How to Cite:
Sharif, M. M., Nasreen, S., Farooq, N., Izhar, M., Malik, T., & Dhedhi, N. A. (2023). Effectiveness of topical application of 15% salicyclic acid and 0.1% diphencyprone combined in an ointment form for treatment of plantar warts. *International Journal of Health Sciences*, *7*(S1), 1438–1446. https://doi.org/10.53730/ijhs.v7nS1.14366

Effectiveness of topical application of 15% salicyclic acid and 0.1% diphencyprone combined in an ointment form for treatment of plantar warts

Mariam Muhammad Sharif
Consultant Dermatologist, Memon Medical Institute Hospital, Karachi Pakistan

Saba Nasreen
Assistant Professor, Baqai Medical University, Karachi Pakistan
Corresponding author email: simsfcps@gmail.com

Nadia Farooq
Assistant Professor Dermatology, Baqai Medical University, Karachi Pakistan

Madiha Izhar
Assistant Professor Dermatology, Fazaiya Ruth Pfau Medical College/ PAF Hospital Masroor, Karachi Pakistan

Tooba Malik
Classified Dermatologist, PNS Rahat Hospital Karachi, Assistant Professor of Dermatology BUM&DC, Karachi Pakistan

Naseem Amin Dhedhi
Consultant Family Medicine, Razi Alkhidmat Hospital, CBR Town, Islamabad Pakistan

Abstract---Objective: To determine the Effectiveness of topical application of 15% salicyclic acid and 0.1% Diphencyprone combined in an ointment form for treatment of plantar warts. Place and Duration: This Descriptive, case series was held in Dermatology outpatient department, Abbasi Shaheed Hospital Karachi. Method: A sample size of 80 patients with plantar warts were included as calculated by exact 95% confidence interval. Results: Total 80 patients of plantar warts were enrolled. 40 (50%) were females and 40 (50%) were males, with mean age of 31 yrs. 65 patients (81.25%) showed positive response to treatment with combined DPCP and salicyclic acid, while remaining 15 (18.75%) had some mild adverse reactions. Conclusion: As Plantar wart is a common problem in all populations

therefore more randomized trials should be done on combined chemical treatments for better outcomes.

Keywords---human papillomavirus (HPV), diphencyprone (DPCP).

Introduction

Warts are common in the world's population. Its prevalence is unknown, but it is estimated that 7-12% of the population is affected by warts[1-2]. The prevalence in school-aged children is 10-20%. These are the mucous membranes and skin benign growths occurred due to the human papilloma virus (HPV). A plantar wart also called Verruca plantaris is a wart that occurs on the toes or soles of the feet[3]. It is generally self-limiting, but management is usually suggested to relieve symptoms (like pain), reduce transmission and shorten the duration of the disease[4-5]. There are many methods of treating warts. Treatment can be divided into medical and ablative. Ablative methods include the destruction and surgical excision by laser, liquid nitrogen and electrodexification while medical treatment involves the use of keratolytic agents such as salicylic acid, immunomodulators, and chemotherapeutics useful for treatment, such as topical retinoid or 5-FU[6-7].

Local immunotherapy included the controlled initiation of an allergic contact reaction in the wart itself, can be performed with potent haptens such as dinitrochlorobenzene (DNCB), dibutyl square acid ester (SADBE) or diphencyprone (DPC)[8-9]. Topical immunotherapy is the influential treatments for warts with minimum scarring. These agents often cause non-therapeutic allergic contact reactions, therefore patient compliance and physician attention and expertise are required for good results with minimal side effects[10]. A 2016 study evaluated the effects of various topical treatments for non-genital skin warts in healthy individuals, finding a general lack of evidence for the effectiveness of some treatments in others. Another study was also performed on patients with palmoplantar warts treated with a patient-applied ointment consisting of a combination of 15% salicylic acid and 0.1% difencyprone (DPCP) in white soft paraffin, with a 92% success rate for removal of the wart[11]. Two studies in which a dermatologist used PDCP at regular intervals showed response rates (87.7% and 88%) similar to the previous study[12].

The purpose of our study is to reassess the effectiveness of this combination in treating plantar warts in patients admitted to a tertiary hospital, as electrical cauterization and cryotherapy are not available in our local hospital or in the private sector. snowy. and if it proves to be similar in effectiveness in international trials, it will be used in more patients.

Methods

This Descriptive, case series was conducted in Dermatology outpatient department, Abbasi Shaheed Hospital Karachi for 6 months duration from January 2021 to June 2021. A sample size of 80 patients with plantar warts were included as calculated by exact 95% confidence interval.

Inclusion criteria

- Age over 20 years.
- Either gender.
- Clinically two or more plantar warts which will be small lesion as pencil eraser or larger > 2inches, that appears on the foot sole and resembles typically a cauliflower, with tiny black petechiae (tiny hemorrhages beneath the skin) in the center and is painful on applying direct pressure.
- Duration > 2 days.

Exclusion criteria

Following group of patients were excluded from this study:

- Age < 20 yrs
- Pregnant patient.
- Patients previously sensitized to DCP
- Patients with active eczema.
- Immunocompromised patients.
- Those who have not given written consent for inclusion in the study.

Patients were selected conferring to the exclusion and inclusion criteria, the risks and benefits of the study were explained to them, and a detailed Performa (attached at the end of the abstract) was completed after consenting to participate in the study. Patient's name, age, gender and telephone number were recorded by the investigator. The DPCP (diphenylcyprone) and salicylic acid used in our formulation were obtained from commercial suppliers who were instructed to prepare 10g of 15% salicylic acid and 0.1% DPCP in white soft paraffin. Patients (or their assistants) were educated to apply a small amount of the mixture to the wart surface daily at night, then covering the area with paper tape, remove the tape next morning, and wash the area. Patients or their assistants were warned about the side effects of PDCP. The patients were given a questionnaire and told to complete it until the warts were removed. Patients were followed for the first, second and sixth weeks and then for 4 months until the treated wart was successfully removed. Patients' pain was assessed using a visual analog scale (provided in the performance), and a size reduction > 2 mm from baseline was considered effective. Patients who miss their follow-up visit and/or do not return the questionnaire will be contacted by phone to maximize the follow-up population.

Data analysis was done with SPSS version 20. Statistical analysis was expressed as frequency and percentage. Effect modifiers such as gender, age group and clearance time were controlled by stratification and chi-square test. A p value less than 0.05 will be considered significant. Frequency and percentage will be calculated based on gender and activity while the mean and standard deviation will be calculated based on the age and duration of the warts before treatment.

Results

A total of 80 patients were selected in this analysis. Out of all patients 40 were male and 40 were females with M:F ratio being equal. (table 1).

Table 1
Demographic variables

Variables	Mean± SD (n = 80)
Gender Male: female	1.5 ± 0.503 (n=1:1)
Age mean ± SD	31±.7.48
Duration of illness	< 2 months

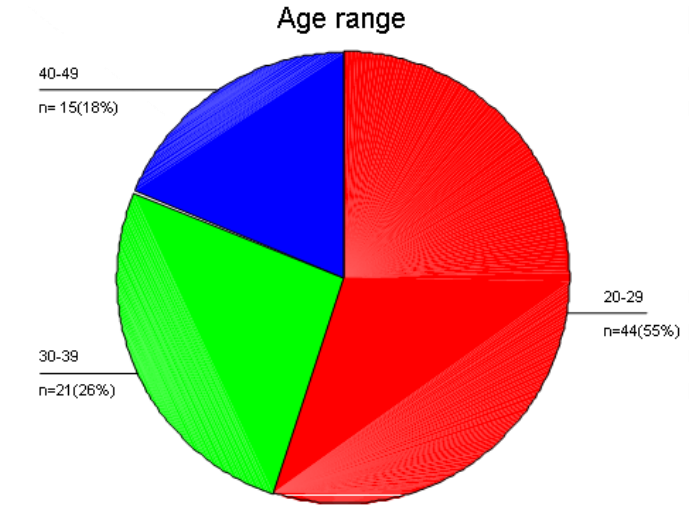

Figure 1. Age distribution

Of 80 patients 44 (55%) were in 20-29years age group while 21 (26%) were in 30-39yrs and 15 (18%) patients belong to 40-49 yrs (fig. 6). Mean age of total patients was 31 years ± 7.48 years. The duration of warts prior to therapy was mostly <2 months nearly in 80% of the patients while the remaining 20% had duration of > 2 months. The duration of wart clearance was within 8 weeks in 60 of the cases (75%), and the rest 18 (22.5%) had within 8-12 weeks and only 2 (2.5%) had duration of clearance of wart of 12-16 weeks. Of 80 patients 56 (70%) of the patients presented with painful warts while the rest 15 (18.75%) with discomfort due to warts and remaining 9 (11.2%) due to disfiguring complain on feet due to warts.

Table 2
Effectiveness of DPCP and salicyclic acid

Variables	Percentage (n =80)
Efficacy positive response	65 (81.25%)
Not effective	15(18.75%)

The reduction in size of wart was < 2mm in almost nearly all the patients and Out of 80, 65 (81.25%) reported to have the complete removal of the wart while 15 (18.75%) developed mild reactions with local redness in 7 (8.75%), pruritus in 8 (10%). The patients developing mild reactions were given symptomatic treatment from anti-allergic and anti-inflammatory drugs, but no response was noted in them. The number of males who responded to treatment were 35 (%) and remaining were females i-e; 30 (%) who responded to treatment. The age distribution of responders was greatest among 20-29yrs i-e; 41 while the rest is shown in table 3. Patient had an average of four follow ups over a six-month period.

Table 3
Distribution of effectiveness according to age and gender

Variables	Number of patients with response positive (n = 65)	P value
Sex distribution • Male • Female	Wart clearance n= 35 n= 30	0.334
Age distribution • 20-29yrs • 30-39 yrs • 40-49 yrs	 41 15 9	 0.007

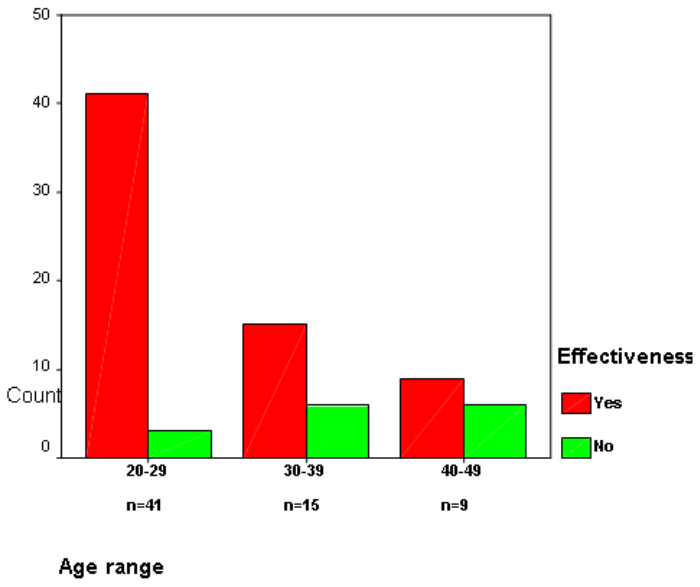

Fig 2. Effectiveness

Discussion

Plantar warts are benign skin growths caused by HPV types 1, 2, 4, or 63, affecting approximately 7-10% of the US population, with a peak incidence between 2 and 12 months of age, at age 16. While the global coverage varies from country to country, ranging from 3.4% to 4.5% in the UK and up to 22% for 16-18-year-old in Australia[13]. Around two million people in Wales and England visit their GP for skin warts treatment every year, costing at least £40 million a year[14].

While most plantar warts will go away on their own without treatment, many patients seek treatment for a number of reasons, such as inability to play sports and other daily activities, pain. About 25% of warts disappear spontaneously within two months, 32% within three months, and 67-76% within 2 years. Formerly infected patients are at greater risk of developing new warts than those who have never they had not been infected[15-16]. Current treatment is aimed at eliminating the signs and symptoms of HPV infection, as there is no cure and treatment does not affect the infection[17]. While some warts may regress on their own, they can be a source of physical discomfort and infectious disease. Therefore, many patients seek medical help[18].

There are many ways to treat warts, ranging from the least painful, cheapest and time consuming to the most invasive and expensive treatments for resistant common warts. Salicylic acid is considered a first-line therapy with a cure rate of 70-80%[19]. Some other over-the-counter topical medications are also effective, for example dibutyloxquanic acid, also called as diphencyclopropenone (DCP) and square acid dibutyl ester (SADBE) are contact sensitizers, trichloroacetic acid is a corrosive compound that results in necrosis of the tissue, aminolevulinic acid (ALA) treats flat warts[20]. It is a photosensitizer that is used topically in blue light combination for photodynamic therapy and systemic agents such as cimetidine, retinoids, in addition to topical immunotherapy with antigens such as mumps, candida and USP trichophytin[21]. Other alternative treatments that have been shown to be effective in treating warts include adhesive therapy, hypnosis, hyperthermia, garlic, and vaccines. Other alternative treatments have been promoted as an effective method of treatment but little or no clinical evidence on their effectiveness is present, they include duct tape occlusion therapy, podophyllin application and apple cider vinegar application[22]. While the surgical therapy is reserved for refractory warts like cryosurgery, pulse dye laser and electro-desiccation and curettage.

Despite all these treatments, optimal treatment is lacking because of deficiency of high quality RCTs. Cochrane skin group assessed different treatment groups and found that treatment for cutaneous warts are mostly weak because of poor reporting and methodology[23]. The treatment decision should be based on the daily case basis according to physician experience, patient preference, and evidence-based medicine. The two most common used strategies are over the counter prescribed salicyclic acid and physician prescribed cryotherapy.[24] The Cochrane review rated salicyclic acid to be safe and effective with high cure rates and few adverse effects from six randomized controlled trials and found to have 75% cure rate compared to 48% placebo. Various preparation s of salicyclic acid are available, over the counter preparations include less than 17% strengths however

physician prescribed can contain up to 70%[25]. Cryotherapy was also used widely as a primary care treatment in cutaneous warts in many studies, and Cochrane review found it no more superior to salicyclic acid. The highest cure rates of cryotherapy are achieved when applied for two to three weeks. Studies comparing two treatments found them equally effective with no difference in effectiveness of the two. However, studies on combined treatment of cryotherapy and 70% salicylic acid were very effective and showed 89% eradication rate in 86.2% of patients[26].

Diphencyclopropenone (DPCP) is a contact immunotherapy agent usually used in resistant verrucae. In 2002 cure rate of 87.7% was reported on resistant palmoplantar warts. Buckley et al. used 2% DPC for plantar warts and 0.1% for digital warts and achieved clearance of all lesions in 86% of cases after an average of five treatments with a resolution time of 5 months[27]. However, Armor 0.1% diphencyprone and 15% salicylic acid in white soft paraffin has shown wart removal times of four weeks to four months. Our study was consistent with its warts clearance time but response was variable with slightly more than half of the patients showed complete removal of wart after the application of combined DPCP and salicyclic acid[28]. The wart clearance was higher among males than females and most commonly among age group younger and middle aged. Study conducted in 2016, found higher response rate and absence of scarring and few local side effects after treatment with DPCP in treatment of recalcitrant warts and majority tolerated treatment. Armour in 2006 also reported good response to treatment with combined DPCP and salicyclic acid. Our study was consistent with above findings with only few side effects reported after combined application of both DPCP and salicyclic acid.

Conclusion

The problem of plantar warts is a very common problem and more randomized trials should be done on chemical treatments for better outcomes.

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