

Effectiveness of Autoinoculation in Patients with Multiple Warts Presenting at a Tertiary Care Hospital

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ABSTRACT

Objective: To determine the effectiveness of autoinoculation in patients with multiple skin warts.

Study Design: A Quasi-experimental study.

Place and Duration of study: Dermatology department of PNS Shifa Hospital, from April to October 2021.

Methodology: Ninety-six patients with multiple warts were enrolled in this study after informed consent. Under strict aseptic measures and local anaesthesia, wart tissue was removed and crushed on a glass slide with the scalpel. Autoinoculation was done on flexor aspects of bilateral forearms after making a subcutaneous pocket which was then stitched. Patients were assessed at monthly intervals for 03 months and after 01 month of the last autoinoculation to see sustained response. Effectiveness was recorded according to ordinal scale; worsening of lesions/no response at <50% resolution/partial response at >50%-<100% resolution and complete response at 100% resolution.

Results: Complete response was observed in 88 (91.66%) of the cases, no response was observed in 2 (2.1%) cases where as 6 (6.3%) showed worsening. All patients were compliant with the follow-up. No new eruptions were observed.

Conclusion: Autoinoculation is a minimally invasive and cost-effective procedure with excellent response to wart. It also decreases recurrence by generating viral-specific immunity.

Key Words: Viral warts, Autoinoculation, Multiple, Immunotherapy, Verrucous, Treatment, HPV, Resistant.

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INTRODUCTION

Warts are mucocutaneous outgrowths commonly involving the skin. The causative agent belongs to a class of double-helical DNA viruses; Human Papilloma Virus (HPV).¹ The incidence of warts is estimated to be between 3-13% in the western world.² Though precise statistical data with regard to the prevalence of warts in Pakistan is not available, it is one of the most common viral infections seen in the dermatology clinic.³ Various clinical types are common warts (verruca vulgaris), filiform warts (digitate wart), flat warts (verruca plana), plantar warts and genital warts. Warts are contagious and spread by touch or contact to the person himself and others. They most commonly involve extremities, scalp, face, neck, and genital area. Therefore, greatly affects patient's quality of life by causing social embarrassment and fear of negative appraisal in public.⁴

Although some viral warts regress spontaneously, most of them require treatment. Various modalities are used to treat warts, such as electrocautery, chemical cautery, cryotherapy, CO₂ laser ablation, retinoids, podophyllin, podophyllotoxin, hot nitric acid, intralesional bleomycin, imiquimod, oral zinc, immunotherapies such as BCG vaccine, MMR vaccine and HPV vaccines all have been tried. No treatment, either single or multiple, has proven to be 100% effective.^{5,6}

Recurrence and persistence are common as most of the treatment modalities only treat the growth without generation of specific immunity against the causative agent, leading to pain, scars, and prolonged morbidity. Therefore, the ideal treatment is aimed at removal of warts without recurrence along with the avoidance of aggressive procedures. This may be achieved by exposing the virus to immune mediators and subsequently enhancing the immune system.^{7,8}

Autoinoculation is a novel procedure, which helps in treating warts by stimulation of cell-mediated immune response against HPVs.⁹ It initiates delayed hypersensitivity reaction to the wart tissue with a surge of Th1 cytokines and viral-specific antibodies resulting in clearance in majority of the patients.⁶ It has found to be 53.33% effective in the treatment of warts.⁹ It is done by extraction of wart tissue with subsequent implantation in the

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uninvolved skin.^{9,10} Hence, autoinoculation is a simple procedure that does not require any expensive or specialised materials. In this study, the authors plan to assess the effectiveness of autoinoculation as a therapy for multiple warts. Therefore, if found effective, autoinoculation can be recommended as a standard treatment modality for warts. Moreover, there is a paucity of data in Pakistan in this regard. Hence this study will be a valuable contribution in this regard.

METHODOLOGY

This experimental study was conducted at the Dermatology Department of PNS Shifa Hospital, from April 2021 to October 2021. Approval was taken from the hospital research ethics committee (ERC/2020/Derma/033), with prevalence of 53.33%, the authors calculated a sample size of 96 patients with the assistance of World Health Organisation sample size calculator, with a confidence level 95% and margin of error 10%.

Patients of either gender with >3 warts belonging to the age group 12 years to 65 years were registered in the study by non-probability consecutive sampling technique.

Patients who have taken any therapy for warts in the past one-month, immunosuppressed state and pregnant or lactating ladies were excluded.

After obtaining written informed consent from the patients, clinical history and demographic details were noted. Detailed clinical examination of the patients, including the diagnosis, site, size, number and duration of lesions were noted. Under local anaesthesia and aseptic measures, autoinoculation was performed by removing a piece of wart tissue with the help of a scalpel blade no.15. The wart tissue was cut into small pieces. A small incision was given in the flexor aspect of the forearm bilaterally followed by creating a pocket in subcutaneous tissue in which pieces of wart tissue were introduced. The wound was closed with 4/0 polyglycolic acid violet suture and secured with dressing. The stitch was removed after 01 week. The patient was followed at monthly intervals for 3 months and after 01 month of the last autoinoculation to see a sustained response. If no response was achieved at 01 month, monthly autoinoculation was repeated with a maximum of 03 sessions. Effectiveness was recorded according to ordinal scale of 1 to 4, worsening of lesions, no response (<50% resolution), partial response (>50%- <100% resolution) and complete response (100% resolution).

Descriptive statistics were calculated by using the Statistical Package for the Social Sciences version (SPSS) 28. The quantitative variables were presented as Mean \pm SD while the qualitative variables were noted as frequency and percentage. Stratification of effect modifiers like gender, age, socioeconomic status, education, site of lesions, number of lesions and duration of disease was achieved. Post-stratification chi-square test was implemented. A p-value ≤ 0.05 was contemplated as statistically significant.

RESULTS

Out of the patients enrolled in the study, 66(68.8%) were males and 30(31.3%) were females. The age group of the patients ranged from 12 years to 65 years with mean age of 34.20 ± 11.98 years. Twenty-six (27.1%) belonged to socio-economic group with monthly earning <20,000 PKR, 61(63.5%) befitted group with monthly income 20,000-50,000 PKR, and 9(9.4%) belonged to group with monthly earning >50,000 PKR. The majority of patients 47(49%) got their education till higher education level, 19 (19.8%) secondary, 27 (28.1%) primary, and 3 (3.1%) were illiterate. Characteristics of warts including duration, size, site, and number of lesions are shown in Table I.

Table I: Baseline characteristics of warts in study population (n=96).

Characteristics	Number of patients (%)	
Size of lesion		
<0.5cm	6(6.25%)	
0.5cm-1cm	72 (75%)	
>1cm	18(18.75%)	
Duration of lesion		
≤ 12 months	65(68%)	
>12months	31(32%)	
Mean \pm SD	14.06 \pm 7.71	
Number of lesions		
<10	28(29.2%)	
10 - 20	60(62.5%)	
>20	8(8.3%)	
Site involved	Yes	No
Face and neck	33(34.4%)	63(65.6%)
Hands	32(33.3%)	64(66.7%)
Feet	30(31.3%)	66(68.7%)
Arm	22(22.9%)	74(77.1%)
Genitals	19(19.8%)	77(80.2%)



Figure 1: Response to autoinoculation (a) at presentation, (b) at 01 month, (c) at 02 month, (d) at 03 month.

The number of lesions was calculated at month 1, at month 2, at month 3 and after 1 month of the last autoinoculation. The mean number of lesions was 13.85 ± 5.95 , 4.43 ± 5.03 , 1.60 ± 3.41 , 0.60 ± 2.04 and 0.16 ± 0.84 at month-1, at month-2, at month 3 and after 1 month of the last autoinoculation respectively. There was an excellent response to treatment (Figure 1) as shown in Table II.

Table II: Response to treatment.

Effectiveness	At 01 month n (%)	At 02 months n (%)	At 03 months n (%)	After 01 month of last autoinoculation
No response	12 (12.5%)	4(4.2%)	2(2.1%)	2(2.1%)
Partial response	43 (44.8%)	20(20.8%)	0	0
Complete response	36 (37.5%)	71(74%)	88(91.66%)	88(91.66%)
Worsening	5(5.2%)	1(1%)	6(6.3%)	6(6.3%)
No of lesions (Mean±SD)	4.43±5.03	1.60±3.41	0.6±2.04	0.6±2.04

Only 2 (2.1%) patients developed an infection at the recipient site within 01 week of the procedure. They were managed with daily wound dressing and systemic antibiotic (amoxicillin 875mg + clavulanic acid 125mg), following which the recipient site healed without any sequelae.

In this study, effectiveness was found to be 88(91.66%) while 2 (2.1%) of the patients failed to show any response to the treatment, and 6(6.3%) showed worsening of lesion. The results showed no significant association of effectiveness with the number of lesions, duration and site of lesion, gender, socio-economic status and education.

DISCUSSION

Refractory viral warts are problematic to cure and cause serious psychological impacts on the patient. Although warts regress spontaneously, most cases require therapeutic interventions, but recurrence rates are higher.¹¹ Selective immunodeficiency or altered immune state of the patient might lead to recrudescence in wart.¹² The target of the modality should aim for complete clearance of warts and boost the immune system to deal effectively with the virus and have life-long immunity against HPV that prevents the recurrence of warts.¹³

Autoinoculation was first explained by Shivkumar *et al.*, who implemented it in 60 patients with warts and achieved a total clearance rate of 44(73.3%) with most of the patients showing complete response in 2 months.¹⁴ Gulanikar *et al* documented the success rate of autoinoculation in 22(88%) patients within a follow-up time of 3 to 6 months in his report.¹⁵ This study showed even better response with complete response in 88(91.66%) at 03 months. In this study, autoinoculation was performed in bilateral forearms, unlike most previous studies in which the unilateral forearm was selected as the recipient site.^{11,14} Hence, it can also be elicited that this technique enhanced immunity and resulted in higher rates of effectiveness.

Narayanan *et al.*, in their study, showed a complete response in 15(60%) patients with genital warts.¹⁶ In this study, complete clearance was 17(89.5%) in patients with genital warts respectively.

Earlier studies have reported that palmoplantar warts are problematic to deal with. Faleiro *et al.* in their study reported a complete response in 17(82.3%) patients who had palmoplantar warts.¹⁷ In the present study, 28(93.33%) patients with plantar and 31(96.87%) patients with palmar warts had complete clearance. In a study by Shirodaria and Mathews,

immunofluorescence of plantar warts showed a much higher incidence of stainable virus antigens. This could account for the better response of palmoplantar warts seen in our study as also mentioned by Mary *et al.* in their study.¹⁸

Additionally, in the present study, there was no significant relation between treatment response with age, gender, size, and number of lesions similar to the study by Abdelmonaem *et al.*¹⁹

In the present study 2(2.1%) patients showed no response despite three sessions of autoinoculation. This unsatisfactory result might be due to a specific immune deficit to the virus in absence of generalised immune compromise as discussed by Narayanan *et al.*¹⁶

Adverse events of this autoinoculation are very few such as pustules, hypertrophic scar formation at the site, and post-inflammatory hypopigmentation or hyperpigmentation. In this study 2(2.1%) of the patients experienced infection at the site of autoinoculation whereas in the study done by Taneja *et al.*, 2(13.33%) of the patients developed an infection at the site of the reception.²⁰ However, it did not have any significant effect on the treatment response.

The main limitation of this study was relatively small sample size therefore more studies in future with larger sample size are required. Another drawback comprised of a single-centre experience. It was governed in an urban environment therefore; the results might not extrapolate to mass populations.

CONCLUSION

This study showed excellent response, 88(91.66%), to autoinoculation. It is a simple, safer, and cost-efficient technique with minimal trauma and complications that can be used in simple set-ups as a useful method for the treatment of warts.

ETHICAL APPROVAL:

Ethical approval was obtained from the Ethical Review Committee of PNS Shifa Hospital prior to initiation of the research work.

PATIENTS' CONSENT:

Informed consent was obtained from patients for the treatment of warts and the use of data for research purposes.

COMPETING INTEREST:

The authors declared no competing interests.

AUTHORS' CONTRIBUTION:

UA: Design of the work, acquisition, analysis, interpretation of data for the work, and accountable for all aspects of the work.

NA: Revising the work critically for important intellectual content, conception, and design of the work.

MT: Revising the work critically for important intellectual content.

FH: Data collection and interpretation, and drafting the work.

AHS: Revising the work critically.

OF: Analysis and interpretation of data, revising the work critically.

All the authors have approved the final version of the manuscript to be published and equally accountable for all aspects of the work.

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