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An Overview of Various Lines in The Treatment of Warts: Review Article

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ABSTRACT

Background: Human papillomavirus (HPV) infection, which can be obtained through direct contact with an infected person or through exposure to the environment, is the most prevalent cause of warts. For example, they can be categorized into common warts, plantar warts, and genital warts based on appearance or location. Common warts have been treated with a variety of invasive and non-invasive methods, both destructive and immunotherapeutic. Cryosurgery, surgical excision, electrocautery, and laser ablation are all examples of destructive therapies. Medical compounds like salicylic acid and trichloroacetic acid are also destructive, as is formaldehyde and 5-flurouracil.

Objective: To make an overview of various lines in the treatment of warts.

Methods: The databases were searched for articles published in English in 4 data bases [PubMed – Google search - Google scholar- science direct] and Boolean operators (and, or, not) had been used such as [Human papillomavirus, treatment of warts, warts] and in peer-reviewed articles between 2009 and 2021.

Conclusion: A wide range of treatments are currently available to help individuals with warts, whether as a single treatment or in combination.

Keywords: Human papillomavirus, Warts, Treatment

INTRODUCTION

HPV is the primary cause of warts, a common skin condition. For both patients and practitioners, plantar warts are a source of irritation because no one treatment works for everyone. More than two years of treatment has failed to get rid of recalcitrant warts, thus they're referred to as "recalcitrant." Treating recalcitrant patients with immunotherapy and preventing its recurrence have been good outcomes [(1)].

HPV is thought to be present in the bodies of 40% of the world's population. Plantar warts affect 14% of the general population each year. When it comes to plantar warts, young people are more likely to have them due to a variety of factors, the most common of which are immunodeficiency or overuse of public showers and/or public restrooms [(2)].

The aim of the review article was to make an overview of various lines in the treatment of warts.

Methods:

A search strategy has been performed to determine the related literature. overview of various lines in the treatment of warts. Relevant keywords included: treatment of warts, and warts more synonymous key words had been used.

These databases were searched for articles published in English in 4 data bases [PubMed – Google search - Google scholar- science direct] and Boolean operators (AND, OR, NOT) had been used such as [Human papillomavirus, treatment of warts, warts] and in peer-reviewed articles between January 2009 and October 2021; a 13-year date range was selected, and no language limitations, and filtered in selected data basis for the last 13 years, however, the range of time interval for researches is wide as there's scarcity of data on the particular reviewed, accurate and depth in the retrieved literature.

Documents in a language apart from English have been excluded as sources for interpretation was not found. Papers apart from main scientific studies had been excluded: documents unavailable as total written text, conversation, conference abstract papers and dissertations.

Evidence:

Treatment of warts:

At least 30 percent recurrence after therapy appears to be successful is the most disturbing aspect of wart management, presumably due to resurgence of virus from surrounding tissue reservoir. Both destructive and immunological operations have a success rate between 65 and 85 percent, although no single treatment is 100% effective in all patients [(1)].

There are efficient Local destructive techniques for the treatment of warts, including cryotherapy, electrocautery, and laser. However, scarring, dyspigmentation, or recurrence make these therapies impractical for patients with many lesions. Host immune status, age, HPV serotype, and site of infection all have a role in resolving the infection. In immunocompetent individuals, a wart or verruca can disappear within two years of the onset of symptoms [(2)].

For the most part, warts can be treated with either a typical aggressive way, such as chemical cautery or cryotherapy or electro-cauterization or

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surgical removal; or an immunotherapeutic method, which is based on activating the immune system [3].

It is the wart itself that is targeted by destructive means rather than the HPV. Both physical and chemical approaches can be used to destroy tissue. A bigger incision, scarring, and dyspigmentation are common side effects of destructive treatments because they kill infected and non-infected keratinocytes in the same place [4].

A) Destructive methods:

- **Chemical procedures:**

1) Salicylic acid:

In the treatment of viral warts, salicylic acid (SA) formulations are the most commonly used preparations Exfoliation is promoted by SA, although at high quantities it can cause irritation to the skin. Before applying salicylic acid and occlusive tape, paring is performed. In collodion or polyacrylic bases, SA concentrations range from 10% to 26% in commercial formulations. Lactic acid is frequently added. Many patients find it to be an excellent first-line treatment due to its low cost and lack of discomfort [5].

2) Trichloroacetic acid and monochloroacetic acids:

The epidermis and upper papillary dermis are destroyed by trichloroacetic acid, a caustic that coagulates skin proteins throughout the skin layers. The skin and dermis then rejuvenate, with fresh collagen synthesis and restoration of elastic tissue.Trichloroacetic acid is applied topically and must be allowed to dry until a white frosting develops. Adverse effects include burning sensation during application, dryness, fissuring, and contact sensitivity [2].

3) Cantharidin:

Cantharidin is a blistering chemical that causes acantholysis and intra-epidermal skin blistering after 24–48 hours of exposure. Desmosomal attachment breakdown and exfoliation of virus-containing tissue are the mechanisms of action. Plantar warts can be effectively treated by podophyllotoxin, salicylic acid, as well as cantharidin [6].

4) Phenol:

Caustic phenol (carbolic acid) penetrates deeply into the tissue, producing a white crust on top of it. Reconstitution of HPV gene suppression transcription complexes can be facilitated by polyphenols, powerful antioxidants. Burning, discomfort, erythema, depigmentation, scarring, and infection are all possible side effects [7].

5) Glycolic acid:

Peeling agents such as glycolic acid, α-hydroxy acid, are used in cosmetics. In 20 patients aged 7–16 years with persistent face flat warts, an open research using SA 2 percent coupled with glycolic acid 15 percent indicated an 8-week cure rate of 100 percent [8].

6) Pyruvic acid:

To get rid of the outer layers of the skin, pyruvic acid is an excellent keratolytic agent. It's 70% ethanol, 70% of which is used. When used with salicylic acid, extreme caution must be exercised to prevent the eroding of healthy skin [2].

7) Formic acid:

Because of its dehydrating properties, formic acid has been linked to the deterioration of tissue. The most common side effects include moderate irritability. Extensive chemical damage can be caused by extended exposure or application under occlusion [9].

8) Retinoids:

Desquamation and peeling of the skin are caused by retinoids, vitamin A derivatives that govern epidermal proliferation and differentiation. As powerful immunomodulators, retinoids can also be used to treat skin conditions. Acitretin or isotretinoin are used both systemically (0.5 to 1 mg/kg/d for a maximum of 3 months) and topically (tretinoin or tazarotene at a dosage of 0.05 percent administered once daily) for the treatment of plane warts, as well as for the treatment of other skin lesions. Dryness of the skin and mucosa, cheilitis, and temporary increases in serum amino transferase and triglyceride levels are the most prevalent side effects of treatment with systemic retinoids [10].

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- **Physical methods:**

1) Cryotherapy:

One of the most frequent methods in medical practise is cryotherapy, which uses liquid nitrogen to treat patients. In randomised trials, the reported cure rate for warts at all sites is highly variable, with an average of 49% [11].

Warts are specifically targeted by this treatment. Preparation prior to cryotherapy for plantar warts is more effective. It takes 5–30 seconds to freeze the wart with liquid nitrogen until a halo of frozen tissue forms around it. A maximum of six treatments can be given every two to three weeks. Bleeding, scarring, discomfort, burning, and erythema were among the most common side effects recorded [12].

As a "in vivo dendritic cell vaccination," cryotherapy can load dendritic cells, causing a "abscopal effect" and an immunological response throughout the body [12].

2) Surgical excision:

Because of the possibility of scarring, surgical excision is not the best option. Cures under local anaesthetic may be effective in those who have a

single plantar wart that causes both physical and psychological suffering [9].

3) Lasers:

Recalcitrant warts can be treated with laser therapy, according to some experts. However, because to the expensive expense, this technique can only be utilised as a last resort. CO2 laser, pulsed dye laser (PDL), and Er: YAG lasers are all used to treat warts. By coagulating blood arteries and creating ischemia within the lesion, the dye laser causes more precise damage, making it a better option for wart removal [13].

Bloodless removal of vascular lesions can be achieved by using a laser to evaporate and coagulate them. Warts are reduced in size and the lesional skin is prepared for the use of topical medicines such as imiquimod, 5-FU creams, or cidofovir cream [14].

4) Photodynamic therapy (PDT):

PDT works by inducing an inflammatory response and then destroying tissue as a result of the resulting oxidative stress. Warts should be covered with an occlusive polyurethane dressing for four hours after using 5-aminolevulinic acid 20% cream. An irradiation time of 20 minutes using a light source that emits between 590 and 700 nanometers of light per square centimetre is then applied to the wart. The most common side effects include erythema, a burning feeling, and pain [15].

B) Antimitotic agents:

Wart growth is inhibited by antimitotic drugs, which stop the proliferation of infected keratinocytes.

1) 5-fluorouracil (5-FU):

When administered topically, 5-fluorouracil inhibits viral DNA and RNA production while also reducing epidermal proliferation. Every two weeks, it can be injected into the lesion with local anaesthetic and used topically [16].

It can be used to treat warts that are resistant to other treatments (30-95 percent). Onycholysis and blistering in periungual lesions are the most prevalent side effects of 5-fluorouracil, whether used topically or intralesionally [16].

2) Bleomycin:

Streptomyces verticillus produces a group of similar glycopeptide antibiotics known as bleomycin. It is cytotoxic because it inhibits DNA by producing free radicals. anti-tumor, antiviral, and antibacterial properties [17]. 0.1 percent Bleomycin for three injections with a 96.10 percent cure rate demonstrated highly effective and safe in the treatment of palmoplantar and periungual warts. Bleomycin has been approved by the FDA. Bleomycin's most common side effects include pain at the injection site, scarring, and pigmentation changes [18].

3) Podophyllin and Podophyllotoxin:

At a dosage of 10% to 25% in alcohol or benzoin, podophyllin is an antimitotic drug that causes tissue necrosis. After a few hours of application, it is reapplied every week for up to six weeks. Neurotoxicity and myelotoxicity make it contraindicated in paediatric patients [4].

C) Antiviral agents:

DNA polymerase is competitively inhibited by the nucleoside analogue Cidofovir. A direct antiviral impact can be achieved by using this product. It is integrated into the viral DNA during endocytosis, inhibiting replication. Warts can be effectively treated with a topical solution of cidofovir 1 percent [11].

DISCUSSION

Both warts contagiosum are likely to resolve spontaneously, but as clearance can take months or years, treatment is usually sought for cosmetic reasons, pain or, particularly for warts, interference with function. Warts contagiosum lesions are often asymptomatic, but can become inflamed and pustular and lesions may number over a hundred [5].

Current knowledge of the numerous remedies for warts is not based on much strong evidence, even though many treatments are in regular use. Where treatment trials have been placebo controlled, a 20–30% response rate is expected for placebo treatment.

The treatment of cutaneous warts can incur significant costs due to the high prevalence of the disease and the use of more than one or repeated treatments before achieving satisfactory clearance [8].

There is some evidence that geographical variations may occur in predominant wart virus strains. and it is possible that there are differences in response to treatment between different strains of human papillomavirus (HPV) [11].

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 [15].

Kwok et al. [19] highlighted the neutral comparison between cryotherapy and salicylic acid. 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.

CONCLUSION

A wide range of treatments are currently available to help individuals with warts, whether as a single treatment or in combination. A wide range of treatments are currently available to help individuals with warts, whether as a single treatment or in combination.

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