

Evidence for Clinicians is coordinated by the Child Health Field of The Cochrane Collaboration. The Cochrane Collaboration has been a leader in promoting the use of systematic reviews in health care decision making since its establishment in 1993. The Child Health Field was formed in 2000 to spearhead the dissemination of evidence from Cochrane reviews for use by those responsible for the care of children and youth, as well as to raise the profile of evidence-based medicine within child health. We began publishing our Evidence for Clinicians columns in Paediatrics & Child Health in 2002, and have been delighted to have this ongoing opportunity to present evidence relevant to the practice of Canadian paediatricians and family physicians.

We will be introducing a new format for Evidence for Clinicians in mid-2014. An advisory group of paediatricians and family practitioners will help us to select the most interesting and relevant Cochrane reviews and work through various means of presenting that evidence to our readers. Of course, your thoughts and opinions will be vitally important to us, and you can contact us at any time by e-mail at child@ualberta.ca.

Child Health Field, The Cochrane Collaboration

Are salicylic formulations, liquid nitrogen or duct tape more effective than placebo for the treatment of warts in paediatric patients who present to ambulatory clinics?

Lindsey Craw MD FRCPC FAAP¹, Aileen Wingert BA MPH², Irene Lara-Corrales MD MSc¹

Cutaneous warts are common in the general population. Salicylic acid (SA), cryotherapy and duct tape are commonly used to treat warts. Current, high-quality evidence suggests that topical SA is effective compared with placebo, and is the preferred first-line treatment in children due to ease of application and minimal side effects. The evidence does not suggest that cryotherapy is more effective than SA, and it is associated with more side effects. Duct tape has not been shown to be superior to placebo and side effects, including redness, itching, eczema and bleeding, are possible. Treatment of warts for a child should be aimed at reducing symptoms or improving appearance while minimizing side effects. Risks and benefits should be discussed with care providers. Because warts often resolve spontaneously within a period of months to years, it is acceptable to recommend no intervention.

PART A: EVIDENCE-BASED ANSWER AND SUMMARY

Cutaneous warts, caused by the human papilloma virus (HPV), are common in the general population (1). Bare feet in change rooms and swimming pools expose individuals to a greater risk of plantar warts; however, spread within families and classrooms also appears to occur. Parents often seek treatment for their children or present with complications of treatment (2). Topical SA and liquid nitrogen (cryotherapy) are two options often used as first-line treatments (1). SA is a peeling agent that is painted on warts (1). Liquid nitrogen is usually sprayed on warts to cause freezing, thereby damaging cells and vascular supply, and possibly stimulating the immune system (1).

A previously published Cochrane review (3) was updated in 2011 (1) and identified a total of 85 trials (8815 participants) assessing topical treatments for cutaneous warts. Only four of the included trials involved children alone; the findings are based

primarily on studies involving adults and children combined (1). Many of the studies contained a high risk of bias in at least one area of trial design (eg, inadequate reporting of randomization, inadequate concealment of allocation, lack of participant or personnel blinding and/or incomplete loss to follow-up) (1). Outcomes for 18 studies were assessed at ≤ 6 weeks, which is generally considered to be inadequate for the detection of clinical cure or recurrence (1). Six studies (486 participants) comparing SA with placebo showed a modest increase in the chance of clearance of warts for all sites (RR 1.56 [95% CI 1.20 to 2.03]), which was higher on the hands (RR 2.67 [95% CI 1.43 to 5.01]) than on the feet (RR 1.29 [95% CI 1.07 to 1.55]) (1). Three studies (227 participants) comparing cryotherapy with placebo found no significant difference (RR 1.45 [95% CI 0.65 to 3.23]), with one trial reporting an unusually low cure rate for warts on the hands and another reporting a high cure rate in the no-treatment group (1). In four trials (532 participants), 'aggressive' cryotherapy (multiple freezes or longer duration of freeze) was more effective than 'gentle' (brief freeze) cryotherapy (RR 1.90 [95% CI 1.15 to 3.15]), but with more reports of adverse events (pain, blistering, scarring, skin irritation, skin pigmentation and crust) (1). Applying duct tape over warts is a less invasive treatment that gained support after a single trial of silver duct tape showed favourable outcomes compared with cryotherapy (RR 1.52 [95% CI 0.99 to 2.31]) (1).

However, two additional trials (198 participants) in the updated review comparing clear duct tape occlusive treatment with placebo indicated no significant effect (RR 1.43 [95% CI 0.51 to 4.05]), with one trial reporting adverse events in the intervention group (redness, itching, eczema and bleeding) (1). Limited data from several studies comparing the treatment methods (SA, cryotherapy and placebo) with one another provide inconsistent, and sometimes contradictory, evidence of effectiveness. Further

¹Department of Pediatrics, Hospital for Sick Children, University of Toronto, Toronto, Ontario; ²Cochrane Child Health Field, Department of Pediatrics, University of Alberta, Edmonton, Alberta

Correspondence: Dr Irene Lara-Corrales, Department of Pediatrics, University of Toronto, 555 University Ave, Toronto, Ontario M5G 1X8.

Telephone 416-813-7654 ext 4864, fax 416-813-7909, e-mail irene.lara-corrales@sickkids.ca

Accepted for publication October 3, 2013

methodological limitations in these studies make it difficult to draw conclusions on overall treatment efficacy.

PART B: CLINICAL COMMENTARY

Warts, caused by HPV, are a very common problem affecting 10% to 20% of children at some point in time (2). The peak incidence occurs between 12 and 16 years of age (2). Warts are harmless and will resolve spontaneously within months to years; however, they can be painful and unsightly, which prompts patients to seek treatment. It is important to remember that all treatments available for warts aim to cause an immune reaction toward the HPV virus but do not actually kill the virus; therefore, the optimal length of treatment or the time for warts to fully resolve is not easy to predict.

Topical SA is our recommended first-line treatment in children. It is available in over-the-counter formulations, is inexpensive and, of particular importance in children, its application is not painful. At the concentrations indicated for home use, side effects are minimal and mainly include skin irritation. This treatment can be applied at home by patients or parents, and evidence suggests that it is more effective than placebo, particularly for warts on the hands. Compliance with this treatment is a problem because the application should be continued until the wart resolves, which typically takes at least 12 weeks. For very large warts, higher concentrations of SA can be compounded, but this should be applied by physicians and not prescribed for use at home.

Cryotherapy is considered by some to be a first-line treatment. However, the evidence does not suggest that cryotherapy is more effective than SA, and it is associated with more side effects including pain and blistering. Therefore, cryotherapy should be reserved for second-line therapy for older patients who can tolerate the discomfort associated with this treatment without needing to be restrained. A eutectic mixture of local or topical anesthetic (eg, eutectic mixture of local anesthetic [EMLA], liposomal lidocaine) may be considered before the procedure for pain management, although this does not completely control pain. We recommend application with cotton-wool buds as opposed to spray guns (4) because the use of spray guns is associated with increased pain. Longer freeze times, while more effective, lead to greater side effects, and a balance needs to be achieved. Shorter intervals

between treatments also cause more side effects. Consider treating every three to four weeks because there is no evidence that shorter treatment intervals lead to improved outcomes (3).

The evidence does not suggest that duct tape is superior to placebo for the treatment of warts (1). Anecdotally, many believe that the use of duct tape alone or in conjunction with SA (with duct tape over the SA) is effective. We occasionally recommend duct tape with SA, but not duct tape alone. Possible side effects include redness, itching, eczema, bleeding and other skin reactions (1).

There is either insufficient evidence or the risks outweigh the benefits of the other treatments (ie, laser, imiquimod, interferons, intralesional antigens, surgery, podophyllin and cantharidin) that have been proposed for the treatment of warts. We do not recommend use of these therapies as first-line treatment for warts.

When a child presents for assessment of warts, treatment should be guided by the number, location and symptoms associated with their warts, taking into consideration the child's immune status and any comorbid conditions. Overall goals of therapy include a reduction in symptoms or an improvement in appearance, which need to be balanced with minimizing side effects (2). Spontaneous resolution over a period of months to years is the typical outcome; therefore, it is acceptable to recommend no intervention. Risks and benefits should be discussed with parents and care providers. Follow-up of sustained clearance of warts should be standardized at a minimum of three to six months after treatment (1). Treatment of complex cases should be directed by a dermatologist.

REFERENCES

1. Kwok CS, Gibbs S, Bennett C, Holland R, Abbott R. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev* 2012;(9):CD001781.
2. Herman BE, Corneli HM. A practical approach to warts in the emergency department. *Pediatr Emerg Care* 2008;24:246-51; quiz 52-4.
3. Gibbs S, Harvey I. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev* 2006;(3):CD001781. Update in: *Cochrane Database Syst Rev* 2012;(9):CD001781.
4. Boull C, Groth D. Update: Treatment of cutaneous viral warts in children. *Pediatr Dermatol* 2011;28:217-29.

*The Evidence for Clinicians columns are coordinated by the Child Health Field of the Cochrane Collaboration (www.cochranechildhealth.org).
To submit a question for upcoming columns, please contact us at child@ualberta.ca.*