Warts and All: A Treatment Update for Verruca Vulgaris

BY PETER A. LIO, MD

In the event that one begins to wax overly poetic about dermatology and how glamorous a specialty it can be, one needs only to think about one of our most routine conditions to break the reverie: verruca vulgaris, the common wart. Although it is reported that some two-thirds of warts will resolve without any treatment at all within two years, it seems certain that the unhappy remaining third will present to dermatologists.

WEIGHING ALL OPTIONS

Warts are extremely common viral infections of the skin, making up some 21 percent of all dermatology referrals. Their causative agent, the human papillomavirus (HPV), represents a very large group of more than 100 types. Clinical features are roughly related to the HPV type and the anatomic site of infection, with HPV type 1 being associated with plantar warts, for example. Although the warts are often well-defined lesions, HPV may be present at distant body sites and may persist for years.

Although they may be benign and self-limited for the most part, warts can be the root of significant morbidity at times: beyond their unsightly appearance, in one study over half of patients reported moderate to severe discomfort from their warts. The inconvenience and expense of seeking care argues for the impact of warts on patients as well.

It is somewhat disheartening, then, that in the recently updated Cochrane Review on treatments for warts the authors conclude: “Overall, providing a useful idea of ‘what works’ from such a wide range of studies was difficult as many studies were of poor quality.”

Thus, it is with the words of Celsus echoing in our minds that we examine some of the best recent data in an attempt to provide relief: Satius est enim ancess auxilium experiri quam nullum – “It is better to try a doubtful remedy than to try none.” And we are left with quite a few “doubtful remedies” in this domain, unfortunately, and a seemingly endless number of possibilities. I will highlight a handful of favorites below.

Topical salicylic acid (SA) remains the champion of the literature: inexpensive, easy to apply at home, relatively safe, and with efficacy data that trumps nearly everything else. While its mechanism of action is not fully understood, the most compelling hypothesis is that it helps initiate an immune response to the viral infection by its irritant properties. However, it is widely available over-the-counter, and many patients try (and fail) this home remedy before presenting to dermatology, meaning that a great deal of this robust literature is made instantly irrelevant. Why do the warts seem to ignore the evidence? One important detail is that SA comes in a variety of concentrations and formulations: there is the suggestion that at least a 50 percent concentration is necessary to achieve optimal cure rates. Additionally, several studies suggest a combination of SA with 5-fluorouracil as being particularly effective, with cure rates around 63 percent, though more data are needed to substantiate this finding.

Cryotherapy, which entails administering cold damage to warts, usually with liquid nitrogen, has long been performed by dermatologists and primary care physicians alike. What may be surprising, however, is that robust supporting evidence for cryotherapy is actually fairly recent. Two papers, in 2010 and 2011 in particular, helped cement the role of cryotherapy in the treatment of warts. Bruggink, et al. noted that in 2010 the consensus was that evidence favored topical SA application over cryotherapy. In their study of 30 primary care practices and 250 participants in the Netherlands, however, they found cure rates of 39 percent in the cryotherapy group vs. 24 percent in the SA group and 16 percent in the no treatment (“wait-and-see”) group after 13 weeks.

Another study in 2011 suggested that cryotherapy was as effective as SA (our aforementioned champion). While this
ultimately bolstered the efficacy of cryotherapy, finding 14 percent clearance of plantar warts at 12 weeks in 240 patients in each group, it did not show that cryotherapy was superior to SA. Notably, one author objected to the fact that the study used “gentle cryotherapy” rather than standard cryotherapy, which could have significantly weakened the effect of cryotherapy. A relationship between the aggressiveness of cryotherapy and its efficacy has been shown, supporting the author’s point.

As with many therapies in dermatology, however, combinations are commonly used. Cryotherapy once or twice per month in the office is often paired with daily SA home therapy. Accordingly, there are trials suggesting that this combination is more effective than SA alone. This is, for better or for worse, a common starting regimen in the dermatology office. What to do when these fail?

Intralesional injection of bleomycin has been shown in several studies to be more effective than cryotherapy. However, in aggregate, the data are confusing and uncertain. With varying study designs, treatment concentrations, and techniques, intralesional bleomycin is not yet clearly effective. Still, this method with cure rates of up to 94 percent is a powerful “last resort” when patients have failed numerous other therapies.

Injections can be very intimidating for patients and have significant potential for pain and morbidity. The evidence for propolis—the resinous substance that honey bees collect from plants and use as a glue of sorts—is thus a strangely compelling alternative. Zedan, et al. found that given as an oral supplement (500mg/day) in a single-blind study of 135 patients, 73 percent of common warts were cured versus only eight percent in the placebo group.

Similarly, zinc has been shown to have some effect on warts, both topically and orally. Two trials of topical zinc found a higher cure rate compared to distilled water placebo and comparable to a low-concentration of SA with lactic acid, making a trial of zinc oxide diaper paste an inexpensive and appealing possibility. Oral zinc sulfate supplementation (10mg/kg/day, up to 600mg) has a dramatic study that found an 86.9 percent complete clearance rate in patients with recalcitrant warts; they also noted that in all of the patients, serum zinc levels were low. A follow-up study in 2009, however, could not replicate these results and found that the zinc sulfate group was no better off than placebo, but did have significantly higher gastrointestinal side-effects. One could speculate that there may be a subgroup of patients who will respond, who are likely zinc deficient.

**FILLING IN THE BLANKS**

In navigating this mire of partial data, varying results, and manifold possibilities, we continue to hope to find safe, inexpensive, and highly effective treatments for our nemesis, the wart. Topical SA, cryotherapy, intralesional bleomycin, oral propolis, and topical and oral zinc represent a large and varied armamentarium for the challenges of warts in the clinical setting, with reasonable evidence to justify their use. With luck, as more data are acquired, we will fill in the blanks with better information about specific approaches, combinations that yield synergies, and suitable second- and third-line options, as well. Undoubtedly, this will make for happier patients and dermatologists.

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**References**