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A Study On The Efficacy Of Immunotherapy By Using Tuberculin Protein In The Treatment Of Viral Wart

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ABSTRACT

Wart is a common dermatological problem, caused by a Human papilloma virus (HPV). There are various treatment modalities available for the treatment of wart. They are various destructive therapies, viricidal therapies, antimitotic therapies and folk and traditional therapies are available. Recently, immunotherapy is widely used for the treatment of wart, Purified protein derivative of tuberculin (PPD) and mycobacterium w (Mw) vaccine can be useful for the treatment of verruca due to its ability to trigger the cell mediated immunity (CMI), especially in countries like India where the majority of population is sensitized to tuberculin due to high prevalence of the disease and mandatory BCG vaccination. PPD is commonly used in Mantoux test, has been recognised as a promising therapeutic method for the treatment of recalcitrant and recurrent warts. Patients who failed to achieve cure even after 5 or more cycles of first- and second-line therapies of wart over a period of 6 months were selected. For each patient, minimum 2 large warts were selected and was injected with 0.1 ml of 10 IU PPD intra lesionally. A total of 6 sessions at 2-week intervals were given and all patients followed up for 3 months. The study period was from August 2022 to August 2023. All the 50 patients completed the study.93% of the patients showed complete clearance in the injected wart and 73% showed complete clearance in injected as well as distant warts. Immune therapy is a safe and cost - effective method for the treatment of recalcitrant and recurrent warts.

Keywords; immune therapy, warts, tuberculin protein, PPD

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INTRODUCTION

Wart is a common dermatological condition caused by Human papilloma virus (HPV) which belongs to a DNA virus of papova virus family. Cutaneous warts are more common in teenagers and adults. The incidence is 2% - 20% in school children and 10% in adults and the incidence decreases with advancing age. Warts are more common in immunocompromised individuals, in these patients' warts are usually resistant to conventional therapies and there is an increased potential of developing malignancy. Current available treatment modalities of warts are destructive therapies like curettage, electrical and chemical cautery, cryotherapy and various antimitotic agents (bleomycin, retinoids, podophyllin, 5-fluorouracil) are also useful for the treatment of warts [1]. Oral zinc, cimetidine, contact sensitizers dinitrochlorobenzene (DNCB), diphenylcyclopropenone (DCP) intralesional interferon, various vaccines like MMR, BCG and purified protein derivative of tubercule bacilli or dermatophyte fungi are the immunotherapeutic agents used in the treatment of warts [2]. The ideal treatment method should be cost effective, remove the lesion quickly, without pain, scar and recurrence. Few methods fulfil most of the criteria and none can achieve all. Ablative methods like cryotherapy, electrocauterization have recurrence rate of 30% due to lack of immune response produced. Contact sensitizers can produce adverse effects like allergic contact dermatitis, urticarial reaction and pigmentary disturbance.

Immunotherapeutic agents act by stimulating the immune system and so have lower recurrence. Immunotherapy has the advantage of not only cure the injected lesion, but also achieve the clearance of distant untreated lesions [3]. Usage of autologous vaccine is limited due to its oncogenic potential. Intralesional injection of purified protein derivative (PPD) from non-tuberculous mycobacteria stimulate the delayed hypersensitivity reaction not only to mycobacterial protein and also against the virus, leading to regression of the wart [4]. According to the WHO statistics, in 2015, 40% of Indian population are infected with TB. So, cell mediated immunity against PPD of tuberculous bacilli develop swiftly, which validates its use as an ideal immunotherapeutic agent against warts.

METHODOLOGY

50 patients with multiple warts (> 5 NUMBERS) had been included in this study based on the inclusion and exclusion criteria. It is a randomised, uncontrolled, non-comparative and single blinded study with a period of 1 year. (August 22 to August 23).

Inclusion Criteria

- Patient having multiple cutaneous warts (>5) at various sites of the body
- No history of any other method of treatment within the last 1 month

Exclusion Criteria

- Children < 12 years
- Pregnant and lactating mothers
- Immunocompromised patients
- Patients with acute febrile illness, chronic liver and renal failure
- Patients who are hypersensitivity to BCG
- Patients who are Mantoux negative (< 5mm induration).

Written informed consent had been obtained and patient name, age, sex, occupation, duration of the lesions, any drug intake and previous history of treatment for wart was recorded. Selected patients had been thoroughly examined for the type, site, number of warts. Pretreatment Mantoux injection 2 TU (tuberculin unit) PPD had been given in the forearm to identify prior sensitivity for PPD. In a patient with multiple wart maximum five warty lesions had been treated. 0.1ml of 10 TU PPD was given intralesionally in the larger warts or mother wart. Intralesional PPD injection had been given at 2-week intervals for a maximum of 6 sessions. On each follow up patients had been examined for partial or complete regression of the wart, any new lesions and any adverse effect observed was recorded. Photographic documentation was done before the procedure and at each session. If all the warts including the distant warts are completely cured before 6 sessions of injections, then the treatment had been stopped. On the other hand, if only the injected warts were cured before 6 sessions of injections, the

procedure had been continued on the injected cured wart site to observe the distant wart clearance rate. Results was assessed at the end of 3 months as:

- Complete clearance – Clearance of all the lesions.
- Partial clearance – Clearance of more than 50% of the lesions
- No clearance – Clearance of less than 50% of the lesions.

The patients had been followed up for 3 months after treatment to look for any recurrence

RESULTS

• All the 50 patients completed the study.
• Male – 30 ; Female – 20 (Ratio 3:2)
• Average age of patients – 35. 3 years (range 18- 55 years).
• Average duration of warts – 2.2 years (1 -5years).
• Mantoux reactivity in the patients strong : > 15 mm → 8 weak : 6 – 15 mm → 7.

Types of Wart	Total number of patients	Complete clearance	Partial clearance	No clearance
Verruca vulgaris	31	28	1	1
Verruca plana	4	3	1	0
Palmar wart	9	9	0	0
Plantar wart	6	6	0	0
Total	50	46 (92 %)	2 (4%)	1 (2%)

Table 1: Table showing clearance rate in various type of warts.

Time of clearance	No. of patients showing complete clearance in injected warts	No. of patients showing complete clearance in injected and distant warts
End of 2nd week	0	0
End of 4th week	0	0
End of 6th week	12 (24%)	10(20%)
End of 8th week	15(30%)	9(18%)
End of 10th week	18(36%)	14(28%)
End of 12th week	3(6%)	3(6%)
Total no. of patients	48 /50 (96%)	30/50 (72%)

Table 2: Table showing number of sessions and response rate

Of all the 50 patients taken for the study, 92 % of the patients achieved complete clearance whereas 4 % had partial clearance. 96% patients showed complete clearance of the lesion injected with PPD and 72 % patients showed clearance in both injected as well as distant lesions. 90.3% of verruca vulgaris lesions resolved completely and only 1 patient showed no response. Palmoplantar warts showed 100% clearance. 38% of our study patients had taken any type of destructive treatment for wart prior to three months of our study. Warty lesions did not respond or recurrence occur within 3 months in these patients.

High pre-treatment mantoux reactive(>5mm induration) patients achieved earlier cure compared to negative(,5mm induration) pretreatment mantoux reactive patients.

Immunotherapy with PPD was well tolerated by all the patients.

- 95% patients had mild pain and edema of injected site after 2 days of injection which resolved spontaneously within 3 days for three days.
- 5% patients developed severe pain, erythema and edema , which was treated with oral analgesics and topical emollients.

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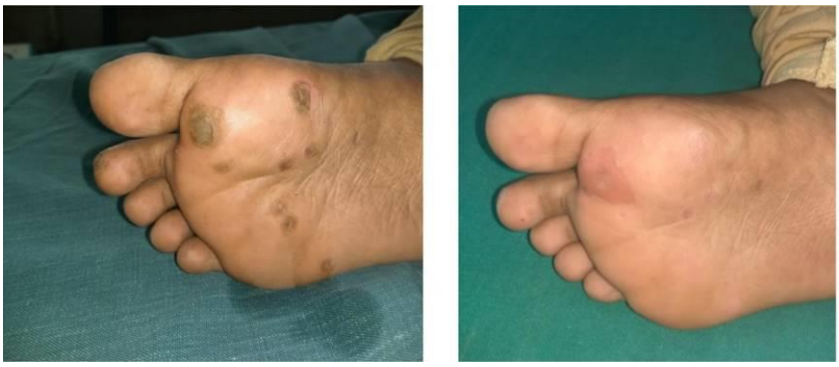
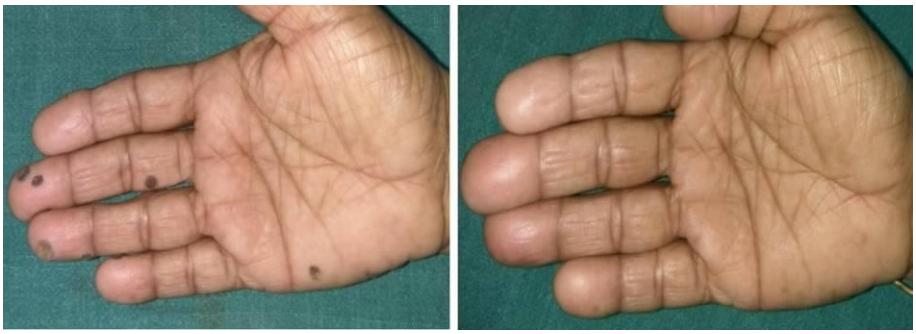
Eczema at injection site was developed in two patients and was treated with emollient and mid potent topical steroid. 5 patients developed hypopigmentation at injected site which resolved spontaneously in 2 months. Ulceration and scarring was not observed in any of the treated patients.

Before Treatment After Treatment (end of 4th session)



Complete clearance of plantar wart.

Before Treatment After Treatment (end of 5th session)



Complete Clearance of Palmar Wart

Before Treatment After Treatment (after 5th session)

Complete clearance of verruca vulgaris of scalp with eczematous changes

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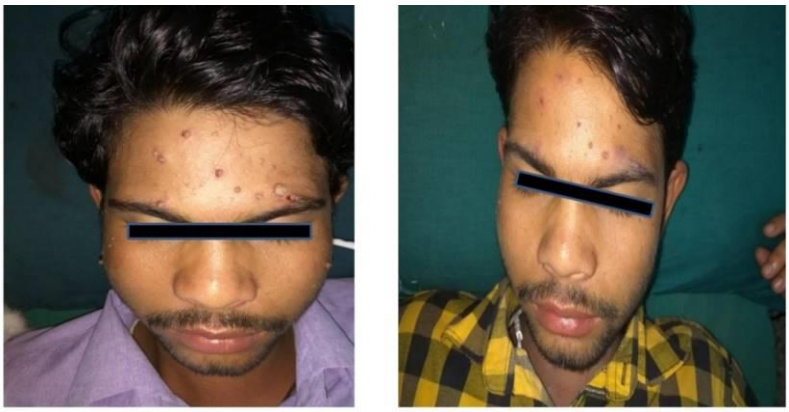
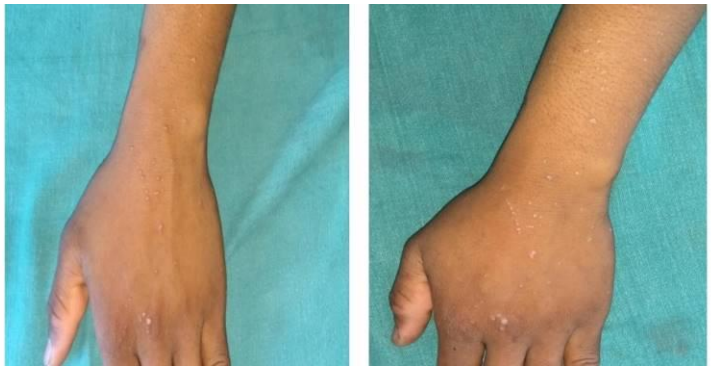
Before Treatment End of Treatment



Partial Clearance of Facial Warts

Before Treatment After Treatment (at the end of 3rd week)



Complete Clearance of Verruca Plana with Post inflammatory hypopigmentation

DISCUSSION

Immunotherapy activate the delayed T cell mediated immunity of the patient against HPV. So both treated and untreated lesions were resolved with immunotherapy, in contrast to traditional destructive methods. The PPD injected in the wart tissue leads to the release of pro inflammatory cytokines. This attract the antigen presenting cells which recognises both the PPD and the HPV antigen and immunity against this is produced. This leads to the inflammation and regression of warts. .It employs the ability of immune system to recognise certain viral and fungal antigens [5]. In a study conducted by Wananukul et al complete clearance of injected warts was found to be 93% which is similar to our study and clearance rate of distant warts was found to be 87% [6]. In another study conducted by Saoji et al , a complete clearance of injected warts was found to be 76 % [4] . In Nimbalkar et al study, a result of 80% clearance of injected warts was seen [7, 8].

CONCLUSION

Intralesional PPD is safe, cost effective and well tolerable method for treating recalcitrant and recurrent wart.

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