

Cantharidin Use Among Pediatric Dermatologists in the Treatment of Molluscum Contagiosum

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Abstract: Cantharidin is cited often in the dermatology and pediatric literature as a valuable treatment option for molluscum contagiosum (MC). However, there have been no prospective, randomized, vehicle-controlled trials that have been able to quantify cantharidin's efficacy in MC. The purpose of this study was to determine the breadth of usage of cantharidin, most frequently used protocols, and common side effects seen with use of cantharidin. An eighteen question survey was administered to the Society of Pediatric Dermatology. The survey sought to evaluate treatments used in MC and experiences with cantharidin including: protocol, side effects, specific products used, and satisfaction with cantharidin. A total of 300 surveys were distributed via email, 101 surveys were initiated, and 95 (94%) of these were completed. Cantharidin, imiquimod, benign neglect, curettage, cryotherapy, and retinoids were the most common approaches to pediatric MC reported by respondents. Ninety-two percent of respondents reported satisfaction with cantharidin's efficacy, but 79% reported side effects, with discomfort/pain and blistering being the most common. Cantharidin is a common modality in the treatment of MC among pediatric dermatologists. While efficacy data is still lacking, subjective satisfaction with cantharidin is reported. Cantharidin remains a viable treatment option for children with MC.

Many general pediatricians and pediatric dermatologists have encountered the dilemma of how to best deal with children (and parents of children) who suffer from molluscum contagiosum (MC). Molluscum contagiosum can spread through close skin-to-skin contact, and many patients autoinoculate themselves, making MC a dynamic disease. Molluscum contagiosum infection can last anywhere from several months to 4 years (1).

Though self-limited and not life-threatening, molluscum lesions can be symptomatic, unsightly, and quite embarrassing. Parents sometimes seek treatment to decrease symptoms and/or improve the cosmetic appearance.

There is large debate about the standard of care and optimal treatment for MC. Because it is a self-limited disease, treatment options for MC attempt to minimize

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side effects while speeding recovery time. Some advocate watchful waiting or benign neglect (2). However, some parents desire a pro-active approach, and there still exists the potential for spread to other susceptible children, especially those with atopic conditions who may develop severe disease.

Cantharidin is cited often in the dermatology and pediatric literature as a valuable treatment option (1,3–5). However, there have been no prospective, randomized, vehicle-controlled trials that have been able to quantify cantharidin's effectiveness in MC. Moreover, like many therapeutic interventions used in dermatology, there does not seem to be one standard protocol to which the majority of practitioners adhere. The purpose of the following survey was to determine the breadth of usage of cantharidin, the most frequently used protocols, and common side effects seen with use of cantharidin.

MATERIALS AND METHODS

Our Institutional Review Board found that our survey was exempt from HIPAA and written consent requirements on November 13, 2007. An eighteen question survey was administered to the Society of Pediatric Dermatology (SPD) via the Internet site <http://www.surveymonkey.com>. The survey was sent out via the SPD listserv on January 23, 2008 to its 300 members.

RESULTS

Demographics

A total of 300 surveys were distributed via e-mail, 101 surveys were initiated, and 95 (94%) of these were completed. It is unknown what percentage of these respondents were resident physicians versus board-certified dermatologists. Fifty-four percent of respondents spend more than three-quarters of their time seeing pediatric patients.

Office Visits for Molluscum

Most respondents answered that they typically see one to five or 6 to 10 cases of MC a week (36% and 33% respectively). Twenty-four percent of practitioners saw greater than 11 cases of MC per week, and 7% saw less than one case per week.

Most Commonly Used Therapies for Molluscum

A list of 16 possible treatments for MC was provided as answer choices (Fig. 1). Respondents were allowed to indicate all therapies that they had used in the past, and

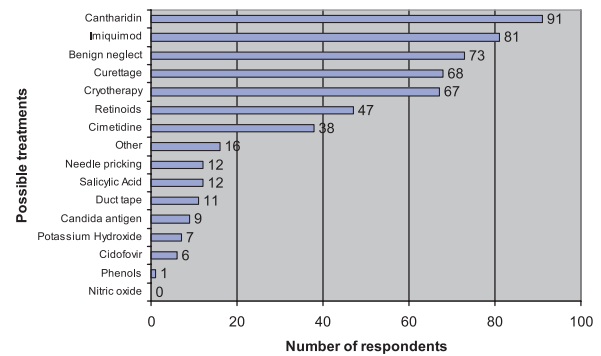


Figure 1. Treatments used by pediatric dermatologists in molluscum contagiosum.

an “other” category was provided to allow fill-in answers. It should be noted that podophyllin, pulsed dye laser, and variations of a tape method, apple cider vinegar, Klaron[®] lotion (Dermik Laboratories, Berwyn, PA, USA), Vaseline[®] (Unilever, London, UK), and Compound W[®] (Prestige Brands, Irvington, NY) preparations, gentle hyfcreation in the operating room, and combinations of the above were written in the “other” category.

Cantharidin Protocols in the Treatment of Molluscum

Seventy-five percent of respondents reported that they do not usually occlude molluscum lesions with tape after treating with cantharidin. Twelve percent reported that they sometimes occlude lesions with tape. In the open-ended question, “When using cantharidin, how many hours do you have your patients wait before washing it off?” 45% of respondents instruct parents to leave cantharidin on between 4–6 hours before washing it off, 26% of respondents tell parents to leave it on for < 4 hours, 7% suggest between 6–12 hours, and 11% do not recommend washing off or recommend waiting until the next day. Another 11% leave it up to the patient's response, giving a recommended maximum time, but having patients wash it off sooner if he/she developed blisters or pain before the recommended maximum time.

Fifty percent of respondents have patients return to clinic every 3–4 weeks for reapplication of cantharidin. Thirty-five percent of respondents have patients come back every 4–8 weeks, and 11% have patients return every 2 weeks. Twelve percent reported that they have patients come back as needed, or tailor treatment to an individual patient's response. Participants were asked how many lesions they treat with cantharidin during the first and subsequent visits (Fig. 2). In both the first and subsequent visits, 31.2% and 49% of respondents, respectively, treated more than 21 lesions at a time.

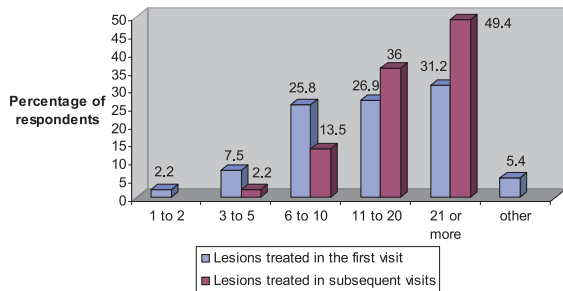


Figure 2. Number of lesions treated at the first and subsequent visits.

Participants were asked an open-ended question: “How many times will you treat a patient with cantharidin before deeming a patient a treatment-failure?” If a respondent answered with a range of numbers, the highest number was taken as representative of the maximum amount of treatments. Thirty-two percent of respondents reported that they would treat three to four times, 19% treated five to eight times, and 15% reported treating two times. Nine percent stated that they have no limit, and will treat until the lesions are gone or until the patient doesn’t return for follow-up. Interestingly, 19% of respondents commented that they have never had a treatment failure. One respondent stated, “Cantharidin never fails, [but] a patient’s immune system may not cooperate.”

Commercial versus Compounded Product

Physicians can either have cantharidin compounded by a local pharmacist for use in clinic, or they can purchase it from an independent commercial manufacturer. Seventy-six percent of respondents report that they use a commercial product.

Forty-nine percent of those who use a commercial product use Canthacur[®] by Paladin Labs Inc (Montreal, Canada), and 31% use Cantharone[®] by Dormer Laboratories (Rexdale, Canada). Six percent and 2% of respondents use Canthacur PS[®] or Cantharone Plus[®], respectively. Finally, 14% of those who use a commercial product were not able to identify the product they used.

Satisfaction

Ninety-two percent of respondents reported satisfaction with cantharidin’s efficacy in treating MC. Although only seven responded that they were not satisfied, 14 entered information in the optional text box that was provided to explain such dissatisfaction with cantharidin. Reasons for being unsatisfied with cantharidin include: “too many problems associated with its use,” “no evidence in the literature to support its use,” repeated clinic visits necessary, variable and unpredictable response,

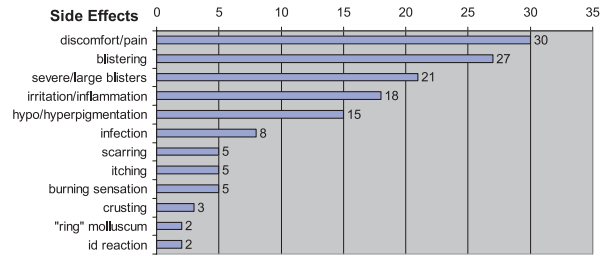


Figure 3. Side effects reported with cantharidin use.

concerns about “horror stories,” too vigorous of a blistering response, poor efficacy, postinflammatory hyper- and hypopigmentation, and “is less reliable than pulsed dye laser, which is one-shot treatment and guaranteed.”

Side Effects

Seventy-nine percent of respondents reported that their patients have experienced side effects when treated with cantharidin and each respondent was able to specify and describe the specific side effects seen in a text box (Fig. 3). There was one report of each of the following: “molluscum pits,” rash, subcutaneous nodule in the dermis that spontaneously resolved, blistering at nontreated or distant sites, fever/irritability, chemical lymphangitis, and one patient who experienced anuria lasting 1 day after facial application of cantharidin.

Reasons for Not Currently Using Cantharidin

Practitioners that indicated that they do not currently use cantharidin were asked for their reasons. Although 12 indicated they no longer use cantharidin, only three practitioners responded. Reasons included: lack of familiarity or comfort with the product, unavailability of the product, and belief that there are too many adverse reactions.

Limitations

Our survey was a descriptive survey and was not validated. Not every respondent answered every question, but percentages reported are of those who responded to that particular question. It is possible that respondents may not have significant experience dealing with MC or cantharidin, but the skip pattern implemented in our survey should have directed them to only the appropriate areas of the survey that were relevant to their practices.

DISCUSSION

Molluscum contagiosum is a common and relatively benign disease that incites debate among practitioners

about the best approach to its treatment. Some defend watchful waiting, contending that it may even be harmful to subject children to the side effects of medication for a benign disorder. Even those who support therapy do not agree on the best treatment or regimen. Our survey sought to look at the use of cantharidin, a commonly cited therapy for molluscum that is anecdotally reported as being quite effective, but has no efficacy data in the literature to support its use. We targeted physicians who would be most likely familiar with cantharidin and who are usually the recipients of multiple referrals. Pediatric dermatologists inherently encounter a selection bias and typically tend to see children with worse, more stressful disease for both the patient and parent.

Cantharidin is a topical vesicant that has been used in the treatment of MC since the 1950s. When applied topically by a professional, it produces a small intraepidermal blister that heals without scarring. In 1962, an FDA amendment required manufacturers to submit efficacy data for their products. Because of the financial implications of submitting a new drug application for a nonpatentable compound, no such data was submitted by the manufacturers of cantharidin, and as a result, cantharidin was removed from the U.S. market in 1962. **Subsequently in 1997, cantharidin was added to the FDA "Bulk Substances List" which permits the compounding of cantharidin by a physician or pharmacist on a customized basis for individual patients** (6).

Despite some of the historical issues with the FDA, the overwhelming majority of respondents (99%) have used, or currently use, cantharidin in the treatment of MC. Additionally, the majority of those that use cantharidin were satisfied with its results (92%). It is interesting to note that 19% of respondents wrote in that they had never had a treatment failure. Such strong statements represent some of the anecdotal efficacy information that can be encountered in a literature review.

It should be noted that most respondents (79%) reported side effects. Though many reported blistering as a side effect, it can be assumed that some did not explicitly write in blistering since it is an almost-expected effect of cantharidin therapy. Whether the respondents observing/reporting more severe side effects are those who use a more aggressive approach with cantharidin is unclear. For example, do those who see more severe side effects leave cantharidin on for longer periods of time before washing, use a PS solution (a mixture of salicylic acid 30%, podophyllin 5%, and cantharidin 1%), or occlude lesions with tape? It is also unclear whether every respondent only reported side effects seen in their own patients, or also reported what they have heard from their colleagues.

While blistering and discomfort can easily be attributed to cantharidin, it will always be difficult to determine

if some of the more rare side effects are coincidental, or are truly related to cantharidin use. Nonetheless, with patient safety in mind, we should remember all potential side effects when choosing a medication for patients.

There was no one standard protocol followed by respondents, though most responses only varied in the amount of time cantharidin was left on the skin, and the number of times a provider would treat a patient. Interestingly, the "Notes" section of the package insert for Canthacur[®] advises to only treat one to two lesions during the first visit to assess patient sensitivity to the product (7). As is seen from the survey results, the majority of practitioners (93%) treat many more than two lesions during the first visit; in fact, most (31%) treated 21 or more lesions at the first visit. Possible reasons may include confidence in and reproducibility of cantharidin's clinical course, desire to avoid additional office visits, or lack of clinical encounters of patients with hypersensitivity to cantharidin.

Cantharidin's history with the FDA as well as the lack of efficacy data may be why it is not often used in the primary care arena. Our survey shows that cantharidin is a common modality in the treatment of MC amongst pediatric dermatologists. While a standard protocol is still lacking, most pediatric dermatologists use somewhat similar protocols, and the variations are reflected in the results of our survey. While efficacy data is still lacking, the results of this survey, our own personal experience (unpublished data) and a retrospective study done by Silverberg et al (3) seem to show subjective satisfaction with its results amongst pediatric dermatologists and parents. Treatment options should always be individualized to specific patients, but cantharidin remains a viable option for children with MC.

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