

Cutaneous Warts Treatment Modalities

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Abstract

Warts are common problem in the communities and caused by many types of human papilloma virus. There are many modalities of treatment in which none was shown to be perfect and only few were based on high-level clinical trials. Treatment should be individualized in practice depending on many factors like immunity status, age, number, and sites of the warts, with generally being less costly and with no pain. Treatments can be traditional, destructive, virucidal, antimetabolic and immunomodulatory. Salicylic acid being most widely used due to effectiveness and convenience with little side effects. Remission and recurrence can seem unpredictable for warts treatments.

Keywords: Warts, Treatment, modalities.

1. Introduction

Warts are common viral disease which are ubiquitous in humans and caused by many subtypes of the Human papilloma viruses (HPV). Table one represents the types of cutaneous warts. ⁽¹⁾

Human papilloma viruses are double stranded DNA viruses that can be transmitted through skin to skin or sexual contact. The infection is localized to squamous epithelial cells of the skin and the mucous membranes. ⁽²⁾ Incubation period may range from weeks to years. These warts are highly dependent on immunity of the host, being widely spread in immunocompromised patients like in HIV positive ones. ⁽³⁾

Warts affect 7 -10% of general population, with peak prevalence in 12 to 16 years. 20%

of school-aged children are affected. ⁽¹⁾⁽²⁾

Common warts represents 70% of all warts types. ⁽¹⁾ These warts can be single with no concern to the patient, but can be self-inoculated to other body parts if there is simple scratch where the virus can be implanted forming a new wart. ⁽²⁾

Warts tend to disappear spontaneously (i.e. self-limited), within almost 2 years in almost 70% of immunocompetent hosts, without leaving a scar. ⁽¹⁾⁽³⁾ Warts treatment modalities are also ubiquitous; although they are evidence based and are considered official guidelines, only few have been proved by high quality randomized clinical trials (HRCT).

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The management plan depends on many factors, treatment modality side effects (especially pain), age of the patient, number of the warts, site of the warts, duration since presence, skill of the doctor in the technique used and more importantly, the immunity of the patient.⁽²⁾

Recurrence after treatment is another problem; this is usually due to reactivation of the latent virus. Previously infected patients have more risk of developing warts than those who had never.⁽²⁾

We should concentrate on the fact that treatment should not cause more discomfort than the wart itself.⁽³⁾

Therefore, the ultimate aim of the treatment includes removing all the warts, being

painless, being without scars and giving lifelong immunity.⁽²⁾

Procrastination of treatment is an option if it is not meeting the below criteria. It is desirable to have an effective and painless treatment that shows rapid results in children.⁽³⁾

Warts can be resistant to treatment; Recalcitrant warts that have been present for over 6 months are more resistant to treatment than warts present for less than 6 months.⁽²⁾

Indication for warts treatments are⁽⁴⁾:

1. Patient's desire or fear from spread.
2. Symptomatic or disfiguring warts
3. Large in numbers or size.
4. Immunocompromised patients.

Table 1: Warts types and their causative agent.⁽¹⁾

Disease	Associated HPV Type
Planter warts	1, 2, 4, 63
Myrmecia	60
Common warts	1, 2, 4, 26, 27, 29, 41, 57, 65, 77
Common warts of meat handlers	1, 2, 3, 4, 7, 10, 28
Flat warts	3, 10, 27, 38, 41, 49, 75, 76,
Intermediate warts	10, 26, 28
Epidermodysplasia verruciformis	2, 3, 5, 8, 9, 10, 12, 14, 15, 17, 19, 20, 21, 22, 23, 24, 25, 36, 37, 47, 50

HPV: human papilloma virus

2. Treatment modalities:

2.1. Non-medical treatment:

1. Education: As there is no 100% effective treatment for warts, patients should be properly educated about the natural history of the disease to avoid future conflicts in the patient doctor relationship. In addition, patient is advised to minimize trauma, such as avoid picking or nibbling around the periungual area. The patient is discouraged

from making the wart's area wet, like in swimming pool or frequent dishes washing.⁽³⁾

2. Garlic extracts: It is shown in one study to be effective, as Garlic has anti-proliferative properties. It was associated with complete remission after 3-4 months in one placebo-controlled study.⁽⁵⁾

3. Duct tape: Warts are taped during the day and are left open to air in the night. One study has shown that this treatment modality is more effective than cryotherapy when applied for six days cycles for 2 months (putting the tape for 6 days then change it). The warts will usually disappear within the first month. Warts at other areas may also regress, which may be the effect of immunostimulation that occurred due to occlusion. ⁽²⁾⁽³⁾

4. Paring: used by the patient if the surface was soft after getting out of the bath. ⁽³⁾

2.2. Destructive therapy

This therapy aims to remove or damage the lesion. Some avoid the usage of this method as fear from kobenerization. ⁽²⁾ They are not the same as virucidal therapy.

They can be surgical, chemical or physical.

2.2.1 Surgical therapy

1. Curettage and cautery: Should not be used as standard therapy. Used in case of single wart after freezing. Although they have 65-85% success rate, they have 30% risk of recurrence and scarring.

This method is best avoided in plantar warts to avoid the risk of scarring, but are best used in the filiform warts in the face and the limbs. ⁽¹⁾⁽²⁾

2.2.2 Chemical therapy

1. Silver nitrate: it is available as over the counter drug in the United Kingdom, it is associated with 43% cure rate with additional 26% after one month of application. ⁽²⁾

2. Salicylic acid: A keratolytic agent, it slowly destroys the virus-infected cells. This type of treatment is considered the first line therapy.

It is widely used since it is convenient, cheap, minimally painful and effective. It is

available as over the counter drugs. The disadvantage is that it requires long-term adherence. There is risk of systemic toxicity in children so should be used in limited areas and in lower concentrations.

Patient should be educated that he should sink the wart with warm water for 5 minutes, then rub it with pumice stone then apply the preparation. This is repeated daily. It is used for 3 months. Cure rate is 75%. ⁽¹⁾⁽²⁾⁽⁶⁾

3. Cantharidin: An acantholytic and necrotic to the epidermis. It has cure rates as high as 80%, with no side effects except for blister formation that will resolve alone within 2 weeks. They are effective against common, plantar and periungual warts. Applied for 24 hours, covered by tape and then repeated after 1 to 3 weeks. ⁽²⁾

4. Cryotherapy: includes exposing the area to freezing liquid nitrogen for seconds, it take several sessions. This cause destruction of HPV infected cells by inducing local inflammation, thereby triggering the immunity. It is considered second line therapy if home treatments are failed. It is repeated each 3 weeks until the wart is disappeared. ⁽¹⁾⁽²⁾ It is painful and recommended only for adults. ⁽³⁾

Cryotherapy is available for the treatment of common warts in primary care and dermatology offices. ⁽²⁾

It is no more effective than other modalities of treatment in the conclusion of several studies done, especially when compared to salicylic acid. Although some practitioners claim that is more effective than what is prescribed by these studies. ⁽⁶⁾

Side effects include pain, damage to nerves, tendons, hyperpigmentation or hypopigmentation, annular warts and risk of

recurrence. It should be used cautiously in patients with poor circulation. ⁽²⁾

This type of therapy has the highest quality of clinical evidence (A, I). ⁽⁶⁾

5. Hot water: Immersion in hot water (48-Celsius degree) has been reported to improve plantar and hand warts. Applied for 45 minutes 2 to 3 times weekly. ⁽¹⁾

6. Radiofrequency ablation: It serves moderate effectiveness for warts treatment. ⁽²⁾

7. Infrared coagulation: Directly applying infrared source by contact with the lesion. This method yielded remission of female condyloma acuminata with only about 10.8% recurrence rate. It cures the wart by necrosis. It is cheaper, safer, and easier administered than CO2 laser therapy. ⁽²⁾

8. Laser therapy: Idea of using the laser is that the cells will absorb the laser through the water molecules. This will produce thermal effect that destroys the infected cells. ⁽²⁾ They are expensive treatments reserved for recalcitrant warts. it carries a risk to healthcare workers infection as warts are present in the plume of the laser.

In CO2 laser, treatment may be useful for periungual and subungual warts that are recalcitrant to other treatments. It has also been found that it is useful in immunosuppressed patients. Adverse effects of this treatment in immunocompetent patients include postoperative pain, prolonged healing time, and scarring. ⁽²⁾

It is no more effective than cryosurgery or electrosurgery. ⁽¹⁾

In Erbium:Yttrium/Aluminum/Garnet (Er:YAG) laser: Warts in a variety of locations

have been successfully eliminated in 75% of patients after a single treatment, with a 25% relapse rate within 1 year after. ⁽⁷⁾

In pulsed dye laser, the laser causes microvascular destruction of dilated capillaries of warts, it causes less post-operative pain & scarring compared to CO2 laser. ⁽²⁾

9. Photodynamic therapy: The idea is exposing the warts to photosensitizing substance, and directing a light toward it. It is used in the treatment of mucosal, common, plantar and flat warts.

It is has a high quality clinical evidence (B, I) in describing its effectiveness. ⁽²⁾

10. Electrosurgery: Can also be effective but associated with scarring and pain. EMLA cream (which contains lidocaine) can be used for anesthesia for flat warts. Lidocaine injection is usually required for thicker warts, especially palmar/plantar lesions. ⁽¹⁾

2.3. Virucidal treatment:

1. Glutaraldehyde: Although it causes skin hyperpigmentation, it is as effective as salicylic acid with cure rate of 70%. ⁽²⁾

2. Formaldehyde: damages the upper layer of epidermis & the virion. It has been concluded that it is no more significant than placebo with cure rate of 65%. ⁽²⁾

3. Formic acid: Type of acids extracted initially from red ants. One study concluded that it has a cure rate of 92% compared to 6% in placebo, after applying 85% of formic acid.

4. Cidofovir: Antiviral drug that inhibit DNA synthesis. It is very useful in warts treatment in HIV patients.

2.4. Antimitotic treatments:

1. Bleomycin: a DNA and protein synthesis inhibitor, used mainly in resistant warts that failed other lines of treatment. It can cause significant systemic toxicity and it is not used in immunocompromised patients, pregnant, children and those with vascular diseases. It causes pain, erythema in the injection site. It is dependent on the immune system and could only have an effect in immunocompetent patients. Bleomycin efficacy varies between studies and ranges from 16 to 90% cure rates on variety of different wart types. ⁽²⁾

2. Retinoids: it affects epidermis differentiation, viral transcription and affects local immunity (immunomodulatory), Treatment of warts with a tretinoin cream resulted in 85% clearance in a series of children as compared to 32% spontaneous clearance in placebo controls. ⁽²⁾

It is very suitable for plane facial warts. The patient should not shave here. ⁽³⁾

3. Podophyllin & podophyllotoxin: Mainly used in anogenital warts, which shown to be effective by the effect on the microtubules of the infected cells disrupting their replication, it can be used to treat resistant warts especially when combined with Er:YAG laser. ⁽²⁾⁽⁷⁾

2.5. Immunotherapy:

1. Oral Zinc sulphate: as known in the literature, Zinc is important for immunity, based on this, a placebo-controlled clinical trial was attempted using oral zinc sulphate (10 mg/kg daily) to treat recalcitrant warts. Complete clearance was reported in 87% of the treatment group versus no clearance in the placebo group. ⁽²⁾

2. Intralesional Injection of Interferon: is also effective, as it can stimulate immune system. It is usually reserved for patient with resistant warts. ⁽²⁾

3. 5-Fluorouracil (5-FU): It is an anti-proliferative agent; it is used in adjunction with epinephrine and lidocaine to reduce pain and systemic absorption. It has a cure rate of 70%. ⁽²⁾

4. Cimetidine: An immunomodulatory H2 receptor blocker was shown to inhibit T suppressor cells, thereby enhancing immunity. Although that in all double-blinded placebo controlled studies, it was shown that it has a cure rate of 26% but not significant when compared to placebo. ⁽²⁾

5. Imiquimod: Imiquimod 5% cream is an immunomodulatory that may stimulate cytokines, including interferon- α , interleukin-1, interleukin-6, tumor necrosis factor- α , granulocyte-macrophage colony-stimulating factor, and granulocyte colony-stimulating factor. It is used for sites that are not thickly keratinized. ⁽²⁾

It is used in less thickened warts; in plantar and palmar warts, frequent paring maybe required. ⁽¹⁾

6. Bacillus Calmette-Guérin Therapy: it stimulates local immunity; it is effective against anogenital warts with 30% recurrent rate. ⁽²⁾

7. Vaccines of HPV: are developing rapidly for the treatment of venereal warts. ⁽²⁾

2.5. Therapy combination:

It is used to reduce the risk of recurrence, especially for genital warts, many regimen can be used like combination of salicylates with imiquimod and cryotherapy, or laser with anti-mitotic agents. ⁽²⁾

Conclusion:

Warts are common worldwide problem caused by human papilloma virus. There are many modalities of treatment in which none was shown to be perfect. Treatment should be individualized in practice depending on many factors like immunity status, age, number and sites of the warts, with generally being less costly and with no pain. Treatments can be traditional, destructive, virucidal, antimitotic and immunomodulatory.

Author recommendations:

After adequate education for the patient, and if there was an indication for intervention, the doctor should use:

1. Hot immersion method for plantar & plantar warts, combined with salicylic acid.
2. For single wart, either cautery or duct tape maybe useful.
3. in multiple plane facial warts: Tretinoin cream should be used. The patient should not shave.
4. Resistant cases are dealt with laser\ intralesional agents.
5. For less educated patients who refuse medical\surgical, treatment, garlic treatment method is used.
6. Oral retinoids are used when there are multiple warts, especially in immunocompromised patients.

For all patient, Zinc sulfate prescription is advised.

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