Efficacy of intralesional Purified Protein Derivative (PPD) in the treatment of multiple warts.

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ABSTRACT
Cutaneous warts are a common dermatological condition caused by the human papillomavirus (HPV) strains 1, 2, 4 and rarely 57. Although it is a benign condition, it causes disfigurement, pain, discomfort, has a tendency to koebnerize, and can be transmitted to others. This makes adequate and timely treatment important. There are several conventional treatments available which include electrosurgery, cryotherapy and topical medications like imiquimod which show variable responses. Our study evaluated the effectiveness and associated side effects of intralesional PPD for the treatment of multiple warts in a group of 20 patients. This is done as a form of immunotherapy. It was administered at a dosage of 0.1ml into each lesional site every two weeks until the clearance of lesions or up to a maximum of 6 injections. We observed a marked response in 5%, moderate response in 75% and no response in 20% of our study population with no complications. On comparison to previous similar studies, the accuracy of our observed results for efficacy and observed side effects was reinforced. Hence proves to be a modality of treatment that should be more widely used for the treatment of warts as it is cheap, safe, less stressful and comparatively more effective.

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INTRODUCTION
Verrucae are one of the most common cutaneous viral infections caused by human papillomavirus (types 1, 2, 4, 7 and 57) (Ljubojevic and Skerlev, 2014). They are benign tumours which commonly involve the skin and epithelial tissues (Drake et al., 1995). Treatment of warts is painful though many modalities are available; which include keratolytic (salicylic acid 10 to 26% with lactic acid) (Sterling et al., 2014), cantharidin (Bunney et al., 1976; Miller and Brodell, 1996); electrosurgery (Kuykendall-Ivy and Johnson, 2003) and cryotherapy (Burge et al., 1996), and the cons are amplified with multiple and recalcitrant warts. The ideal aim of treatment is removing the wart without recurrence, to avoid mutilating procedures and to help the body’s immune system to deal with the infection better, producing lifelong immunity against the viral infection (Sterling et al., 2001). Immunotherapy is defined as a type of biological therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. In our study, we were looking to induce or enhance immunity against the virus. With this as the background, we surveyed to determine the efficacy of intralesional PPD for the treatment of cutaneous warts. PPD or tuberculin stimulates the cell-mediated immunity nonspecifically by activating Th1 cells, NK cells, and cytokine production; production of IL-12 as a process boosts the cell-
mediated immunity and contributes to the mechanism of action (Saoji et al., 2016). It was injected intralesionally at a dose of 0.1ml into each lesional site at two-week intervals until complete clearance of lesions or for a maximum of six sittings.

Figure 1: Showing single skin colored verrucous papule present over the right thumb before Inj.PPD.

Figure 2: Showing marked response following completion of treatment.

Figure 3: Showing single hyperpigmented verrucous plaque on the palm of left hand before Inj.PPD.

Figure 4: Showing moderate response following completion of treatment.

Figure 5: Showing multiple verrucous plaques around periungual region of left thumb before Inj.PPD.

MATERIALS AND METHODS

Trial design
Randomised open study on the efficacy of intralesional PPD in the treatment of multiple warts with the approval of the ethical committee.

Study population
Twenty patients attending the dermatology OPD who were clinically diagnosed with verruca Vulgaris are included in the study as per the following inclusion & exclusion criteria.

Inclusion criteria
Table 1: Response following intralesional ppd injection

| Response     | No of patients (n=20) | Percentage (100%) |
|--------------|-----------------------|-------------------|
| Marked response | 1                     | 5%                |
| Moderate response | 15                  | 75%               |
| No response  | 4                     | 20%               |

Out of the 20 patients in our study, 1 patient showed marked response, 15 showed moderate response and 5 patients showed no response.

Table 2: Complications following intralesional ppd injection

| Complications | No of patients (n=20) | Percentage (100%) |
|---------------|-----------------------|-------------------|
| No            | 20                    | 100%              |
| Yes           | 0                     | 0%                |

None of the 20 patients developed any complications and only experienced mild pain and immediate erythema post injection which subsided within a few hours.

Figure 6: Showing marked response following completion of treatment.

Patients selected are those attending the Department of Dermatology, Venereology & Leprosy at Saveetha Medical College & Hospital who gave consent for the study.

Patients having multiple warts (verruca Vulgaris) (>1).

Male and female patients of age group 18 to 61 years having warts (>1).

Exclusion criteria

Those who did not give consent for the study.

Pregnant females and lactating mothers.

Children under 18 years.

Immunosuppressed individuals.

Patients having any chronic systemic illness.

Genital and perianal warts.

Ulcerated or inflamed warts.

Patients with hypersensitivity to antigens.

Methodology

Twenty patients with clinically diagnosed verruca Vulgaris were included in the study. Patients were selected according to inclusion and exclusion criteria. Written informed consent was taken before they participated in the study. Detailed history including name, age, sex, address, contact number, marital status, occupation, history of medication was noted. Patients were thoroughly examined, and the size, location of all the lesions documented on the first visit. All the patients were advised not to take any treatment other than the medication prescribed in our study.

The individuals were injected with an intralesional PPD (Tuberculin Diluted) of 0.1ml on lesional sites with an insulin syringe once in every two weeks till there was complete clearance or for a maximum of six injections (3 months).

The response parameters of the wart on each visit were noted every fortnight. On each follow-up, patients were examined for evidence of partial or complete regression of their lesions by noting down the size of the wart, the appearance of any new lesions, any adverse effects and to ensure that the patients are not using any other treatment. Photographic documentation was done before the procedure and then periodically up to the end of treatment Figures 1, 2, 3, 4, 5 and 6.
Results were assessed at the end of three months. The primary outcome measure was the complete disappearance of all the lesions without residual scarring. Complete disappearance occurs when the thickening, hyperkeratosis is no more evident, and the normal skin markings return.

The results were assessed as

1. Marked response
Responders who showed greater than 75% outcome.

2. Moderate response
Partial responders who showed 25 to 75% outcome.

3. No response
Those who showed less than 25% outcome. Non-responders were treated with alternate treatment modalities.

RESULTS AND DISCUSSION

Twenty patients who attended the Dermatology OPD at Saveetha Medical College and were clinically diagnosed with verruca Vulgaris and gave written informed consent were enrolled in this study. All 20 patients completed the study.

The mean age in our study group was 25.45, with a majority of the patients of the male gender (60%).

In our group, the most predominant type of wart were common warts (55%) followed by periungual warts (15%).

The efficacy of Inj PPD in our study was 80% (Table 1), and this is similar to other previous studies such as that done by Milante RR, Venida-Tablizo A and King-Ismael D (Milante et al., 2019) (79%) and S. Wananukul et al (Wananukul et al., 2010) (67%).

All patients in our study experienced pain during the administration of the injections but had no complications (Table 2).

CONCLUSIONS

There are various modalities which had been tried for the treatment of warts, one of which is intraleisional immunotherapy. In our study, we used intraleional immunotherapy with Inj PPD, and the results obtained showed its efficacy as well as other comparative advantages which include; its ease of administration, less time consuming, cost-effectiveness, minimal local tissue injury and no complications.

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Conflict of interest

We know of no conflicts of interest associated with this study.

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