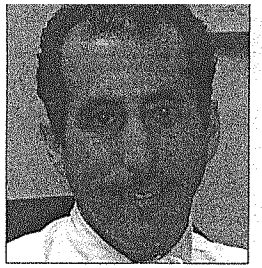
Edward A. Bell

Update on pharmacotherapy of cutaneous warts

by Edward A. Bell, PharmD, BCPS

Cutaneous warts, or verrucae, are a common problem seen in pediatric offices. Although most warts will spontaneously clear within 2 years, warts can have a significant effect upon a child's emotional well-being, especially if one or more are located on easily seen areas, such as the hands or face. Plantar warts may result in discomfort when walking. Thus, children with warts will likely seek help for treatment. As several pharmacotherapies are available for wart treatment, including products available over-the-counter, pediatric clinicians should be familiar with these agents' efficacy and safety profiles.

Cutaneous warts result from infection with HPV. Several HPV types have been known to result in wart formation, with common warts primarily resulting from infection with HPV-2, and plantar warts resulting from infection with HPV-1.

Several pharmacotherapies are available and have been evaluated to treat warts, although some are limited by unclear efficacy or product cost (Table). Several agents are easily available as OTC products — salicylic acid, cimetidine, zinc and, more recently, cryotherapy products. Of these, evidence for efficacy is most abundant for salicylic acid, the only agent categorized as safe and effective for self-treatment by the FDA. Compared with other products that are available only by provider prescription, efficacy evidence also is most abundant for salicylic acid.

Salicylic acid

Salicylic acid has keratolytic activity, and at higher concentrations (>6%) it provides additional destructive activity to surrounding tissue. As salicylic acid has many uses (eg, acne, removal of calluses and corns, dandruff, psoriasis), it is available in a variety of products and strengths. Although products are available as cream, foam, gel, liquid, pad, patch or shampoo formulations, many of these are labeled for uses other than treatment of warts. Several products are specifically labeled for treatment of warts (eg, Tinamed Wart Remover, Dr. Scholl's Clear Away 1-Step Wart Remover, DuoFilm Wart Remover Liquid) and are available in concentrations up to 40% salicylic acid. Compound W may be the most recognizable product, and is available as liquid, gel and pad formulation products.

Several controlled trials have evaluated salicylic acid for wart treatment in children and adults, and a systematic review of randomized controlled trials of salicylic acid and other local treatments has been published.

In this review, six placebo-controlled trials evaluating salicylic acid (376 patients) were included, with data demonstrating a favorable outcome of salicylic acid over placebo (cure rate of 75% vs. 48%, respectively). The authors of this review concluded that, despite the inclusion of 50 trials evaluated for all wart treatments, few data were available to adequately produce treatment recommendations for most agents.

Most of the trials employed poor methodology or reporting. Good data from controlled trials were found only to support the efficacy of salicylic acid, these authors additionally state. A recently published Cochrane Review of topical treatments for cutaneous warts (85 trials of 8,815 patients) concluded that despite weak methodology for many trials, several newly published trials provide some good efficacy evidence for salicylic acid, and that it has a "modest therapeutic effect."

Many products containing salicylic acid are available in strengths of 12% to 15% or greater, they are inexpensive, and it seems reasonable to begin therapy at this concentration. Plantar warts may respond better to products with higher concentrations of salicylic acid (ie, 40%). As salicylic acid may degrade surrounding healthy tissue, resulting in pain, applying a layer of petrolatum around the wart to protect healthy tissue has been suggested. Some beneficial effects should be noticed after 1 to 2 weeks of use, although total wart removal may require up to 12 weeks of consistent therapy.

Cryotherapy

Cryotherapy is likely the most commonly used office-based treatment for cutaneous warts (eg, liquid nitrogen). In the systematic review discussed above, 16 trials of cryotherapy were assessed, and few data were available from placebo-controlled trials. These few data demonstrated no difference in outcome between cryotherapy and placebo. Data from additional trials comparing cryotherapy with salicylic acid found similar efficacy, however. As use of cryotherapy can depend upon provider technique and skill of application, some evidence from published studies reveals that "aggressive" therapy may be more effective than "gentle" therapy. A recently published Cochrane Review concluded that fewer data support efficacy for cryotherapy as compared with use of salicylic acid, and cryotherapy may be more likely to result in adverse effects.

Several new products using cryotherapy are available OTC to consumers, and include Wartner Wart Removal System and Compound W Freeze Off. These products contain dimethyl ether and propane (DMEP), and not liquid nitrogen. Some data from a published trial demonstrate similar efficacy of DMEP and liquid nitrogen. Compound W Freeze Off is labeled for use in children aged 4 years and older, and contains eight applications (approximately $35-$40).

Duct tape

Application of duct tape has been suggested by some as a nontraditional method to treat warts. One randomized study compared silver duct tape with cryotherapy in children (n=51), and found silver duct tape to be more effective. Additional controlled trials did not find an efficacy difference between plain duct tape and placebo, however. As silver can have antimicrobial effects, this may explain outcome differences among these studies.

Other pharmacotherapies

Other pharmacotherapies have been evaluated, including products available OTC and by prescription. Zinc is known to have beneficial regulatory effects upon the immune system and has been evaluated to treat warts. Several controlled studies have demonstrated a beneficial effect of zinc sulfate in wart resolution, although most patients in these studies were zinc-deficient. The effect of zinc in patients who are not zinc-deficient is unknown.

Cimetidine, an H2 antagonist available OTC, has been evaluated in the treatment of warts. Although one small, uncontrolled trial demonstrated efficacy of cimetidine for wart treatment in children, several controlled trials did not demonstrate efficacy of cimetidine treatment as compared with placebo.

Imiquimod, an immune response modifier labeled for genital warts and some skin carcinomas, has demonstrated efficacy in several small studies for treatment of common warts unresponsive to other treatments. Imiquimod cream is expensive. Additional pharmacotherapeutic agents and other treatments (eg, laser, photodynamic therapy) also have been evaluated and have shown some benefit, including injected immune-stimulating antigens (eg, mumps or *Candida* antigen), cidofovir and podophyllotoxin.

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The use of topical retinoids (ie, tretinoin cream) has shown some efficacy from an uncontrolled trial. These treatments are described in more detail in an excellent review by Boull. ■

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Wart Removal Therapies

Therapy	Products	Comments
Salicylic acid	• Available in many dosage forms and strengths	• Inexpensive and easy to use • Product with most efficacy data from controlled studies • The only OTC product recognized by the FDA as safe and effective
Cryotherapy	• Commonly used in pediatric offices as liquid nitrogen • Additionally available as OTC products using DMEP	• Fewer data to support efficacy • Can be painful when applied • Efficacy may depend highly upon clinician skill of application
Duct tape	• Studied as silver tape and transparent duct tape	• Silver duct tape may have efficacy • No demonstrated efficacy with transparent duct tape • Questionable role – use above therapies first
Cimetidine	• Available OTC	• No proven efficacy • Do not use
Zinc sulfate	• Available OTC	• Can be effective for patients with zinc deficiency • Unknown efficacy for patients who are not zinc-deficient

Source: Bell EA