

The Effectiveness of Cutaneous Wart Resolution with Current Treatment Modalities

Sarah A. Ringin

Department of Medicine, University of Notre Dame, Sydney, NSW, Australia

Abstract

Non-venereal warts are a frequent dermatological presentation with potential spontaneous regression in immunocompetent adults and children within 2 years. Evidence shows that conventional wart treatments are not a guaranteed treatment modality and can carry concerns regarding safety. The aim of this literature review was to identify the most effective treatments for wart resolution to guide clinical practice while identifying areas for further research.

A systematic literature review was performed to determine the current treatment modalities for non-anogenital cutaneous warts in immunocompetent individuals and their effectiveness. Articles were categorized into one of eight groups depending on anatomical location, population age, or recalcitrant status with ranked levels of evidence.

This literature review highlights a variety of treatments for non-venereal warts shown to be effective. In this instance where optimal evidence-based treatments are not available, clinical experience determines the most appropriate clinical practice.

Further reproducible immunotherapy research on wart resolution is required to enable clear comparisons of these treatment modalities to conventional methods. Future clinical practice will require the human papillomavirus type to target the wart treatment accordingly; however, further research is required to determine these correlations.

Keywords: Recalcitrant, treatment, verruca, warts

INTRODUCTION

Verruca lesions are strategically named depending on their location: face, shins and dorsum of hands (verruca plana), soles of feet (verruca plantaris), common warts (verruca vulgaris), and surrounding nails (periungual verruca). Verruca lesions are caused by a localized infection of the keratinocytes by the human papillomavirus (HPV), which is a small deoxyribonucleic acid virus of the papovavirus family.^[1] There are more than 150 different types of HPV identified with the majority of verruca vulgaris lesions caused by HPV types 1, 2, 4, 27, or 57 and verruca plana lesions by HPV types 3 or 10.^[1] Viruses can be treated with antiviral agents; however, there is often a reliance on the body's defense mechanisms to control the spread and subsequent effects of viruses. Interestingly, there is selective research determining the HPV type for a cutaneous wart before targeting treatment accordingly.^[2]

Verruca lesions are identified as “recalcitrant” if they were resistant to an initial treatment method, clinically requiring an alternative therapy.^[3] In immunocompetent individuals, spontaneous regression of warts is influenced by the rate of resolution, for example, host immunity, HPV type, and site of infection. However, treatment for instant eradication is favored over spontaneous resolution as natural resolution is found to be successful in only 40% of patients within 2 years.^[4]

The literature has shown that conventional treatments used in everyday practice are uniformly unsuccessful and carry concerns regarding safety.^[3] A Cochrane review by Kwok *et al.*^[4] completed a meta-analysis of the topical treatments for cutaneous warts. They found that liquid

Address for correspondence: Dr. Sarah A. Ringin,
University of Notre Dame,
Sydney, NSW, Australia.
E-mail: sarah.ringin@gmail.com

Access this article online

Quick Response Code:



Website:
www.jcasonline.com

DOI:
10.4103/JCAS.JCAS_62_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Ringin SA. The effectiveness of cutaneous wart resolution with current treatment modalities. *J Cutan Aesthet Surg* 2020;13:24-30.

nitrogen cryotherapy had the same effectiveness as placebo; salicylic acid may be more effective on the hands and feet compared to placebo and no significant difference was found between salicylic acid and cryotherapy on all areas of the body. These findings are concerning for medical practitioners and for patients receiving treatment.

Over the past decade, interest in more sophisticated and focused wart treatments targeting the immune response to HPV has attracted considerable interest compared to the destructive and irritant approaches currently used.^[5] Current verruca vulgaris research is focusing on immune-manipulation methods to determine their effectiveness. These include 5-fluorouracil, dinitrochlorobenzene, intralesional bleomycin, intralesional interferon, photodynamic therapy, and intralesional antigen.^[4] Many of these new immunotherapy interventions have an unknown mechanism of action; however, these new immunotherapy interventions show positive signs of wart clearance at the site of injection and systemically.^[5]

This literature review is first to collate relevant articles over 10 years categorized into anatomical locations with recalcitrant and non-recalcitrant warts segregated. This will provide clarity on the effectiveness of treatment modalities for non-venereal wart resolution.

MATERIALS AND METHODS

The following electronic search method was undertaken on March 22, 2017 following the PICO format to answer the question: What are the current treatment modalities for non-anogenital cutaneous warts in immunocompetent individuals and how effective are they?

- Population: Immunocompetent individuals with non-anogenital cutaneous warts.
- Intervention: Wart treatment modalities.
- Control: No intervention.
- Outcome: Resolution of warts.

The EBSCOhost platform was used to search the relevant articles published between 2007 and 2017 using medical subject headings (MeSH) for the following databases: MEDLINE, CINAHL, and Academic Search Premier.

A total of 759 articles were retrieved from the databases combined. Filters of English language, peer reviewed articles, published since 2007, and “human only” were applied leaving 500 articles.

Primary relevance assessment was conducted to exclude the following:

1. Molluscum contagiosum warts, anogenital warts, respiratory warts, oropharynx warts, and any other type of wart other than cutaneous warts.
2. Immunocompromised patients.
3. Absent effectiveness of the treatment modality measurements.

4. Meta-analysis, systematic reviews, literature reviews, or editorial articles.

The primary relevance assessment removed 414 irrelevant articles by title, 27 by abstract, and 14 by full-text review. The remaining 43 articles were used for analysis with an additional 17 articles from manually searching relevant systematic review and meta-analysis articles. In total, 60 articles were deemed relevant for analysis. Each article was ranked according to the National Health and Medical Research Council (NHMRC) Evidence Hierarchy and categorized into the following groups depending on the anatomical location, population age, and recalcitrant status.

1. Verruca vulgaris and verruca plantaris treatment.
2. Recalcitrant verruca vulgaris and verruca plantaris treatment.
3. Pediatric verruca vulgaris treatment.
4. Recalcitrant pediatric verruca vulgaris treatment.
5. Verruca plana treatment.
6. Recalcitrant verruca plana treatment.
7. Periungual verruca treatment.
8. Recalcitrant periungual verruca treatment.

FINDINGS

Verruca vulgaris and verruca plantaris treatment: 34 articles

There were 19 Level II randomized control trials comparing varying treatment methods for verruca vulgaris lesions, as summarized in Table 1. Khozeimeh *et al.*^[6] compared intralesional *Candida albicans* antigen and liquid nitrogen cryotherapy. There was a statistical significance in wart resolution with immunotherapy more successful. Shaheen *et al.*^[7] found that purified protein derivative (PPD) and measles, mumps, and rubella (MMR) vaccine were statistically more effective than a saline injection for wart eradication; however, there was no statistical significance between PPD and MMR groups. Bruggink *et al.*^[8] in a study of 406 participants, compared monochloroacetic acid (MCA) with cryotherapy on common warts and cryotherapy plus 50% salicylic acid on plantar warts. The study found no significant difference between the treatments for common or plantar warts; however, 212 participants did not adhere to the study protocol. A previous study by Bruggink *et al.*^[9] found that cryotherapy was more effective for common warts than salicylic acid and the “wait-and-see” policy, but there was no difference in wart eradication between these treatments with plantar warts. Zamanian *et al.*^[10] compared intralesional MMR vaccine and normal saline finding a statistical difference in the second and third visits with fewer lesions in the interventional group. However, 30% of the MMR group had influenza type side effects. A similar study by Nofal *et al.*^[11] compared intralesional MMR and saline

Table 1: Effective treatment methods for verruca vulgaris and verruca plantaris lesions

	Treatment modalities (only Level II studies included)	Effective?
Immunotherapy	<i>Candida albicans</i> antigen	Yes: compared to cryotherapy
	PPD	Yes: to placebo. Same as MMR
	MMR	Yes: to placebo. Same as PPD
	Monochloroacetic acid (MCA)	No: compared to cryotherapy and salicylic acid
	Bleomycin	Yes: to placebo, cryotherapy
	Interferon- α injection	Yes: to placebo
	5-FU+LE	Yes: to placebo
Conventional	Liquid nitrogen cryotherapy	Yes: compared to salicylic acid and "wait-and-see" Unsure: same as salicylic acid, pulsed dye laser, and phenol No: compared to bleomycin
	Salicylic acid	Unsure: same as cryotherapy
Other	10% silver nitrate	Yes: to placebo
	Pulsed dye laser	Unsure: same as cryotherapy
	Local hyperthermia	Yes: placebo
	Phenol	Unsure: same as cryotherapy
	Duct tape occlusion	No: to placebo
	Zinc oxide	No: compared to salicylic acid + lactic acid

finding a statistical significance in therapeutic response with MMR being more effective. However, this was not the case with recalcitrant warts. Mohamad *et al.*^[12] compared the MMR vaccine to saline in plantar warts with a statistical significance found for MMR having significant clearance. Cockayne *et al.*^[13] compared cryotherapy and salicylic acid for plantar wart treatment finding no group more effective with relatively low clearance rates. Soni *et al.*^[14] compared intralesional bleomycin and saline finding a statistical significance in resolution rate at 12 weeks in the intervention group. Dhar *et al.*^[15] compared intralesional bleomycin and cryotherapy and found that bleomycin was significantly more effective than cryotherapy. Another previous study by Adalatkhah *et al.*^[16] compared bleomycin and cryotherapy noting that bleomycin intralesional injection was more effective than cryotherapy. Akhyani *et al.*^[17] compared pulsed dye laser (PDL) with cryotherapy and found no statistical significance between both interventions for complete remission. Huo *et al.*^[18] studied local hyperthermia on plantar warts finding a statistical significant difference in cure rates for the local hyperthermia compared to a sham red dot without heat. Aksakal *et al.*^[19] studied sublesional interferon- α injection in common warts finding a statistical significance between the intervention and the placebo as well as a statistical significance in response rate of a single wart more responsive than multiple lesions. Banihashemi *et al.*^[20] compared cryotherapy and 80% phenol solution noting no statistical difference between the treatments. Yazdanfar *et al.*^[21] compared 5-fluorouracil, lidocaine and epinephrine (5-FU+LE) against the placebo of normal saline finding a statistical significance in complete resolution for the intervention group. Ebrahimi *et al.*^[22] compared 10% silver nitrate solution to black ink and found a statistical significant

difference in cure rates in the intervention group as well as a statistical significant cure rate in females over males. Wenner *et al.*^[23] compared duct tape occlusion therapy to placebo moleskin and found no statistical difference between the groups. Khattar *et al.*^[24] compared topical zinc oxide and a combination of salicylic acid and lactic acid. They found no statistical difference between the groups for cure rates.

Three Level III-2 prospective cohort studies were noted. Kaçar *et al.*^[25] compared topical CPS (1% cantharidin, 5% podophyllotoxin, 30% salicylic acid) and cryotherapy for plantar warts noting that topical CPS was significantly more effective than cryotherapy for resolution. Choi *et al.*^[26] compared DCP (1% diphencyprone) to cryotherapy noting a statistical significance in clearance rate in the DCP group at 12 months. Bohlooli *et al.*^[27] compared Fig Tree latex and cryotherapy finding cryotherapy to be more effective for wart reduction.

Twelve Level IV experimental design studies with a one-arm intervention or retrospective experimental studies were analyzed. These research studies were conducted without a control group. These treatments included PPD, MMR vaccine, *Candida* antigen, Nd:YAG, mycobacterium w (Mw) vaccine, intralesional injection of photodynamic therapy, adapalene, CO₂ laser, and homologous autoimplantation.

Recalcitrant verruca vulgaris and verruca plantaris treatment: 14 articles

Four Level II randomized control trials were analyzed, as summarized in Table 2. Dhakar *et al.*^[28] compared Mw vaccine and cryotherapy noting no statistical significance between the two groups. Amirnia *et al.* (2015)^[29] compared intralesional PPD, liquid nitrogen cryotherapy, and saline placebo. They found a statistical

Table 2: Effective treatment methods for recalcitrant verruca vulgaris and verruca plantaris lesions

	Treatment modalities (only Level II studies included)	Effective?
Immunotherapy	Mw vaccine	Unsure: same as cryotherapy
	PPD	Yes: to placebo
Conventional	Liquid nitrogen cryotherapy	Unsure: same as Mw vaccine
	Paring	Unsure: same as IPL
Other	IPL	Unsure: same as paring
	Zinc sulfate	No: to placebo

Table 3: Effective treatment methods for pediatric verruca vulgaris lesions

	Treatment modalities (only Level II studies included)	Effective?
Immunotherapy	5-Fluorouracil cream	Unsure: same as duct tape occlusion
Conventional	–	–
Other	Duct tape occlusion	Unsure: same as 5-Fluorouracil

Table 4: Effective treatment methods for verruca plana lesions

	Treatment modalities (only Level II studies included)	Effective?
Immunotherapy	–	–
Conventional	–	–
Other	50% citric acid	Yes: 0.05% tretinoin
	0.05% tretinoin	No: 50% citric acid

significance in clearance between PPD and the control. Togsverd-Bo *et al.*^[30] compared intense pulsed light (IPL) and paring alone finding no statistical significant difference in clearance rate at 6 weeks. López-García *et al.*^[31] compared oral zinc sulfate and starch placebo finding no significant difference in clearance rates between the two groups.

A Level III-2 non-randomized control trial compared PDL and Nd:YAG for warts eradication finding no statistical significance between the two groups.

Nine Level IV experimental design studies with a one-arm intervention or retrospective experimental studies were analyzed. These studies did not include a control group. The treatments included cantharidin/podophyllotoxin/salicylic acid, MMR vaccine, Mw vaccine, *C. albicans* antigen, PDL, autowart injection, photodynamic therapy, and retinoid.

Pediatric verruca vulgaris treatment: 3 articles

Gladsjo *et al.*,^[33] in a Level II randomized controlled trial, compared 5% 5-fluorouracil cream with duct tape occlusion applied once a day to the same treatment applied twice a day. They found no significant difference in resolution rate between the two groups [Table 3].

Bruggink *et al.*,^[34] in a Level III-2 prospective cohort study, analyzed the “wait-and-see” policy finding 50% of warts were gone in 1 year.

Maronn *et al.* (2008),^[35] in a Level IV retrospective experimental study on 170 patients with no control group, found that 87% had complete resolution with *C. antigen* injection.

Recalcitrant pediatric verruca vulgaris treatment: 3 articles

Two Level IV retrospective experimental studies with no control groups were found. Sethuraman *et al.*^[36] with no control group found a 75% overall clearance rate using PDL. Fernández-Guarino *et al.*^[32] found a 76.4% resolution rate with 3% topical Cidofovir applied twice daily without occlusion.

A nonrated case study (Kellis 2011)^[37] found hypnosis for 6 weeks resolved the warts within 1 week with no recurrence.

Verruca plana treatment: 2 articles

Vali and Ferdowsi,^[38] in a Level II randomized control trial, found that 50% citric acid solution was statistically significant in clearance rate as compared with 0.05% tretinoin lotion; however, no significant difference was noted in the onset of action [Table 4].

A nonrated case study (Bhushan *et al.* 2014)^[39] concluded that 200-mg hydroxychloroquine that was applied twice daily had complete resolution in 40 days.

Recalcitrant verruca plana treatment: 1 article

Kartal Durmazlar *et al.*,^[40] in a Level IV experimental design with a one-arm intervention, noted that all patients had clinical cure within 16 weeks using 0.7% cantharidin solution in acetone solution.

Periungual verruca treatment: 1 article

AlGhamdi and Khurram,^[41] in a Level IV experimental design with a one-arm intervention, found that 86.6% had complete clearance with 1 mL bleomycin at 6 months after treatment.

Recalcitrant periungual verruca treatment: 2 articles

Espana *et al.*,^[42] in a Level IV retrospective experimental study, concluded that 50% of patients had complete clearance with Cidofovir cream application.

A nonrated case study (El-Khayate *et al.* 2011)^[43] concluded complete resolution with systemic acitretin 25 mg applied once daily.

Summary of treatment modality effectiveness

Table 5: Summary of effectiveness	
Cutaneous warts	Effectiveness
Verruca vulgaris + verruca plantaris	Yes: <i>Candida albicans</i> antigen better than cryotherapy Yes: PPD same as MMR, better than placebo Yes: Bleomycin better than placebo and cryotherapy Yes: Interferon- α injection better than placebo Yes: 5-FU+LE better than placebo Yes: 10% silver nitrate better than placebo Yes: local hyperthermia better than placebo ? Salicylic acid, pulsed dye laser and phenol all the same as cryotherapy ? Cryotherapy same as salicylic acid and wait and see
Recalcitrant verruca vulgaris + verruca plantaris	Yes: PPD ? Mw vaccine same as cryotherapy ? Paring same as IPL
Pediatric verruca	None
Recalcitrant pediatric verruca	None
Verruca plana	Yes: 50% citric acid better than 0.05% tretinoin
Recalcitrant verruca plana	None
Periungual verruca	None
Recalcitrant periungual verruca	None

DISCUSSION

Numerous wart treatment modalities have been researched with the aim to identify the most effective treatment for wart resolution. Of the studies each has its own intervention concentration, method protocol, and comparison. Determining the exact effectiveness of these treatments is made difficult with these varying parameters and absent comparison between each intervention.

Appreciating the meta-analysis findings on cutaneous wart treatments, Kwok *et al.*^[4] highlighted the neutral comparison between cryotherapy and salicylic acid to placebo providing a basis for our analysis. This literature review discovers immunotherapy injections for treatment of verruca vulgaris and verruca plantaris lesions as more superior to the conventional methods. The immunotherapy treatments studied in randomized controlled trials considered to be effective include *C. albicans* antigen, PPD, MMR vaccine, and bleomycin. Interferon- α and 5-FU+LE are considered effective treatments against placebo; however, it is unknown how effective they are as compared to other treatment methods. Treatments found not to be effective

include PDL, phenol, duct tape occlusion, and zinc oxide. Furthermore, when treating recalcitrant verruca vulgaris and verruca plantaris lesions there is no well-demonstrated effective treatment.

Pediatric populations still appear to greatly benefit from the “wait-and-see” policy with all other treatment modalities in an experimental phase. Recalcitrant and non-recalcitrant verruca plana and periungual lesions are still in experimental stages with potentially effective citric acid and tretinoin applications.

Interestingly, clinical practice has been known to encompass the use of surgical removal or electrosurgery for treatment of verruca lesions. However, this literature review was unable to appreciate the effectiveness of this modality with the absence of this method published during our search strategy. This is similar to potassium hydroxide, used in the pediatric verruca population, which was also not mentioned in the results.

The findings align with the study purpose of collating systematically searched literature on treatment modalities for wart resolution over the past 10 years. The findings also support the previous systematic review noting liquid nitrogen cryotherapy and salicylic acid treatments no more superior than placebo.^[4]

This literature review has highlighted a variety of treatments for non-venereal warts shown to be effective. In this instance where optimal evidence-based treatments are not available, clinical experience determines the clinical practice. This can include conventional treatments if the deemed necessary even though the current evidence does not clearly support their practice. From this study, we gain a greater insight of the effective treatment modalities for anatomical location, population group, and recalcitrant status. Even though the majority of the research into immunotherapy drugs is still in an experimental stage with varied methods, there is still continued evidence demonstrating their effectiveness. The prediction is that the shift to these experimental treatments will take place in the near future, once formal guidelines and further research is available.

The limitations of this study manifest from the limited optimal evidence (Level II NHMRC hierarchy) currently available on wart treatments. There is a vast availability of experimental studies; however, they do not have a control group to provide any comparison of their effectiveness.

FUTURE DIRECTIONS

Larger, prospective controlled trials of non-venereal wart treatments including immunotherapy injections are required to determine the most effective practice and shape evidence based guidelines. The prediction is that future clinical practice will require the HPV type for each wart to target treatment accordingly;

however, further research is required to determine these correlations.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sterling JC, Gibbs S, Haque Hussain SS, Mohd Mustapa MF, Handfield-Jones SE. British association of dermatologists' guidelines for the management of cutaneous warts 2014. *Br J Dermatol* 2014;171:696-712.
2. Bruggink SC, Gussekloo J, de Koning MN, Feltkamp MC, Bavinck JN, Quint WG, *et al.* HPV type in plantar warts influences natural course and treatment response: secondary analysis of a randomised controlled trial. *J Clin Virol* 2013;57:227-32.
3. Abd-Elazeim FM, Mohammed GF, Fathy A, Mohamed RW. Evaluation of IL-12 serum level in patients with recalcitrant multiple common warts, treated by intralesional tuberculin antigen. *J Dermatolog Treat* 2014;25:264-7.
4. Kwok CS, Gibbs S, Bennett C, Holland R, Abbott R. Topical treatments for cutaneous warts. *Cochrane Database Syst Rev* 2012, Art. No.: CD001781. DOI: 10.1002/14651858.CD001781.pub3.
5. Gibbs S. The trials of treating warts. *Indian J Dermatol Venereol Leprol* 2014;80:495-6.
6. Khozeimeh F, Jabbari Azad F, Mahboubi Oskouei Y, Jafari M, Tehrani S, Alizadehsani R, *et al.* Intralesional immunotherapy compared to cryotherapy in the treatment of warts. *Int J Dermatol* 2017;56:474-8.
7. Shaheen MA, Salem SA, Fouad DA, El-Fatah AA. Intralesional tuberculin (PPD) versus measles, mumps, rubella (MMR) vaccine in treatment of multiple warts: a comparative clinical and immunological study. *Dermatol Ther* 2015;28:194-200.
8. Bruggink SC, Gussekloo J, Egberts PF, Bavinck JNB, de Waal MWM, Assendelft WJJ, *et al.* Monochloroacetic acid application is an effective alternative to cryotherapy for common and plantar warts in primary care: a randomized controlled trial. *J Invest Dermatol* 2015;135:1261-7.
9. Bruggink SC, Gussekloo J, Berger MY, Zaaijer K, Assendelft WJ, De Waal MW, *et al.* Cryotherapy with liquid nitrogen versus topical salicylic acid application for cutaneous warts in primary care: randomized controlled trial. *CMAJ* 2010;182:1624-30.
10. Zamanian A, Mobasher P, Jazi GA. Efficacy of intralesional injection of mumps-measles-rubella vaccine in patients with wart. *Adv Biomed Res* 2014;3:107.
11. Nofal A, Nofal E. Intralesional immunotherapy of common warts: successful treatment with mumps, measles and rubella vaccine. *J Eur Acad Dermatol Venereol* 2010;24:1166-70.
12. Mohamad NS, Badran F, Yakout E. Evaluation of the efficacy of a combination—measles, mumps and rubella vaccine in the treatment of plantar warts. *Our Dermatology Online* 2013;4:463-7.
13. Cockayne S, Hewitt C, Hicks K, Jayakody S, Kang'ombe AR, Stamuli E, *et al.*; EVERT Team. Cryotherapy versus salicylic acid for the treatment of plantar warts (verrucae): a randomised controlled trial. *BMJ* 2011;342:1-7.
14. Soni P, Khandelwal K, Aara N, Ghiya BC, Mehta RD, Bumb RA. Efficacy of intralesional bleomycin in palmo-plantar and periungual warts. *J Cutan Aesthet Surg* 2011;4:188-91.
15. Dhar SB, Rashid MM, Islam A, Bhuiyan M. Intralesional bleomycin in the treatment of cutaneous warts: a randomized clinical trial comparing it with cryotherapy. *Indian J Dermatol Venereol Leprol* 2009;75:262-7.
16. Adalatkah H, Khalilollahi H, Amini N, Sadeghi-Bazargani H. Compared therapeutic efficacy between intralesional bleomycin and cryotherapy for common warts: a randomized clinical trial. *Dermatol Online J* 2007;13:1-3.
17. Akhyani M, Ehsani AH, Noormohammadpour P, Shamsodini R, Azizahari S, Sayanjali S. Comparing pulsed-dye laser with cryotherapy in the treatment of common warts. *J Laser Med Sci* 2010;1:14-9.
18. Huo W, Gao XH, Sun XP, Qi RQ, Hong Y, Mchepange UO, *et al.* Local hyperthermia at 44degrees C for the treatment of plantar warts: a randomized, patient-blinded, placebo-controlled trial. *J Infect Dis* 2010;201:1169-72.
19. Aksakal AA, Ozden MG, Atahan C, Onder M. Successful treatment of verruca plantaris with a single sublesional injection of interferon- α 2a. *Clin Exp Dermatol* 2008;34:16-9.
20. Banihashemi M, Pezeshkpoor F, Yazdanpanah MJ, Family S. Efficacy of 80% phenol solution in comparison with cryotherapy in the treatment of common warts of hands. *Singapore Med J* 2008;49:1035-7.
21. Yazdanfar A, Farshchian M, Fereydoonnejad M, Farshchian M. Treatment of common warts with an intralesional mixture of 5-fluorouracil, lidocaine, and epinephrine: a prospective placebo-controlled, double-blind randomized trial. *Dermatol Surg* 2008;34:656-9.
22. Ebrahimi S, Dabiri N, Jamshidnejad E, Sarkari B. Efficacy of 10% silver nitrate solution in the treatment of common warts: a placebo-controlled, randomized, clinical trial. *Int J Dermatol* 2007;46:215-7.
23. Wenner R, Askari SK, Cham PM, Kedrowski DA, Liu A, Warshaw EM. Duct tape for the treatment of common warts in adults: a double-blind randomized controlled trial. *Arch Dermatol* 2007;143:309-13.
24. Khattar JA, Musharrafieh UM, Tamim H, Hamadeh GN. Topical zinc oxide vs. Salicylic acid-lactic acid combination in the treatment of warts. *Int J Dermatol* 2007;46:427-30.
25. Kaçar N, Taşlı L, Korkmaz S, Ergin S, Erdoğan BŞ. Cantharidin-podophyloxytoxin-salicylic acid versus cryotherapy in the treatment of plantar warts: a randomized prospective study. *J Eur Acad Dermatol Venereol* 2012;26:889-93.
26. Choi MH, Seo SH, Kim IH, Son SW. Comparative study on the sustained efficacy of diphencyprone immunotherapy versus cryotherapy in viral warts. *Pediatr Dermatol* 2008;25:398-9.
27. Bohlooli S, Mohebipoor A, Mohammadi S, Kouhnavard M, Pashapoor S. Comparative study of fig tree efficacy in the treatment of common warts (verruca vulgaris) vs. Cryotherapy. *Int J Dermatol* 2007;46:524-6.
28. Dhakar AK, Dogra S, Vinay K, Sarangal R, Kanwar AJ, Singh MP. Intralesional mycobacterium w vaccine versus cryotherapy in treatment of refractory extragenital warts: a randomized, open-label, comparative study. *J Cutan Med Surg* 2016;20:123-9.
29. Amirnia M, Khodaeiani E, Fouladi DF, Masoudnia S. Intralesional immunotherapy with tuberculin purified protein derivative (PPD) in recalcitrant wart: A randomized, placebo-controlled, double-blind clinical trial including an extra group of candidates for cryotherapy. *J Dermatolog Treat* 2016;27:173-8.
30. Togsverd-Bo K, Gluud C, Winkel P, Larsen HK, Lomholt HB, Cramers M, *et al.* Paring and intense pulsed light versus paring alone for recalcitrant hand and foot warts: a randomized clinical trial with blinded outcome evaluation. *Lasers Surg Med* 2010;42:179-84.
31. López-García DR, Gómez-Flores M, Arce-Mendoza AY, de la Fuente-García A, Ocampo-Candiani J. Oral zinc sulfate for unresponsive cutaneous viral warts: too good to be true? A double-blind, randomized, placebo-controlled trial. *Clin Exp Dermatol* 2009;34:e984-5.
32. Fernández-Guarino M, Harto A, Jaén P. Treatment of recalcitrant viral warts with pulsed dye laser MAL-PDT. *J Dermatolog Treat* 2011;22:226-8.
33. Gladajo JA, Alió Sáenz AB, Bergman J, Kricorian G, Cunningham BB. 5% 5-fluorouracil cream for treatment of verruca vulgaris in children. *Pediatr Dermatol* 2009;26:279-85.
34. Bruggink SC, Eekhof JA, Egberts PF, van Blijswijk SC, Assendelft WJ, Gussekloo J. Natural course of cutaneous warts among primary schoolchildren: a prospective cohort study. *Ann Fam Med* 2013;11:437-41.

35. Maronn M, Salm C, Lyon V, Galbraith S. One-year experience with Candida antigen immunotherapy for Warts and Molluscum. *Pediatr Dermatol* 2008;25:189-92.
36. Sethuraman G, Richards KA, Hiremagalore RN, Wagner A. Effectiveness of pulsed dye laser in the treatment of recalcitrant warts in children. *Dermatol Surg* 2010;36: 58-65.
37. Kellis E. The treatment of warts with a little help from “The Simpsons”: A case example of the treatment of an 11-year-old boy. *Australian Journal of Clinical and Experimental Hypnosis* 2011;39: 181-8.
38. Vali A, Ferdowsi F. Evaluation of the efficacy of 50% citric acid solution in plane wart treatment. *Indian J Dermatol* 2007;52: 96-8.
39. Bhushan P, Aggarwal A, Baliyan V. Complete clearance of cutaneous warts with Hydroxychloroquine: Antiviral Action?. *Indian J Dermatol* 2014;59:211.
40. Kartal Durmazlar SP, Atacan D, Eskioglu F. Cantharidin treatment for recalcitrant facial flat warts: a preliminary study. *J Dermatolog Treat* 2009;20:114-9.
41. AlGhamdi KM, Khurram H. Successful treatment of periungual warts with diluted bleomycin using translesional multipuncture technique: a pilot prospective study. *Dermatol Surg* 2011;37:486-92.
42. Espana LP, de Boz J, Morano TF, Arenas-villafranca J, de Troya M. Successful treatment of periungual warts with topical cidofovir. *Dermatol Therapy* 2014;27:337-42.
43. El-Khayat R, Hague J. Use of acitretin in the treatment of resistant viral warts. *J Dermatolog Treat* 2011;22:194-6.