Is Duct Tape Occlusion Therapy as Effective as Cryotherapy for the Treatment of the Common Wart?

This randomized controlled trial was conducted to assess whether duct tape occlusion therapy is as effective as cryotherapy for the treatment of common warts. Patients 3 to 22 years of age who visited the pediatric clinics on a military base in Washington State with at least 1 common wart on an extremity were approached for study enrollment. Sixty-one subjects were enrolled and randomized to either cryotherapy or duct tape occlusion therapy.

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The cryotherapy group had liquid nitrogen applied to the study wart every 2 to 3 weeks for a maximum of 6 treatments or until wart resolution. The duct tape occlusion group had a small piece of duct tape applied to the study wart, which was left in place for 6 days. This tape was removed on the evening of the sixth day and then replaced the following morning for a maximum of 2 months or until wart resolution. Subjects were instructed to return to the clinic for evaluation every 2 to 3 weeks in the cryotherapy group and every 4 weeks in the duct tape group. Prior to the administration of therapy, each patient had his or her study wart measured with calipers at every clinic visit. Patients who did not follow up at the clinic were contacted by telephone to determine whether their warts had resolved. Ten of the 61 patients who had enrolled in the study were lost to follow-up. At the study's conclusion, a greater proportion of patients in the duct tape group than in the cryotherapy group had complete resolution of their study wart (84.6% vs 60.0%, respectively; P = .05). The investigators concluded that duct tape occlusion therapy is significantly more effective than cryotherapy for the treatment of common warts.

We analyzed this study according to the guidelines provided by the Users' Guide to the Medical Literature published by the American Medical Association. In this analysis, we evaluate the validity of the results, the size and precision of the treatment effect, and the applicability of these results to patient care.

Randomization of Subjects

We asked the following questions: (1) Were patients randomized? (2) Was randomization concealed? (3) Were patients analyzed in the groups to which they were randomized? (4) Were patients in the treatment and control groups similar with respect to known prognostic variables? This study was a randomized, controlled, noninferiority trial. Patients were randomized by a computer-generated code. We assume that randomization was concealed using this method. Although not explicitly stated, we also assume that the outcomes for all patients with complete follow-up were analyzed within their original randomization group. The patients in the 2 treatment groups were similar with respect to sex, age, baseline size of warts, and wart location. As this was a randomized trial, additional unmeasured factors that might have had prognostic significance should be equally distributed between the study groups.

Blinded Assessment

We asked the following questions: (1) Were patients aware of group allocation? (2) Were clinicians aware of group allocation? (3) Were outcome assessors aware of group allocation? Given the nature of the 2 therapies, the investigators could not blind the subjects to group allocation. The study personnel were initially blinded to the treatment groups, as the duct tape was removed before each clinic visit, and both groups were instructed to debride their warts similarly before visiting the clinic. At each visit, study nurses measured and recorded each wart size before determining an individual subject's treatment group and administering the appropriate therapy. While this protocol was designed to maintain the blinding of the outcome assessors, it is possible that having the study nurses both assess the outcomes and administer therapy may have resulted in unblinding of the study personnel over time. However, the caliper measurements should have provided a relatively objective, quantitative measurement of wart sizes.

More importantly, patients who did not follow-up in the clinic were contacted by telephone to report their treatment responses to study personnel. More subjects in the duct tape group reported their outcomes by telephone. Because the subjects were not blinded to their treatment, their qualitative assessment of wart resolution may have been biased. However, because there was no placebo group and because both treatment groups in this study received treatment, it is unclear in which direc-
tion any bias due to the unblinding of parents might go. One might expect it to favor the more conventional treatment, which is, in this case, cryotherapy.

FOLLOW-UP

Follow-up was completed for 51 (84%) of the 61 enrolled subjects. Six patients from the cryotherapy group and 4 patients from the duct tape group were lost to follow-up. The authors did not report when or why these subjects were lost to follow-up. Similarly, the authors did not report patients' adherence to the study protocol. As we will discuss in the following section, the loss of 16% of the patients to follow-up has important implications for interpreting the results of this study.

TREATMENT EFFECT SIZE AND PRECISION

The investigators reported the statistically significant benefit of duct tape occlusion therapy over cryotherapy. Specifically, 83% of patients treated with duct tape and 60% of patients treated with cryotherapy had resolution of their study wart. The reported $P$ value of .05 implies that we can state with 95.2% confidence that these results were not due to chance alone. However, the study did not report the 95% confidence interval (CI), which is the more clinically relevant measure of treatment effect. The 95% CI is calculated using a standard equation based on the number of patients randomized to each treatment group and their outcomes.\(^3\) We calculated that the 95% CI for this study's reported treatment effect is 1.1 to 48.1, and we can state with 95% confidence that the true treatment effect is somewhere between these 2 values. In other words, while this study found a treatment effect of 24.6%, the true treatment effect may be as small as 1.1% or as large as 48.1%. While both the $P$ value and the 95% CI indicate that the observed difference between the 2 groups is statistically significant at the $\alpha=.05$ level, the 95% CI provides a measure of the clinical significance of this difference by defining the range of potential treatment effect.

Because 16% of the patients in the trial were lost to follow-up, it is also important to consider the effect that this missing data could have on the study's results. The magnitude of effect that patient loss to follow-up may have had on this study can be determined by including that 16% of patients in the treatment effect analyses using a range of hypothetical outcomes. The worst-case scenario would be if, at the conclusion of this study, the 6 cryotherapy patients lost to follow-up had wart resolution and the 4 duct tape patients lost to follow-up had residual wart. By adding these 10 worst-case outcomes to the 51 known outcomes, we calculated that wart resolution would have occurred in 73% of patients in the duct tape group and 68% of patients in the cryotherapy group (95% CI, −17 to 28). This 95% CI includes zero, indicating that the 5% difference between the 2 treatment groups is not statistically significant. Therefore, if we take into account the effect that the patients lost to follow-up might have on the results of the study, duct tape therapy would be no more effective than cryotherapy. However, this is a maximally conservative estimate.

GENERALIZABILITY

The study population included patients 3 to 22 years of age with at least 1 common wart located on an extremity who visited the pediatric and adolescent clinics at the Madigan Army Medical Center in Washington State. While this is a unique population presenting to a single center, these results are likely generalizable to most patients receiving treatment at pediatric primary care clinics in other settings. However, the authors did not mention other factors that affect warts' response to therapy, including the duration that the study wart had been present and the patients' prior use of wart removal therapies other than cryotherapy.\(^3\) Therefore, it is unclear whether the results of this study may also be applied to patients with any of these clinical characteristics.

CLINICALLY IMPORTANT OUTCOMES

The study's primary outcome was resolution of the study wart 2 months after initiation of treatment. Adverse outcomes were not specifically quantified, but they were reported to be more frequent and more severe in the cryotherapy group.

Ideally, a study of wart therapy should be long enough to adequately assess both wart resolution and recurrence. The Cochrane review of treatments for cutaneous warts suggests that subjects should be followed up for 6 months to assess cure more completely.\(^4\) The 2-month follow-up in this study may have affected its ability to detect these important clinical outcomes. Although the authors stated that they did not intend to measure wart recurrence, this is nevertheless a clinically important outcome with important implications for treatment efficacy. In 1 prior study,\(^2\) the cure rate of cryotherapy decreased by 26% when study wart presence was reassessed 19 months after initiation of therapy.

There are additional clinically important outcomes that were not assessed in this study. The authors had initially intended to measure the duration to cure as a secondary outcome, but they were not able to do so as a result of erratic patient follow-up. Owing to the small number of patients enrolled in the study, the authors did not compare the response of study warts by their anatomic location.

TREATMENT BENEFITS AND COSTS

There are many potential practical advantages of duct tape treatment over cryotherapy. Duct tape treatment is easily performed at home and seems to be well-tolerated. In addition, it may be more cost-effective than cryotherapy, as duct tape is relatively inexpensive and therapy would not require multiple clinic visits.

CONCLUSIONS

This study has important implications. As the authors conclude, duct tape therapy may be more effective than cryo-
therapy for the treatment of common warts. However, given the percentage of patients lost to follow-up, we calculate that it is possible that there is no difference in treatment effect between the 2 therapies.

Although primary care physicians frequently use cryotherapy for wart removal, a recent Cochrane review that assessed the efficacy of local treatments for cutaneous, nongenital warts found inconclusive evidence to support the efficacy of cryotherapy for this indication.4 The 2 small trials that have compared cryotherapy with placebo failed to demonstrate an advantage of cryotherapy over placebo and were classified by the Cochrane reviewers as low-quality. According to this review, the best available evidence supports the use of topical treatments that contain salicylic acid. Such preparations have been shown to have a modest, but significant, treatment benefit over placebo. However, the 2 trials that have compared the efficacy of cryotherapy with that of topical salicylic acid and/or lactic acid found no significant difference between the treatment groups. In addition, when considering medical therapy for the common wart, it is also important to consider their rate of spontaneous resolution. One large survey of institutionalized children found that 66% of warts spontaneously resolved within 2 years.6

Further studies comparing the efficacy of duct tape therapy with that of both placebo and salicylic acid are indicated. In the meantime, pediatricians may consider presenting duct tape as a therapeutic option to patients with extremity warts who, after discussing the risks and benefits of the various treatment options with their physician (including the option to not treat), request a non-salicylic acid therapy.

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REFERENCES