**Response of Predominantly Recalcitrant Cutaneous Warts to Topical Chemotherapy**

Warts, particularly plantar warts, are often therapeutically challenging. They may disappear when least expected or persist despite months of intensive treatment. The objective of this preliminary study was to assess the response of recalcitrant warts to a topical liquid compound containing chemotherapeutic (antineoplastic) agents (Wart Film Formula 4, NuCara Pharmacy, Waterloo, Iowa) (fluorouracil, levamisole, salicylic acid and 2-deoxy-D-glucose). Each component of this compound has been reported to be helpful separately in the treatment of warts.

With approval of the Mayo Foundation Institutional Review Board, we surveyed all adult patients (> 18 years old) who presented to the Department of Dermatology at Mayo Clinic between 2000 and 2002 with recalcitrant cutaneous warts, mostly involving the feet, and received a prescription for the compound. The survey was conducted by mail and, if no reply, by telephone.

The questionnaire was sent to 280 patients, and 221 (79%) completed it. Responses were analyzed for the 188 patients (85%) who used the compound as prescribed. Of these 188 patients, 155 (83%) had tried other treatments unsuccessfully. In response to the survey, 77 patients (41%) reported that the warts were completely gone (fig. 1), 37 (20%) that the warts were almost gone, 52 (28%) that the warts were the same and 9 (5%) that the warts had increased in number. Eighty-six patients (46%) reported that they were very satisfied with the treatment. Mean duration of therapy was 10.3 weeks (range, 1–60 weeks). No serious adverse effects were reported.

Thus, we observed a high rate of therapeutic success treating predominantly recalcitrant warts with a topical liquid formulation containing chemotherapeutic agents. Use of a liquid preparation is more appealing than the destructive approaches frequently used (liquid nitrogen, electrodessication, curettage, excision, CO2 laser), all of which cause some degree of morbidity. Our patients reported infrequent adverse effects using this compound.

We conclude that this topical formulation, which incorporates two chemotherapeutic agents, is an effective treatment for warts. Although a survey study has limitations, we believe our results warrant further study.

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**Efficacy and Benefit of a 5-FU/Salicylic Acid Preparation in the Therapy of Common and Plantar Warts—Systematic Literature Review and Meta-Analysis**

**Abstract**

**BACKGROUND:** (1) Salicylic acid (SA) and 5-Fluorouracil (5-FU) are effective drugs in wart therapy. (2) In Germany, increasing data on the benefit and the economic efficiency of drugs at Level I of evidence-based medicine are needed.

**METHODS:** Evaluation of the effectiveness and benefits of a drug combination containing 0.5% 5-FU and 10% SA in the therapy of (a) common and (b) plantar warts in form of a two-step procedure—(1) Systematic literature analysis, (2) Meta-analysis of the randomised-controlled studies (RCTs).

**RESULTS:** (1) The efficacy of 5-FU/SA therapy was tested in a total of 625 patients (n=8 RCTs) with common warts and 101 patients (n=4 RCTs) with plantar warts. The therapeutic effect across all studies in common warts was 63.4% response (complete healing) for 5-FU/SA vs. 23.1% for the 5-FU-free controls, respectively. In plantar warts, the response was 63.0% vs. 11.0%. (2) A meta-analysis of n=7 RCTs on common warts (n=325 patients) showed a mean risk difference of 0.42 (CI 0.34-0.50, p < 0.05), thus a significant superiority of 5-FU/SA over SA. A comparable result was also found for plantar warts.

**CONCLUSION:** The combination of 5-FU and SA is an effective and beneficial therapy for common and plantar warts.

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**Fig. 1**

Treatment of recalcitrant plantar warts. (a) Recalcitrant plantar warts in an immuno-suppressed patient with acute lymphocytic leukemia who was receiving chemotherapy. There had been no response to treatment with any of the following agents: salicylic acid for 2 months, liquid nitrogen for 3 months or cantharidin for 2 months. (b) Five months after starting treatment with a topical liquid formulation of salicylic acid, fluorouracil, levamisole and 2-deoxy-D-glucose.
TREATMENT OF VERRUCA PLANTARIS WITH A COMBINATION OF TOPICAL FLUOROURACIL AND SALICYLIC ACID.

Abstract
A medical record review was conducted to determine the clinical outcome and average time to resolution of verruca plantaris in 20 patients treated with twice-daily applications of either 0.5% or 5.0% topical fluorouracil combined with topical 17% and 40% salicylic acid. Seven patients used 0.5% fluorouracil, and 13 used 5.0% fluorouracil. All of the lesions were sharply debrided at regular 1- or 2-week intervals. All 20 patients achieved full clinical resolution in a mean +/- SD of 82.5 +/- 56.6 days. Three patients (15%) had recurrent lesions, which subsequently resolved with repeated treatment. Two patients (10%) developed local dermatitis, which resolved with temporary discontinuation of the medication and the addition of a topical corticosteroid. It was observed that the twice-daily application of topical fluorouracil and salicylic acid is a safe and effective treatment for verruca plantaris.

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TOPICAL 5% 5-FLUOROURACIL CREAM IN THE TREATMENT OF PLANTAR WARTS: A PROSPECTIVE, RANDOMIZED, AND CONTROLLED CLINICAL STUDY.

Abstract
Topical 5-fluorouracil (5-FU) is an antineoplastic antimetabolite that inhibits DNA and RNA synthesis, thereby preventing cell replication and proliferation. This mechanism of action may allow topical 5-FU to be utilized in the treatment of human papilloma virus (HPV). We conducted a study comparing 5% 5-FU cream under tape occlusion versus tape occlusion alone in 40 patients presenting with plantar warts. Nineteen out of 20 patients (95%) randomized to 5% 5-FU with tape occlusion had complete eradication of all plantar warts within 12 weeks of treatment. The average time to cure occurred at 9 weeks of treatment. Three patients (15%) had a recurrence at the 6-month follow-up visit; accordingly, an 85% sustained cure rate was observed. It is concluded that use of topical 5% 5-fluorouracil cream for plantar warts is safe, efficacious, and accepted by the patient.

Salk RS, Grogan KA, Chang TJ.

5% 5-FLUOROURACIL CREAM FOR TREATMENT OF VERRUCA VULGARIS IN CHILDREN.

Abstract
Warts are a common pediatric skin disease. Most treatments show only modest benefit, and some are poorly tolerated because of pain. 5-fluorouracil interferes with deoxyribonucleic acid and ribonucleic acid synthesis, and is used to treat genital warts in adults. Efficacy, safety, and tolerability of topical 5% 5-fluorouracil for treatment of common warts were examined in an open-label pilot study with pediatric patients. Thirty-nine children who have at least two hand warts applied 5% 5-fluorouracil cream (Efudex, Valeant Pharmaceuticals International) once or twice daily, under occlusion for 6 weeks. Assessment of treatment response and side effects was performed at baseline, treatment completion, and 3- and 6-month follow-ups. Hematology measures, liver function tests, and medication blood levels were reassessed at treatment completion. Eighty-eight percent of treated warts improved after 6 weeks of treatment, and 41% of subjects had complete resolution of at least one wart. Treatment response did not differ between once or twice daily applications. Tolerability and patient satisfaction were excellent. No subject had clinically significant blood levels of 5-fluorouracil. At 6 month follow-up, 87% of complete responders had no wart recurrence. Topical 5% 5-fluorouracil is a safe, effective, and well-tolerated treatment for warts in children.

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