RESEARCH ARTICLE

Efficacy and safety of intralesional quadrivalent human papillomavirus vaccine as immunotherapy in management of recalcitrant genital warts in a tertiary health care center of North India

Sumir Kumar¹, Onkar Singh¹, Sukhmani Kaur Brar², Sukhpreet Kaur Gill¹

¹Department of Dermatology, Venerology and Leprology, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India, ²Department of Skin, Fortis Medcentre, Chandigarh, Punjab, India

Correspondence to: Onkar Singh, E-mail: onkar.rajoa@gmail.com

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ABSTRACT

Background: Warts are common epidermal outgrowths caused by various strains of Human Papilloma Virus (HPV) and are spread by direct or indirect contact. Although they undergo spontaneous remission in 60–70% of cases over a period of few years, the cosmetic disfigurement, tendency to spread, and associated poor quality of life warrants intervention.

Aim and Objectives: The purpose of this case study was to explore the efficacy of Intralesional quadrivalent HPV Vaccine as immunotherapy in management of genital warts.

Materials and Methods: Twelve subjects of genital warts were enrolled from outpatient department of dermatology. Intralesional HPV vaccine was administered at 3 weekly intervals till three sittings or till the resolution of the lesions occurs, whichever was earlier. Results were measured in the terms of reduction in the number of the lesions, size of lesions or appearance of the new lesions. Follow-up was done at 3 weeks, 6 weeks, 9 weeks, 6 months, and 1 year. Any side effects seen during the study were recorded.

Results: Eleven out of 12 patients showed complete resolution. Side effect observed was only pain and that too during the injection. Only one patient had recurrence.

Conclusion: Immunotherapy is a simple, cost effective, and non-ablative mode of treatment for genital warts with better efficacy, tolerability, and less recurrence rate.

KEY WORDS: Genital Warts; Human Papillomavirus; Immunotherapy

INTRODUCTION

Genital warts are common benign dermatological conditions caused by Human Papilloma Viruses (HPV) 6, 11, 16, 18, etc.[1] Their prevalence varies according to geographical locations. In India, it is estimated to be around 1.07%, similar to world prevalence. They can cause significant disfigurement, are sexually transmissible to others and have a high recurrence rates. Different modalities are available for the treatment of warts such as electrocautery, microsurgery, or topical therapies in the form of local application of trichloro acetic acid (TCA), salicylic acid, and glutaraldehyde.[2] These are locally destructive, requiring frequent applications to individual lesions, which can not only be traumatic to the patient but also increase the number of medical visits. As a result, there has been a demand for safer modalities to treat recalcitrant warts. Immunotherapy presents an alternative approach to management of warts as it provides an ease of application but even distant lesions get resolved with application to a single lesion. Immunotherapy has been undertaken with Imiquimod, Mycobacterium w vaccine,[3] B.C.G vaccine, zinc, HPV[4] and auto implantation therapy.[5] There has been paucity of data on the efficacy of HPV vaccine in genital warts.
MATERIALS AND METHODS

Institutional ethical committee approval was taken before start of the study. Twelve patients with genital warts were enrolled from the dermatology department of a tertiary health care center from July 2019 to November 2020. Diagnosis in all the patients was made clinically. Informed and written consent was taken from each patient. Detailed history including duration of lesion, family history, history of recurrence of lesions or any comorbidities was taken from the subjects and they were subjected to routine clinical investigations. Patients who had used any treatment modality for warts within 3 months as well as pregnant/lactating women were excluded from the study. Size of the lesions, number of the lesions, and photographic record were maintained at each visit. 0.1 ml of Intralesional quadrivalent HPV vaccine was injected into the base of largest lesion using insulin syringe (30 G) under aseptic conditions. Three injections were to be given at 3 weekly intervals or till the resolution of lesions whichever occurred earlier. Follow-up was done at 3 weeks, 6 weeks, 9 weeks, 6 months, and 1 year.

RESULTS

Results were measured in terms of absolute reduction in number of lesions and recurrence or appearance of new lesions. Majority of the patients in our study were between 35 and 50 years of age. Females and males were almost in similar numbers who participated in the study. Only three patients had positive family history in our study. The results of this study demonstrate the positive correlation between the resolution of genital warts and immunotherapy with intralesional quadrivalent HPV vaccine.

Complete resolution of the lesions occurred in 11 out of 12 patients. Table 1 demonstrates the epidemiological profile of our study as well as results achieved by HPV vaccine used in the genital warts. Figure 1 shows multiple genital warts in the retropositive female at baseline. Figure 2 shows complete resolution of lesions at 6th week. Figure 3 shows multiple warts at baseline on the shaft of penis of the patient, while Figure 4 shows complete resolution at 6th week. Figure 5 shows an extensive condyloma acuminata at the glans penis, diagnosis was made clinically but biopsy was done to rule out S.C.C and intralesional HPV vaccine was given, complete resolution was achieved after 3rd injection. Figure 6 shows complete resolution after 3rd injection.

Significant side effects were not observed in our study. Only pain was observed and that too during the procedure. Only 1 patient had mild erythema which improved in few hours. No other side effect was observed. One patient showed recurrence of few lesions.

| Age (years) | Sex | Duration of lesion (in months) | Size of the largest lesion | Comorbidities | Family history of wart | Prior treatment taken | No. of lesions at baseline | No. of lesions at 3 weeks (1st visit) | No. of lesions at 6 weeks (2nd visit) | No. of lesions 6 months after last injection | Recurrence | Side effects |
|------------|-----|-------------------------------|---------------------------|---------------|------------------------|-----------------------|--------------------------|--------------------------------------|----------------------------------------|---------------|-------------|
| 27         | M   | 24                            | 0.8 cm                    | None          | None                   | Podophyllin           | 8                        | 5                                    | 2                                      | None          | Pain, None  |
| 50         | F   | 12                            | 0.5 cm                    | HIV           | None                   | Chemical cautery      | 8                        | 5                                    | 2                                      | None          | None        |
| 34         | M   | 9                             | 0.3 cm                    | None          | None                   | Electrocautery        | 5                        | 3                                    | 4                                      | None          | None        |
| 36         | M   | 4                             | 1 cm                      | None          | Present                | Electrocautery        | 5                        | 10                                   | 2                                      | None          | None        |
| 45         | F   | 18                            | 0.8 cm                    | None          | None                   | Electrocautery        | 5                        | 2                                    | None                                 | 1            | None        |
| 37         | M   | 23                            | 0.5 cm                    | DM            | Present                | Surgical excision     | 5                        | 2                                    | 5                                      | None          | None        |
| 48         | M   | 6                             | 0.6 cm                    | None          | None                   | Electrocautery        | 5                        | 3                                    | None                                 | None          | None        |
| 46         | F   | 8                             | 0.7 cm                    | None          | None                   | Electrocautery        | 5                        | 3                                    | 6                                      | None          | None        |
| 45         | M   | 13                            | 3.5 cm                    | None          | None                   | Podophyllin           | 5                        | 6                                    | 3                                      | None          | None        |
| 51         | F   | 16                            | 0.8 cm                    | DM            | None                   | Chemical cautery      | 6                        | 4                                    | None                                 | None          | None        |
DISCUSSION

In our study, complete resolution of lesions occurred in 11 out of 12 patients while one patient showed recurrence. Pain was the only side effect observed at site of injection. Almost all of the patients had history of prior treatment and one of them was retro-positive also, since genital warts tend to be extensive as well as resistant in such patients, the findings of our study assume significance in management of genital warts in such patients. Furthermore, one of the patients had
an extensive condyloma acuminata on glans penis which was mimicking squamous cell carcinoma, immunotherapy was offered and complete resolution of lesions occurred.

Genital warts continue to be a serious issue worldwide in spite of availability of different treatment modalities. They cause significant lifelong psychological and physical impact on the patients. The common modalities being used for the treatment of warts cause pain, scarring and are associated with high recurrence rates. Immunotherapy is an emerging treatment option which is non-destructive, easy to administer, and associated with lesser side effects. It works on the basis of evasion of host immune response. The virus is sequestered in upper cornified layers of stratum corneum and cause activation of T suppressor cells. They also further reduce the number of Langerhans cell which further cause proliferation of host cell.

There is strong immune response against the HPV vaccine that not only causes clearance of local wart lesion but also causes the clearance of distant lesions. The vaccine is designed to elicit neutralizing antibody responses which prevent initial infection with HPV but in warts it mainly acts by mounting a cell mediated and humoral response which helps in clearance of warts. Quadrivalent HPV vaccine contains inactive L1 proteins from four different strains 6, 11, 16, and 18 synthesized in the yeast Saccharomyces cerevisiae. Both quadrivalent and bivalent vaccines are routinely used for prevention of cervical cancer in girls since 2006. It is also being used for prevention of ano genital cancer in men in few countries. There are isolated case reports of use of HPV vaccine for recalcitrant warts. Venugopal in his case report described regression of 30 cutaneous warts with use of HPV vaccine at 0, 2, and 6 months. Hayashi et al. described in their study that HPV vaccine may not be an effective treatment modality for all cutaneous warts and the outcome is not determined by the HPV type. Retrospective studies in countries such as Denmark, Australia, and New Zealand, where HPV vaccine was routinely used, revealed a decrease in incidence of anogenital warts. Similarly, nonavalent HPV vaccine has been used in a study for management of cutaneous warts in immunocompromised patients. The results of our study are similar to the results observed in various isolated case reports and case series.

The results of our study reflect on efficacy of intralesional quadrivalent HPV vaccine in the management of genital warts even in immunocompromised patients. The subjects in the study were not offered any other therapy during the study period. Results were measured by reduction in number as well as size of lesions, photographic record was also maintained. The limitation of this study is that number of patients included was less and comparison with an established modality was not done.

CONCLUSION

The study has demonstrated that Quadrivalent HPV vaccine when used as intralesional immunotherapy presents a unique and effective approach toward management of genital warts even in immunocompromised patients. Conventional modalities require frequent and repeated medical consultations, while quadrivalent HPV vaccine is an effective and novel alternative in the long run.

Immunotherapy can be used in genital warts which fail to respond to other modalities. Further studies are required with larger population to evaluate the long-term cell-mediated immune response as well to compare the efficacy of this vaccine with the other modes of immunotherapy in genital warts.

REFERENCES


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