

Topical Cidofovir

A Novel Treatment for Recalcitrant Molluscum Contagiosum in Children Infected With Human Immunodeficiency Virus 1

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF CASES

Two children with human immunodeficiency virus 1 (HIV-1) presented to the dermatology clinic for treatment of disseminated molluscum contagiosum (MC). Both children suffered from severe social isolation because of their facial disfigurement. Their MC lesions were refractory to numerous therapeutic modalities, including liquid nitrogen, cantharidin, and 0.05% tretinoin gel. Both children had MC lesions, elevated viral loads, and low CD4 T-cell counts despite highly active antiretroviral therapy (HAART) for a median of 24 months. Patient 1, an 8-year-old African American boy, had a CD4 T-cell count of 329/ μ L and a viral load of 727050 (log 5.86) HIV RNA copies/mL. Patient 2, a 4-year-old-Hispanic boy, had a CD4 T-cell count of 168/ μ L and a viral load of 429976 (log 5.63) HIV RNA copies/mL.

Both patients exhibited hundreds of umbilicated pearly and skin-colored papules disseminated over the entire body, including the face and perineal area (**Figure**, A and C).

THERAPEUTIC CHALLENGE

Our goal was to develop a minimally scarring, effective nonsurgical method of treating recalcitrant and disfiguring MC in patients with severe immunosuppression and high HIV-1 levels despite HAART.

SOLUTION

Topical 3% cidofovir was compounded as follows: 15 g of cidofovir (75 mg/mL) was mixed with 22.5 g of a combination vehicle (Dermovan; Galderma Laboratory Inc, Fort Worth, Tex). The lesions were treated with topical application of 3% cidofovir in Dermovan once a day, 5 days a week, for 8 weeks. Nonfacial lesions were treated similarly, but they were also occluded with adhesive tape (Scotch 3M) for at least 12 hours. All lesions were treated except those near the edge of the upper and lower eyelids, because the patients refused treatment of this area and to avoid irritation of the conjunctiva. Both patients exhibited redness and painful erosions at the sites of previous lesions 5 to 15 days after the initial application of the drug. Most redness and erosion resolved during the 2-day rest

period. The surrounding perilesional skin appeared to be unaffected by treatment. The lesions healed with superficial scars, postinflammatory hypopigmentation, and hyperpigmentation. Large lesions healed with varioliform scars (Figure, B and D). No systemic adverse effects were noted. During therapy, neither patient developed neutropenia, and their serum urea nitrogen and creatinine levels were within the normal range. After 2 months of treatment, all the lesions that were treated showed complete clinical resolution. There was no evidence of recurrence at the 3-, 6-, and 18-month follow-up visits. There was no statistical difference between the absolute CD4 T-cell counts and viral loads before and at 18 months after cessation of therapy. The CD4 T-cell count of patient 1 was 319/ μ L, and his viral load was 270126 (log 5.43) HIV RNA copies/mL. The CD4 T-cell count of patient 2 was 155/ μ L, and his viral load was 404015 (log 5.61) HIV RNA copies/mL. Also, patient 1 remained clear of MC lesions at 21 months after cessation of therapy. At the end of the study, both patients showed significant improvement in their self-image and resumed their social activities.

COMMENT

Molluscum contagiosum commonly affects children and immunocompromised individuals. The prevalence of MC among HIV-infected individuals ranges from 5% to 18%. Children with acquired immunodeficiency syndrome (AIDS) who exhibit extensive and recalcitrant MC suffer from increased morbidity and disfigurement. Recalcitrant MC in these children represents a therapeutic challenge.

We report the successful use of topical 3% cidofovir in a combination vehicle (Dermovan) in the treatment of recalcitrant MC in 2 children with AIDS. Cidofovir therapy has also been reported to induce clearing of MC lesions in 3 adults with AIDS, 2 of whom were receiving the drug intravenously for cytomegalovirus retinitis, and 1 of whom was being treated topically.¹ Recently, topical cidofovir was reported to be effective in the treatment of MC in a 12-year-old boy with Wiskott-Aldrich syndrome.² More than 75% of the patient's body surface was covered with MC lesions. Within 2 to 3 weeks, the lesions treated with cidofovir showed acute inflammation followed by resolution.



Upper trunk area (A) and perineum (C) before treatment with topical 2% cidofovir. Eighteen months after cessation of therapy, the lesions had healed with postinflammatory hyperpigmentation and superficial scars (B and D).

Cidofovir is a nucleotide analog of deoxycytidine monophosphate that has broad antiviral activity against DNA viruses, including cytomegalovirus,³ herpes sim-

plex virus,⁴ human papillomavirus,^{5,6} and MC.^{1,2} However, it demonstrates no activity against RNA viruses. Cidofovir diphosphate, cidofovir's active metabolite, acts as

a competitive inhibitor of, and an alternate substrate for, DNA polymerase.^{7,8} It inhibits viral DNA polymerase more avidly than human DNA polymerase.⁹ Unlike acyclovir and ganciclovir, cidofovir is not dependent on virally encoded thymidine kinase for activation. In fact, it has been shown that strains of herpes simplex virus that were resistant to acyclovir, ganciclovir, or foscarnet remained sensitive to cidofovir.¹⁰

Several animal studies regarding topical administration of cidofovir are available. Recently, Cundy et al¹¹ investigated the availability of topical cidofovir on abraded and intact skin of rabbits. The bioavailability of topical cidofovir was 0.2% to 2.1% in intact skin and 41% in abraded skin. Furthermore, they found that the bioavailability of cidofovir was enhanced in vehicles containing propylene glycol. In this study, we used Dermovan, a vehicle that contains propylene glycol. We believe that the combination of a vehicle such as Dermovan and occlusion enhanced the optimal delivery of the drug. Most likely, occlusion increased the efficacy and absorption of the drug by increasing the skin surface area, hydration, and temperature and by maintaining a reservoir of the drug in the stratum corneum. The inflammation and erosions produced by this formulation may have further increased the absorption. We decided not to occlude facial skin and mucous membranes, because there is increased absorption of topical formulations in these areas.¹²

Topical application of cidofovir on intact rabbit skin led to negligible systemic exposure to the drug.¹¹ In humans, a systemic adverse reaction has been reported in a single patient treated with intralesional cidofovir (2.5 mg/mL) for recurrent laryngeal papillomatosis.¹³ This individual developed "precardial" complaints, but no cardiac abnormalities were found. The pharmacokinetics of 0.3% and 1% cidofovir gel in subjects with herpes simplex virus has been briefly described.¹ Of note, nephrotoxicity, neutropenia, and metabolic acidosis are potential serious systemic adverse effects of intravenous cidofovir therapy.¹⁴

In this study, topical cidofovir was effective in the treatment of generalized MC in 2 children with AIDS. Our 2 patients had refractory MC despite extensive treatment with HAART. Most nucleoside analogs are relatively specific for HIV, except lamivudine, which also has shown activity against hepadnaviruses.¹⁵ None of the agents that target HIV has known predicted antiviral activity against MC. Although both our patients received concomitant HAART during their topical cidofovir therapy, there was suboptimal control of HIV-1 viral replication. It is unlikely that HAART was responsible for the resolution of the MC lesions, since there were no significant differences in absolute CD4 T-cell counts and viral loads before or after treatment with topical cidofovir.

To our knowledge, we report for the first time the use of topical cidofovir for generalized and facial MC in children with AIDS. This nonsurgical method avoids the potential significant renal toxicity associated with systemic therapy. Our study suggests that topical 3% cidofovir is a safe and potentially effective treatment in recalcitrant MC in children with AIDS and high HIV-1 levels despite HAART. Double-blind control trials of topical cidofovir in Dermovan for MC in HIV-infected children will confirm our preliminary results.

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Submissions

Clinicians, local and regional societies, residents, and fellows are invited to submit cases of challenges in management and therapeutics to this section. Cases should follow the established pattern. Submit 4 double-spaced copies of the manuscript with right margins nonjustified and 4 sets of the illustrations. Photomicrographs and illustrations must be clear and submitted as positive color transparencies (35-mm slides) or black-and-white prints. Do not submit color prints unless accompanied by original transparencies. Material should be accompanied by the required copyright transfer statement, as noted in "Instructions for Authors." Material for this section should be submitted to George J. Hruza, MD, Laser and Dermatologic Surgery Center Inc, 14377 Woodlake Dr, Suite 111, St Louis, MO 63017. Reprints are not available.

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Correction

Error in Drug Amount. In The Cutting Edge article by Toro et al titled "Topical Cidofovir: A Novel Treatment for Recalcitrant Molluscum Contagiosum in Children Infected With Human Immunodeficiency Virus 1," published in the August 2000 issue of the ARCHIVES (2000;136:983-985), in the first sentence of the "Solution" section on page 983, the amount of cidofovir should have read "15 mL" (not 15 g).