhancing natural killer cell cytotoxicity and stimulating B-cell proliferation. The therapeutic mechanism of duct tape for the treatment of verruca vulgaris has been mostly undetermined, but several theories have been proposed. The lay media often proposes the theory that occlusion results in a deprivation of oxygen to the virus, essentially leading to suffocation. A second theory is that duct tape debrides and debulks the wart. Allen and Dveirin<sup>9</sup> suggested that duct tape may contribute to psychological aspects, thus, it may be more helpful in children than in adults. Additionally, duct tape occlusion creates a macerating and keratolytic environment<sup>10</sup>, which encourages penetration of imiquimod 5% cream.

Thick stratum corneum may inhibit drug penetration, rendering the degree of keratinization, which is a possible explanation for the less impressive results on the common wart. Consequently, duct tape occlusion following the application of imiquimod may be helpful in overcoming this limitation.

In conclusion, imiquimod 5% cream and duct tape occlusion combination therapy is an effective alternative treatment modality for the treatment of the common verruca. Additional studies with larger numbers of patients including randomized double blind trials are required to establish its effectiveness.

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# Selective Elevation of Antibodies to Desmoglein 1 during the Transition from Mucocutaneous to Cutaneous Type Pemphigus Vulgaris

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Dear Editor:

Pemphigus vulgaris (PV) is a group of autoimmune blistering diseases. Three types of PV have been classified in-

cluding mucous PV, mucocutaneous PV (mcPV), and cutaneous PV (cPV). It has been reported that mcPV and cPV exhibit autoantibodies against both desmoglein (DSG)1 and

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