Original Article

Effectiveness of 100% Tea Tree Oil (*Melaleuca alternifolia*) versus Salicylic Acid + Lactic Acid Solution in the Treatment of Common Warts: A Randomized Controlled Trial

Zacaria B. Pario Jr., Lalaine R. Visitacion, Bai Shariffah B. Pandita-Reyes

Department of Dermatology, Southern Philippines Medical Center, Davao, Philippines

Abstract

Background: Common warts are a common malady among patients. Not only does it affect the person physically but also mentally and socially. Several treatment modalities are available; however, the major concerns are the treatment cost and adverse effect profile. Salicylic + lactic acid (SLA) solution is one of the standard treatment modalities owing to its strong keratolytic properties; however, its cost and adverse effects limit its use among patients. A cost-effective and safe alternative treatment is ideal to bring about a more favorable clinical outcome and better patient satisfaction. 100% tea tree oil (TTO) solution was used in this study due to its natural antiviral and anti-inflammatory properties.

Objective: The study aimed to compare the safety and effectiveness of 100% TTO versus SLA solution in the treatment of common warts.

Methods: A total of 17 patients with a total of 74 warts were included in the study. Each wart was assigned to either of the two treatment groups: the SLA group and the 100% TTO group. A treatment period of 6 weeks was used to assess the effectiveness of both treatment groups.

Results: The study showed no significant difference between the SLA solution and 100% TTO in the treatment of common warts. The 100% tea tree group reported lesser adverse effects. Both treatment groups reported favorable treatment satisfaction.

Conclusion: 100% TTO is a potentially safe and cost-effective alternative in the treatment of common warts.

Keywords: Common warts, lactic acid, salicylic acid, tea tree oil, verruca vulgaris

Address for correspondence: Dr. Zacaria B. Pario Jr., Phase 2 Block 10 Lot 11, Villa Candida Subdivision, Bulua, Cagayan de Oro City 9000, Misamis Oriental, Philippines.
E-mail: gozaibepario@gmail.com

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Introduction

Verruca vulgaris (common warts) is a viral infectious skin disease, seen more commonly among children and adolescents between 12 and 16 years of age. It is common worldwide and affects approximately 10% of the population. In school-aged children, the prevalence is as high as 10%–20%.[1] The Philippine Dermatological Society Health Information System recorded 26,708 cases in the last 10 years. Warts were more commonly seen in ages 11–20 years old with female predilection.[2] They are more common among immunosuppressed patients and

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meat handlers. Warts can be transmitted through sexual and nonsexual ways. As a result, warts do not only cause a problem for the patient cosmetically but also the infectious nature of the disease is an added disease burden. In a study by Unal *et al.* conducted in 2016, warts involving areas on the face, hands, and feet have been shown to cause discomfort in 51.7% and a negative effect on social or leisure activities in 38.8% of the subjects. In children and adolescents, warts were found to diminish the quality of life in up to 68.4% of the study population.[1]

The common wart is caused by human papillomavirus (HPV), a virus in the *Papovaviridae* family. The most frequent HPV infection is HPV-2, followed by HPV-4, HPV-7, HPV-26, and HPV-27. The virus gains access to the skin from minor external injury and infects the epidermal cells. The viral particles are released concurrently with exfoliation of the wart, causing spread to other areas. Areas of predilection include the hands and feet with a latency of 3–6 months. It begins initially as a small papule and gradually enlarges and elevates into a verrucous shape. Lesions are usually multiple, but sometimes may coalesce to form a plaque. Dermoscopy is an indispensable tool to diagnose common warts. Dermoscopic features would include papillomatosis, bleeding, linear and dotted vessels, and finger-like projections.[3]

Various treatment modalities are available in the treatment of common warts. Although spontaneous recovery occurs, it usually takes a long time and even years. There is very little tendency for spontaneous healing and will eventually require active intervention. Destructive procedures like cauterization with salicylic acid or surgical methods such as cryosurgery, laser ablation, electrocautery, and excision are used invariably to treat warts. These methods are usually painful, can cause scarring, and show inconsistent outcome with a high frequency of relapse. Contact sensitizers, imiquimod, intralesional interferons, and oral levamisole, cimetidine, or zinc sulfate have also been tried with variable success. Immunotherapy with intralesional antigens or vaccines (Bacillus Calmette–Guerin vaccine, measles, mumps, rubella virus, or measles, mumps, and rubella vaccine) has been tried for the treatment of common warts with encouraging results.[4] Several research have also explored the possibility of using herbal medicines and essential oils in the treatment of common warts. One study by Cruz and Visitacion showed no significant difference between salicylic-lactic acid (SLA) solution and apple cider vinegar in the treatment of common warts.[5] Studies with herb-derived products can provide more options and cheaper alternatives to the management of common skin disorders like common warts. A wider variety of treatment options provide physicians opportunities to better individualize treatments among patients.

Tea tree oil (TTO) is a popular ingredient in a variety of household and cosmetic products. Known for its potential antiseptic properties, it has been shown to be active against a variety of bacteria, fungi, viruses, and mites. The antimicrobial property is mainly attributed to terpinen-4-ol, the major component of the oil. TTO is a pale yellow essential oil extracted from the leaves of the *Melaleuca alternifolia* plant of the *Myrtaceae* family. The antiviral activity of TTO was first shown using tobacco mosaic virus and tobacco plants. Plants were sprayed with TTO or control solutions and were then experimentally infected with the tobacco mosaic virus. After 10 days, there was a noted decrease in the number of lesions in the plants than in the controls.[6] Another study conducted by Garozzo *et al.* showed the potential antiviral activity of TTO. Data showed that TTO has an antiviral activity against influenza A/PR/8 virus subtype H1N1.[7] A case study published in 2008 by Millar and Moore noted the successful treatment of hand wart in a 7-year-old patient. After 5 days, all warts had considerably reduced in size with little deformity to the digit, and after a further 7 days, there was no evidence of the presence of warts, at which point, the treatment was discontinued.[8] Two case reports in 2016 by Alsanad and Alkhamees also showed efficient treatment of warts with TTO in a 14-year-old and 9-year-old boy. For the first case, there was a dramatic reduction in the size of the wart after 3 days, and after 7 days, the wart had totally disappeared. For the second case, the wart needed about 20 days to disappear completely; however, the patient did not comply perfectly with the regimen.[9] A pilot comparative study was conducted in 2016 by Lombos–Serondo *et al.* on TTO and SLA solution. The study assessed 20 subjects, 8–44 years of age. There was no significant difference between the two groups in the resolution rates of common warts. Although these results are favorable to the *M. alternifolia* group, these may be due to the small sample size; hence, a larger study group is recommended in the future. Another factor that is of importance is that of the time amount given in the study for follow-ups. Four weeks is a relatively short period of time given for the complete cure of common warts with the use of topical agents.[10] Thus, this study is conceived to further investigate the antiviral effect of TTO specifically on common warts on a bigger number of subjects and longer period of time.

Objectives

The study aimed to compare the safety and effectiveness of 100% TTO versus SLA solution in the treatment of common warts. The study also aimed to (1) describe the

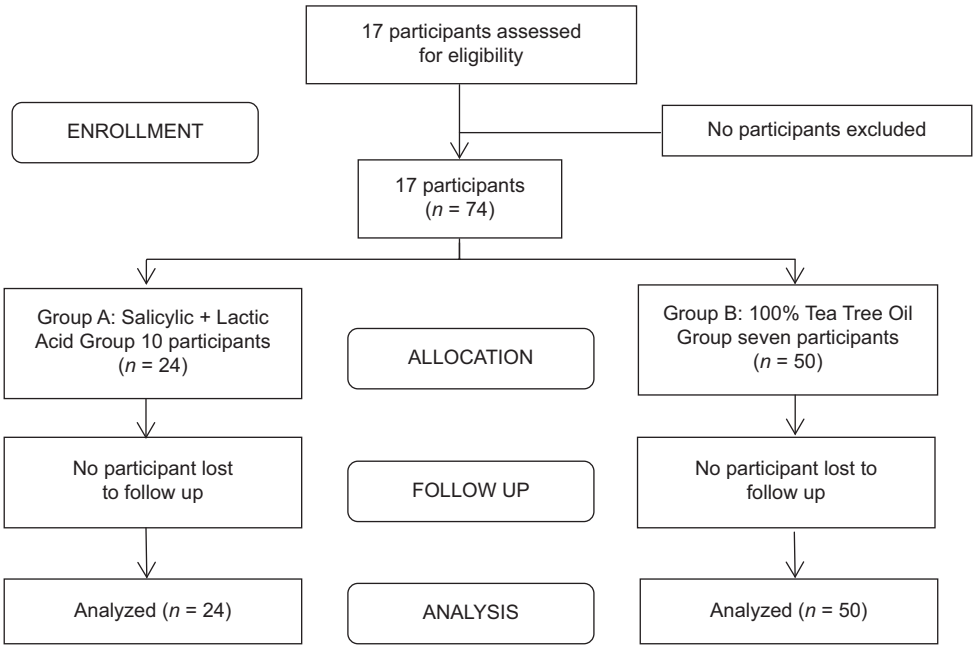

Figure 1: Flow diagram for salicylic-lactic acid solution versus 100% tea tree oil for the treatment of common warts

demographic and clinical characteristics of participants with common warts given 100% TTO versus SLA solution, (2) compare the effectiveness of 100% TTO versus SLA solution in producing complete clearance of the warts in 6 weeks in terms of clinical assessment and dermoscopy, (3) determine and compare the side effects on the use of 100% TTO and SLA solution in patients with warts in terms of pain, erythema, and erosion, and (4) assess patient satisfaction levels using the Visual Analog Scale (VAS) at the end of the treatment period in both groups.

Methods

This was an experimental, prospective, phase 2 randomized, controlled trial on the safety and effectiveness of 100% TTO versus SLA solution in the treatment of common warts. The study was done at the outpatient clinic of the Department of Dermatology in Southern Philippines Medical Center, Davao City. The study included patients diagnosed with common warts aged 5 years old and above. Participants with genital, seborrheic, mosaic, periungual, and filiform warts and participants who used topical agents 2 weeks before or underwent electrocautery or cryosurgery 4 weeks before were excluded from the study. Patients with known mental illnesses, immunodeficiency, and pregnant and lactating women were excluded from the study. The study protocol was submitted and approved by the hospital's Ethical Review Board. The study utilized purposive sampling procedures to select the respondents who were clinically and dermoscopically diagnosed with common warts in the outpatient section.

In this study, commercially available 100% TTO was used. It was compared with the commercially available SLA 167 mg/150 mg solution in the treatment of common warts [Figure 1]. Study interventions were placed in similar-looking opaque 15 ml bottles labeled as either "Solution A" or "Solution B." Participants were assigned with random numbers generated from the website http://www.randomization.com. The initial interview and physical examinations were done by the principal investigator. The participant randomization and dispensing of medications were done by the research assistant. The demographic and clinical profile of the patients was analyzed using descriptive statistics. The mean and standard deviation for continuous data such as the case of age and other relevant parameters measured using a standardized unit of measure. For categorical data such as the case of sex, type of treatment done, and/or procedure, frequency and percent were used to express the variables, and data were summarized using a frequency distribution table.

The number of warts was counted and measured accordingly (<5 or ≥5 mm). Before applying the study interventions, petroleum jelly was applied on the uninvolved areas to protect the normal skin. Participants assigned to either treatment group applied two coats of the solution to warts <5 mm in size and four coats of the solution to warts ≥5 mm in size using a brush applicator and then wrapped with cling wrap. Applications were done at bedtime and left overnight. The procedure was repeated until the warts were cleared. The participants were seen on day 1 (week 0) and were reassessed on day 14 (week 2), day 28 (week 4),

and day 42 (week 6). On each visit, complete physical and cutaneous examinations and photo documentation were done by the principal investigator, including adverse reactions and patient satisfaction to the assigned intervention. Participants who developed adverse reactions were evaluated and given the standard treatment for free.

The primary outcome of the study was assessed by clearance of warts on day 42 (week 6).[10] The outcome was based on the proportions achieving complete clearance of warts on day 14 (week 2), day 28 (week 4), and day 42 (week 6) between the two study groups. The clinical findings were rated as "complete clearance" or "no response."[11] Clearance was considered if skin color and lines were reestablished and warts were no longer visible and palpable. A dermatoscope was utilized to assess the clearance of the wart individually. A *t*-test for two proportions was used to compare significant difference in the clinical assessment, dermoscopy parameters, and presence of erythema and erosion between TTO versus SLA solution. A *t*-test for two means was used to compare the significant difference between the mean pain score of TTO versus SLA solution.

Results

Seventeen participants with a total of 74 warts were included and randomized from September 2021 to December 2021. No participants were excluded. A total of 24 warts in 10 participants were assigned to Group A: SLA solution and 50 warts in seven participants were assigned to Group B: 100% TTO. All participants had a good follow-up and completed the 6-week treatment period.

The profile showed that most participants were female with a mean age of 29 years. The median number of common warts seen on each participant was 3. The median size of warts was 3 mm [Table 1]. The common sites of warts were the dorsal aspect of the hands (33.33%), followed by the palmar aspect of the hand and the plantar aspect of the foot [Table 1].

The efficacy of treatment was evaluated by complete clearance of warts at week 6 [Table 2]. A dermoscopic evaluation was used to assess the complete clearance of warts. Clearance was considered if skin color and lines were reestablished and warts were no longer visible and palpable. In the 100% TTO, 70% achieved complete clearance, and 30% showed no response [Figure 2]. In the SLA group, 70.83% achieved complete clearance, and 29.16% showed no response [Figure 3]. After 6 weeks of treatment, both treatment groups were comparable in producing clinical and dermoscopic clearance.

Adverse reactions were determined among the participants to evaluate the favorable side effects of both interventional groups [Table 3]. Results show a more favorable safety profile for the 100% TTO group. Participant satisfaction [Table 3] was also assessed every follow-up until treatment completion using the VAS. The overall treatment satisfaction was comparable in both treatment groups.

Discussion

Verruca vulgaris (common warts) is a common dermatologic problem. Not only are the treatments expensive but they also incur the risks of different complications such as treatment failure and scarring, which contributes negatively not only to the patient's physical but also mental well-being as common warts can be cosmetically unpleasing. A safe and cost-effective alternative is ideal to address these concerns.

Based on the results of this study, complete clearing coincides with dermoscopic clearing with no significant difference between the two treatment groups. This shows that the two treatment groups are comparable. This supports the previous studies that purported the antiviral properties of TTO. Interestingly, the 100% TTO group reported lesser adverse effects with only one patient reporting mild erythema compared to the SLA group which showed five patients reporting of mild burning pain, and five patients reporting of mild erythema while on treatment. The better safety profile of 100% TTO may be attributed to its potential antiviral and anti-inflammatory

Table 1: Baseline demographics characteristics of the participants and location of warts

Indicator	SLA	100% TTO	Total	*P*
Gender				
Male	4	4	8	0.25
Female	6	3	9	
Age, mean±SD (years old)	33.1±9.65	23.57±12.88	29.18±11.75	
Children (5–12)	0	1	1	0.286
Adolescent (13–17)	0	2	2	
Adult (18–30)	4	3	7	
31–40	4	0	4	
41–50	2	1	3	
51–60	0	0	0	
>60	0	0	0	
Number of warts, median	2	5	3	
Size of warts (mm), median	4	3	3	0.261
<5	17	44	61	
≥5	7	6	13	
Location, *n* (%)	*n*=24	*n*=50		
Hands	13 (54.17)	21 (42)		0.153
Palmar	5 (20.83)	15 (30)		
Dorsum	8 (33.33)	6 (12)		
Feet	8 (33.33)	28 (56)		
Plantar	6 (25)	28 (56)		
Dorsum	2 (8.33)	0		
Lower extremities	3 (12.5)	1 (2)		

SD: Standard deviation, TTO: Tea tree oil, SLA: Salicylic-lactic acid

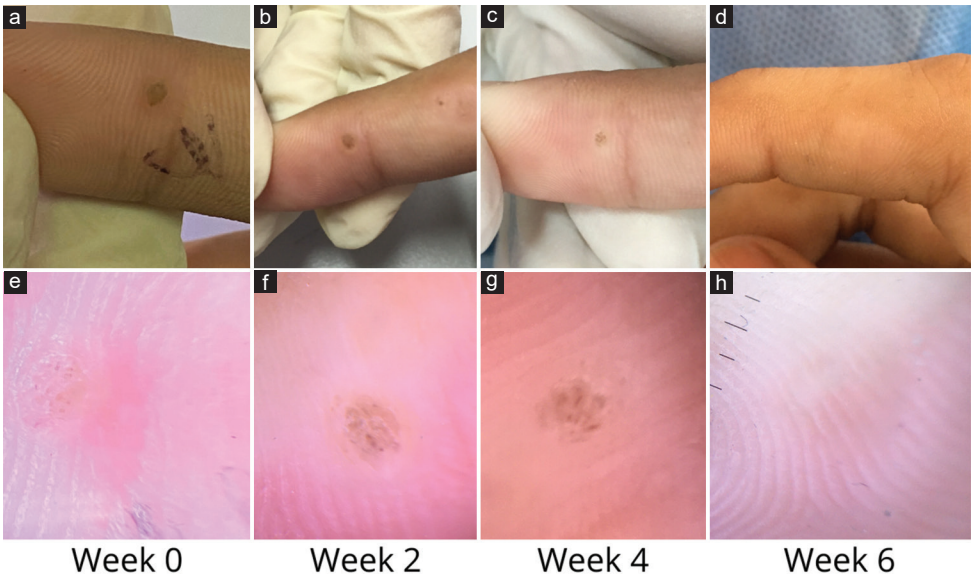

Figure 2: (a-d) 100% tea tree oil. Complete clearance of wart in the right index finger from week 0 to week 6. (e-h) Dermoscopy reveals reestablished skin color and lines.

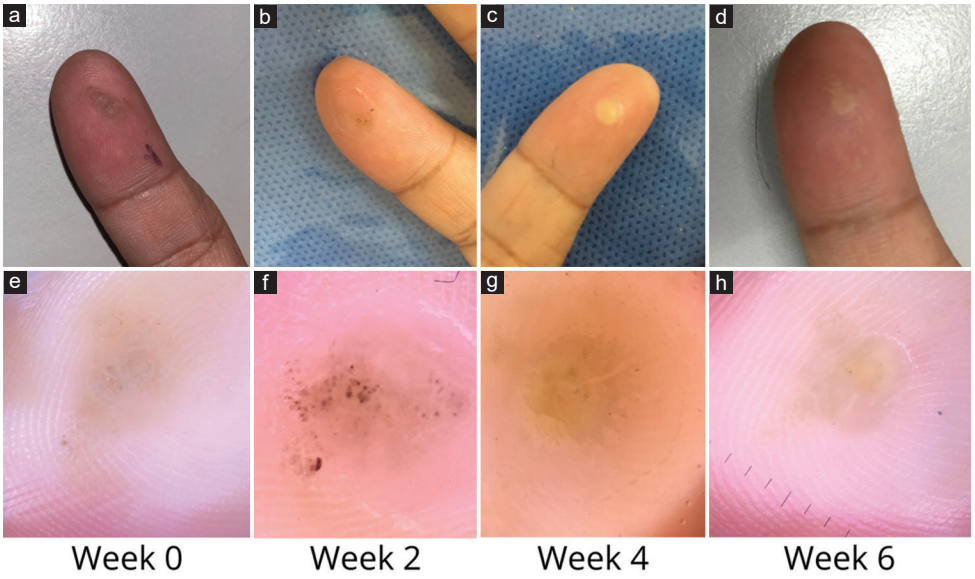

Figure 3: Salicylic-lactic acid solution. (a-d) Complete clearance of warts in the right fifth finger from week 0 to week 6. (e-h) Dermoscopy reveals reestablished skin color and lines.

Table 2: Response to treatment

Location	SLA		100% TTO		*P*
	Complete clearance, *n* (%)	No response, *n* (%)	Complete clearance, *n* (%)	No response, *n* (%)	
Hands	9 (37.5)	4 (16.67)	13 (26)	8 (16)	0.078
Palmar	4 (16.67)	1 (4.16)	10 (20)	5 (10)	
Dorsum	5 (20.83)	3 (12.5)	3 (6)	3 (6)	
Feet	7 (29.16)	1 (4.16)	21 (42)	7 (14)	
Plantar	5 (20.83)	1 (4.16)	21 (42)	7 (14)	
Dorsum	2 (8.33)	0	0	0	
Lower extremities	1 (4.16)	2 (8.33)	1 (2)	0	
Overall	17 (70.83)	7 (29.16)	34 (70)	15 (30)	

TTO: Tea tree oil, SLA: Salicylic-lactic acid

properties as opposed to the strong keratolytic properties of SLA solution. All of these reported adverse effects improved with subsequent applications as they finished the whole 6-week course of treatment. A future study

Table 3: Comparison of adverse effects and participant satisfaction

Adverse effect	Treatment		*P*
	SLA	100% TTO	
Pain, *n* (%)	5 (50)	0	0.029
Week 2	3 (30)	0	
Week 4	2 (20)	0	
Week 6	0	0	
Erythema, *n* (%)	5 (50)	1 (14.29)	
Week 2	3 (30)	1 (14.29)	
Week 4	1 (10)	0	
Week 6	1 (10)	0	
Erosion	0	0	
Week 2	0	0	
Week 4	0	0	
Week 6	0	0	
Clinical outcome	**VAS**		
	0–30, *n* (%)	**40–70, *n* (%)**	**80–100, *n* (%)**
Week 2			
SLA	3 (30)	3 (30)	4 (40)
100% TTO	1 (14.29)	3 (42.86)	3 (42.86)
Week 4			
SLA	3 (30)	3 (30)	4 (40)
100% TTO	0	3 (42.86)	4 (57.14)
Week 6			
SLA	1 (10)	3 (30)	6 (60)
100% TTO	0	3 (42.86)	4 (57.14)

TTO: Tea tree oil, SLA: Salicylic-lactic acid, VAS: Visual Analog Scale

with a placebo group can be helpful to further explore the safety profile of both treatment groups. Although the SLA group reported more adverse effects, there is no statistically significant difference in patient satisfaction toward both treatment groups. A commercially available 100% TTO costs about half a commercially available 15 ml SLA solution. This further makes 100% TTO not only a safe and effective alternative but also a cost-effective alternative treatment for common warts. The study was able to include a limited number of warts due to the pandemic restrictions; to further evaluate the effectiveness of 100% TTO, a larger sample size is recommended. A relatively short treatment period of 6 weeks was done for the study; given the good safety profile of 100% TTO, a longer treatment period is permissible to allow better clearance of warts, especially for warts larger than 5 mm. Posttreatment follow-up care is also warranted to assess the recurrence of common warts.

Conclusion

The study explored the potential of 100% TTO in the treatment of common warts. It was compared to the standard treatment of the SLA solution. The profile showed that most participants were female with a mean age of 33.1 years in the SLA group and most participants were male in the 100% TTO group with a mean age of 23.57 years. Results showed that there was no significant difference between the two treatments based on complete clinical and dermoscopic clearance of warts. It was also noted that participants treated with 100% TTO reported lesser adverse effects than those under the standard treatment. Both treatment groups reported favorable treatment satisfaction.

Based on this study, 100% TTO can be a safe and cost-effective alternative treatment for common warts.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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