Dear Readers:

Recurrent orofacial herpes simplex virus (HSV) infection called herpes labialis (HSL), or cold sores, affects 1 in 3 persons in the western world. Most primary infections occur in childhood then recur as re-activated HSV, a DNA virus, migrates to the lips, face, or oral mucosa, usually from the sensory trigeminal ganglion.

This recurrent infection creates a partial-thickness wound that is usually shorter than the primary episode, progressing through 1 or more of the typical stages: prodrome, redness, papule, vesicle, ulcer, hard crust, and residual swelling/dry flaking before normal skin is restored. “False prodrome” can occur without progressing to the papule stage in up to one-third of episodes. Nonulcerative episodes stopped by the host’s immune response after the papule stage may last only 3 days. Classical ulcerative HSL lesions which progress through the vesicle, ulcer, crusting, and flaking stages last 7-10 days as compared to 5-6 days on average for ulcerative and nonulcerative lesions mixed.

The 24-hour window of opportunity to initiate effective treatment plus variability in HSL lesion severity and related time to heal makes it difficult to study efficacy of the anti-viral agents most commonly used to prevent or treat HSV infection. The HSV lesion is a partial-thickness wound involving epidermis and dermis. Fear of preserving a moist HSL environment is unwarranted so there appears no scientific reason to deny the HSL lesion the benefits of faster healing and lower complications experienced by similar depth wounds dressed with moisture-retentive or “occlusive” dressings. The 2 reports reviewed below summarize recent advances in managing HSL lesions and offer interesting hypotheses for further testing.

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Topical Medications Improve Cold Sore Outcomes


Rationale: The rapid-onset and brief period of HSV replication that trigger recurrent HSL limit the opportunity for antiviral medications to reduce lesion severity. Recognized antiviral agents and their pro-drugs show only a 10% reduction in lesion healing time. New data suggests that episodic treatment may prevent outbreaks.

Objective: Conduct a comprehensive critical review summarizing recent evidence of effects on recurrent HSL epidemiology, pathology, and development, and identify factors important in design of randomized controlled trials (RCTs) exploring agents affecting lesion progression.

Methods: MEDLINE searches identified all clinical studies of episodic HSV treatment reporting epidemiology of herpes labialis excepting cases induced by ultraviolet light exposure. Epidemiology was summarized as number of episodes per individual per year. The authors developed a mathematical model to describe recurrent HSV epidemiology and to test treatment efficacy based on the assumption that each episode of HSL occurs independently of other episodes.

Results: Seven qualifying studies, mostly retrospective surveys, reported that 30% to 45% experienced recurrent HSL among more than 36,000 subjects, including students, adults, blood donors, hospitalized patients, and hospital staff, from 21 countries, mainly Australia, Sweden, the United Kingdom, or the United States. Likelihood of HSL increased with age to 80% to 90% of subjects greater than 50 years of age. One percent to 3% of the population experienced ongoing HSL at any one assessment time. The model estimated that 3.5% of adults experience 1 episode of HSL each year, and 2.7% experience 2 episodes of HSL each year, conservatively suggesting that 600,000 of every million people in the population may experience HSL at least once per year. False prodromes have been reported in 16% of the general population or 26% to 38% of clinical trial subjects applying treatment at earliest prodrome sensation or redness. Healing measures include lesion incidence, duration, and size. All antiviral treatments studied reduced lesion duration by one-half to 1 day (P < 0.01). Prevention efficacy has been reported as protection from ulcerative lesions for acyclovir with hydrocortisone (n = 601) and 2-day valacyclovir (n = 339) treatment. Key parameters improving efficacy are early treatment with an effective dose of antiviral agent, delivered well through the stratum corneum, the skin’s outer layer. Acyclovir iontophoresis through the skin has been studied on a small sample, reporting “a weak trend” toward herpes labialis prevention.

Author’s Conclusions: Topical combined acyclovir and mild corticosteroid is an effective formulation for treating HSL and may also be suggested for genital HSV infection. Including ulcer size in

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outcomes measures and giving “false prodromes” a size of zero would improve reliability of results.

Topical Antiviral or Dressings to Heal Cold Sores


Rationale: Thin hydrocolloid dressings (THD) are effective in managing dermal wounds and provide healing benefits. Prior research revealed multiple healing benefits of using THD during an HSL episode.

Objective: Compare safety and efficacy of topical THD or 5% acyclovir cream (AC) applied from onset of HSL symptoms to healing in managing subjective assessments and healing of HSL episodes in subjects with a history of recurrent HSL.

Methods: In a multicenter, assessor-blinded RCT outpatient subjects covered the HSL site with a topical THD (n = 179) or with AC (n = 172) from the time symptoms were first noticed for up to 10 days, or until the lesion healed, whichever came first. For the primary outcome, non-blinded subjects rated global assessment of therapy (SGAT) on a 0-10 scale, where 0 was “no response” and 10 was “excellent response” to therapy. Subjects also rated specific components that contributed to the global assessment, such as lesion protection, noticeability, and social embarrassment. Clinicians blinded to treatment assessed healing time.

Results: Both treatments were well-tolerated and no significant differences were observed between groups in any response to therapy. High mean SGAT ratings supported good efficacy for both the AC group (8.0) and the THD group (7.9). Median healing time was similar for the 2 groups at 7.03 days for AC-treated subjects and 7.57 for those treated with THD (p = 0.37).

Author’s Conclusions: Thin hydrocolloid dressings and AC therapy are both safe and effective in treating HSL. Thin hydrocolloid dressings can provide a safe, effective method of managing the lesion while protecting it and adding an element of discretion and relief from social embarrassment.

Clinical Perspective: Clear benefits are gained from earliest possible topical application of antiviral agents3,4 or THD4 despite the difficulty of conducting a double-blind RCT comparing a dressing to a topical cream. The 0.5 to 1-day healing advantage offered by early antiviral treatment reached statistical significance in the meta-analysis by Harmenberg and colleagues1 and appears to be a worthy goal of care. Considered together, these findings make one wonder if covering an effective topical antiviral agent with a THD may enhance and/or sustain its delivery by optimizing delivery through the stratum corneum and using its reservoir capacity. A clinician or researcher would need to use a delivery method that limits its physical and/or immunological adhesive interactions with antiviral cream or vehicle.5 This would also provide the HSL lesion moist healing benefits and a viral and bacterial barrier to limit cross-contamination or secondary bacterial infection, while protecting and concealing the potentially embarrassing lesion.

Caution should be exercised before using any occlusive dressing over a topical antiviral-corticosteroid cream because occlusion potentiates topical corticosteroid delivery and effects.6 Related adverse effects are avoided on other types of wounds by using less frequent application or a lower dose of the topical corticosteroid under occlusive dressings with careful professional supervision. These variables remain to be explored on HSL lesions.6

In any case, topical antiviral formulations or THDs offer relief for HSL and potentially for other forms of cutaneous herpes infections.7,8

References: