Clinical Review:

Plantar Warts

Plantar warts are a common problem in adults and children. Though exact data is difficult to come by, one study evaluating the prevalence of warts in the United States found 0.84% prevalence. Children and young adults have a particularly high incidence of warts, with one study in the UK documenting a prevalence rate of 12% in school children ages 4 to 6 years old.1 Warts are often caused by the human papilloma virus (HPV), of which there are over 100 different species. It is theorized that even small abrasions can be enough to allow skin infection with this virus. Common risk factors include things like use of communal showers, regularly contact with meat (as an occupation), and immunosuppression. For most immunocompetent people, warts are harmless and disappear naturally over months or years without treatment, but there are topical treatments that may be utilized to speed up resolution of warts.' In this newsletter, we will be discussing commonly-used treatments for the topical management of plantar warts.

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Warts are often treated by daily application of a topical preparation but may also be treated in-office. Common treatments for warts include salicylic acid, salicylic acid/5-fluorouracil combinations, cidofovir, cimetidine, and topical sensitizers such as diphenylcyclopropenone or squaric acid. Salicylic acid is one of the most common first-line treatments as it is inexpensive and available over the counter. Salicylic acid is thought to be efficacious against warts due to its keratolytic activity allowing it to directly breakdown wart tissue.
Concentrations used to manage warts vary widely, often between 10-60%.2 One review of several studies evaluating topical salicylic acid at 17-60% either as a solo agent or in combination with lactic acid found that salicylic acid had a composite cure rate of about 75% compared with approximately 48% in the placebo arms.3 Most salicylic acid preparations are applied once or twice daily, and recommendations to improve the likelihood of success include soaking the wart and debriding with a pumice stone before application.2

5-Fluorouracil (5-FU) is another common agent used in the management of warts. It may be used as a sort of intralesional injection, but more often it is compounded into topical formulations with or without salicylic acid.2 5-FU works to inhibit DNA and RNA synthesis, thereby preventing proliferation.5 When used together, salicylic acid may assist in breaking down tough wart tissue via its keratolytic capabilities, resulting in improved delivery of 5-FU. One study evaluating the efficacy of a 0.5% 5-FU and 10% salicylic acid combination compared with salicylic acid alone found a 63% cure rate in the combination group versus only 11% in the salicylic acid-only group.4 Another study of 5% 5-FU cream tested the application of 5-FU cream applied twice daily under tape occlusion in patients who had previously failed to see results with a tape- occlusion only treatment. The addition of 5-FU to this regimen resulted in a complete cure rate over twelve weeks with a low rate of recurrence.5 Lastly, one medical record review found 20 patients treated twice daily with 0.5% or 5% 5-FU combined with

salicylic acid 17% or 40%, all patients had their warts debrided every 1-2 weeks. All 20 patients achieved full clinical resolution between 2-3 months. The main adverse effect reported was local dermatitis.6

Cidofovir is a less common topical agent, mainly due to expense, but it's sometimes used for recalcitrant warts. Cidofovir inhibits DNA synthesis and may inhibit wart proliferation via this mechanism.2 One case study in a pediatric patient tested cidofovir 1% cream applied once daily over 8 weeks and found complete resolution of the wart with no recurrence at 6 months and no adverse effects were reported.1 Another observational study evaluated outcomes of patients treated with 3% cidofovir cream applied twice daily. The study found an 80% response rate with a low rate of reccurence.8

Two other active ingredients commonly used in compounded wart treatment preparations include deoxy- d-glucose and cimetidine. Though they are commonly used, there is few studies evaluating the efficacy of these ingredients topically and most data supporting their use are anecdotal. Deoxy-d-glucose is thought to exert anti-viral activity via compromising the ability of the virus to enter the cell.9 Oral cimetidine has also been studied for warts and the proposed mechanism of action is anti-viral activity as a result of cimetidine increasing production of IL-2 and IFN-c.10 Cimetidine is commonly used in these topical formulations at 5-10%, and deoxy-d-glucose at 0.2%.

Other agents, rather than having keratolytic or antiviral mechanisms, work by triggering the immune system to attack the wart. These agents, called contact sensitizers, include squaric acid dibutyl ester (SADBE) and diphenylcyclopropenone (DCP).2 Contact sensitizers such as SADBE and DCP often follow a sensitization schedule. One study of SADBE sensitization treatment with 2% SADBE followed by home application of an 0.2% solution for 3 to 7 nights per week for 3 months found that 58% of patients had complete clearing and 18% had partial clearing. Side effects were generally mild, but erythema at the site of sensitization was common.11 Another study evaluating DCP tested 2% as a sensitizer in adults and 1% as a sensitizer in pediatrics, the patients were then treated with a low concentration of 0.001%, which was gradually increased up to a maximum of 2% with the goal of generating a mild eczematous reaction. The DCP was applied weekly and nearly 70% of patients saw complete improvement over a median of 7.4 weeks.12

Cantharidin (an in-office use only product), is also used commonly for the management of warts. Cantharidin is a caustic substance derived from the blister beetle, and its mechanism of action against warts is causing blister formation and epidermal cell death.2 Cantharidin is generally applied under tape for 24 hours, then applied again after the blister heals in 1 to 3 weeks.2 One study that evaluated cantharidin 1% in combination with 5% podophyllum and 30% salicylic acid compared with cryotherapy tested efficacy of either treatment performed every 2 weeks for up to five sessions. The cantharidin group got 100% wart clearance as compared to 41.7% of the cryotherapy group.13

There is a plethora of options for treating warts available to us with different mechanisms including keratolysis, anti-cell replication, antiviral activity, contact sensitizers, and direct blistering agents. For patients who have not found relief with over-the-counter options, compounded anti-wart therapy can be an important alternative. Check out the Fagron Academy site for related formulas. If you have further questions, follow-up with Fagron Academy Technical Support Services!

Sources:

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The matters discussed herein are for informational purposes only and not intended for the purpose of providing legal advice. You should consult your attorney in case of any questions as to when it is appropriate to compound or regarding any other particular issue discussed or referenced in this document.

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