



COMPARISON OF CLINICAL OUTCOME OF AUTOINOCULATION VS ACITRETIN IN PATIENTS WITH VIRAL WARTS AT TERTIARY CARE HOSPITAL, KARACHI

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ABSTRACT

Background: Viral warts are benign growths on the skin, mucous membranes, and other epithelial tissues caused by various strains of the human papillomavirus (HPV). Autoinoculation and acitretin have shown efficacy in treating multiple viral warts by increasing the immune response and reducing wart's proliferation. Autoinoculation stimulates the body's defense mechanisms whereas Acitretin acts as a systemic retinoid to promote skin regeneration and reduce wart recurrence.

Objective: The present study aimed to compare the clinical outcome of autoinoculation vs acitretin in viral warts patients, at tertiary care hospital, Karachi.

Study Design: Randomized controlled trial

Materials and Methods: This randomized controlled trial investigated 40 viral warts patients in the Dermatology Department of Tertiary Care Hospital, Karachi from March 2024 to August 2024. Eligible participants were randomly assigned to one of the two treatment groups: Group A (Autoinoculation therapy; n =20) and Group B (Acitretin therapy; n=20). Patients in Group A (Autoinoculation therapy) were received autoinoculation therapy. Group B patients administrated with Oral acitretin 0.5 mg/kg body weight/day for a total duration of three months. Efficacy of Autoinoculation and Acitretin therapy measured in terms of complete, partial, and no response. SPSS version 23 was used for data analysis.

Results: Mean age of patients was 27.25 ± 10.32 years. The mean duration of warts disease was 8.78 ± 6.24 months. Cosmetic disfigurement, Itching, and Pain was the most prevalent symptoms of warts. Among 40 warts cases, the common warts were the prevalent type of warts found in 29 (72.5%) followed by Plantar 8 (20%) and plane 3 (7.5%). Regarding the site of wart, hand was the most common site 21 (52.5%) followed by feet 14 (35%). The incidence of complete, partial, and no response in Group A vs. Group B was 5 (25%) vs. 3 (15%), 13 (65%) vs. 11 (55%), and 2 (10%) vs. 6 (30%), respectively. There was no statistical significance regarding side effects in both groups.

Conclusions: This study shows that autoinoculation is a promising treatment for viral warts, resulting in better clinical outcomes and patient satisfaction compared to acitretin. Autoinoculation is considered as one of the effective and safe treatment of viral warts.

Keywords: Viral Warts, Autoinoculation, Acitretin, clinical outcomes

INTRODUCTION

Viral warts are benign growths on the skin, mucous membranes, and other epithelial tissues caused by various strains of the human papillomavirus (HPV). In general, the prevalence of warts varies from 7% to 10% among population that suffer at certain stage of their lives. HPV thrives in hot, humid environments, such as public swimming pools and locker rooms, and spread through direct contact or through small amounts of skin rubbing on the sensitive cornea [1]. Weaken immunity of children and adolescents make them more prone to severe infection and viral warts [2]. Viral warts are hyperkeratotic papules or verrucous lesions on the skin, caused by the human papillomavirus (HPV) and can be found on different parts of the body, such as the legs, arms, face, genitals, or muscles. There are about 180 types of HPV [3]. Different strains of HPV cause warts in different parts of the body. Site-based viral warts classified as common warts (found on the face, thighs, arms, legs, etc.), leg warts, genital warts, genital warts and plane tumors [4].

Treatment of warts usually involves locally destructive treatments, such as salicylic acid, surgical curettage, chemical peels, electrocautery, cryotherapy, hyperthermal therapy, various types of lasers. These treatments aim at destruction warts locally but host anti-HPV does not affect the immune system [5, 6]. Autoinoculation is a relatively new way to treat multiple and simple warts [7]. Vaccination of an excised wart can induce HPV antigen release into the plasma, triggering a prolonged hypersensitivity reaction that clears local and distant lesions. This exposure to viral antigens can stimulate immunity cell-mediated immunity, and virus-specific IgG and IgM antibodies may appear in body [8, 9].

Acitretin is a systemic retinoid that has been used to treat various dermatologic conditions including psoriasis and severe keratinization disorders. In addition, it was used to treat recalcitrant warts due to its ability to modulate cell differentiation and proliferation. Ideally, good treatment should not leave scars [10]. Given the theory that current treatments do not provide a complete cure and the limited literature on the effectiveness of autoinoculation and recalcitrant warts, this study was conducted to compare the clinical outcomes of autoinoculation and acitretin for viral warts in patients.

METHODOLOGY

This randomized controlled trial investigated 40 viral warts patients in the Dermatology Department of Tertiary Care Hospital, Karachi from March 2024 to August 2024. Patients of either gender with >3 warts and aged ≥ 12 years diagnosed with viral warts were enrolled. Patients who have taken any therapy for warts in the past one-month, immunosuppressed state and pregnant or lactating ladies were excluded. Eligible participants were randomly assigned to one of the two treatment groups: Group A (Autoinoculation therapy; n =20) and Group B (Acitretin therapy; n=20). Patients in Group A (Autoinoculation therapy) were received autoinoculation therapy. Under strict aseptic conditions and local anesthesia, the wart's tissue dissected with a scalpel and crushed on glass slides. Autoinoculation was done on flexor aspects of forearms after making a subcutaneous pocket, which then stitched. Patients were assessed at monthly intervals for 03 months to see sustained response. Patients in Group B investigated until three months. Oral acitretin 0.5 mg/kg body weight/day were given to patients for a total duration of three months. Efficacy of Autoinoculation and Acitretin therapy was measured in terms of complete, partial, and no response.

Data analysis was done using SPSS Version 23. Numerical parameters such as age, disease duration, and number of warts were expressed as mean and standard deviation whereas categorical variables were described as frequency and percentages. Clinical outcomes in both groups were compared using Chi-square test by taking p-value of ≤ 0.05 was considered significant.

RESULTS

Mean age of patients was 27.25 ± 10.32 years. The mean duration of warts disease was 8.78 ± 6.24 months. There were 21 (52.5%) male and 19 (47.5%) females. Autoinoculation (group-A) had 11 (55%) male and 9 (45%) females. Both male and females were 10 (50%) in Group-B (Acitretin). Cosmetic disfigurement, Itching, and Pain was the most prevalent symptoms of warts. Among 40

warts cases, the common warts were the prevalent type of warts found in 29 (72.5%) followed by Plantar 8 (20%) and plane 3 (7.5%). Regarding the site of wart, hand was the most common site 21 (52.5%) followed by feet 14 (35%). The incidence of complete, partial, and no response in Group A vs. Group B was 5 (25%) vs. 3 (15%), 13 (65%) vs. 11 (55%), and 2 (10%) vs. 6 (30%), respectively. There was no statistical significance regarding side effects in both groups. Demographic details of patients are shown in Table-I. Comparison of different types of warts illustrated in Figure-1. Comparison of incidence of complete, partial and no response demonstrated in Figure-2.

Table-I Demographic details of patients

| Variables | Total (N=40) | Group A (Autoinoculation therapy) (N=20) | Group B (Acitretin therapy) (N=20). |
|---------------------------|---------------|--|-------------------------------------|
| Age (years) | 31.34 ± 12.26 | 32.56±11.86 | 30.12±12.66 |
| Gender | | | |
| Male | 21 (52.5%) | 11 (55%) | 10 (50%) |
| Female | 19 (47.5%) | 9 (45%) | 10 (50%) |
| Disease duration (months) | 8.78 ± 6.24 | 7.89±5.86 | 9.67±6.94 |
| No. of warts (mean) | 11.46 ± 8.64 | 12.54±7.98 | 10.38±9.3 |
| Wart's sites | | | |
| Hand | 21 (52.5%) | 11 (55%) | 10 (50%) |
| Feet | 14 (35%) | 6 (30%) | 8 (40%) |
| Face | 3 (7.5%) | 2 (10%) | 1 (5%) |
| Hand and feet | 2 (5%) | 1(5%) | 1 (5%) |

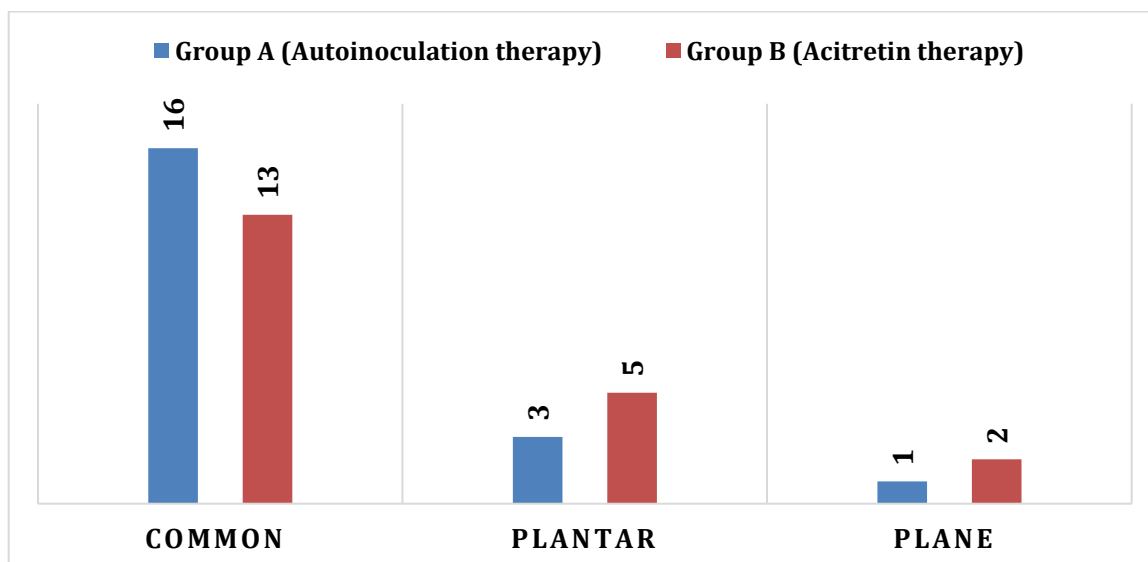


Figure Comparison of different types of warts (N=40)

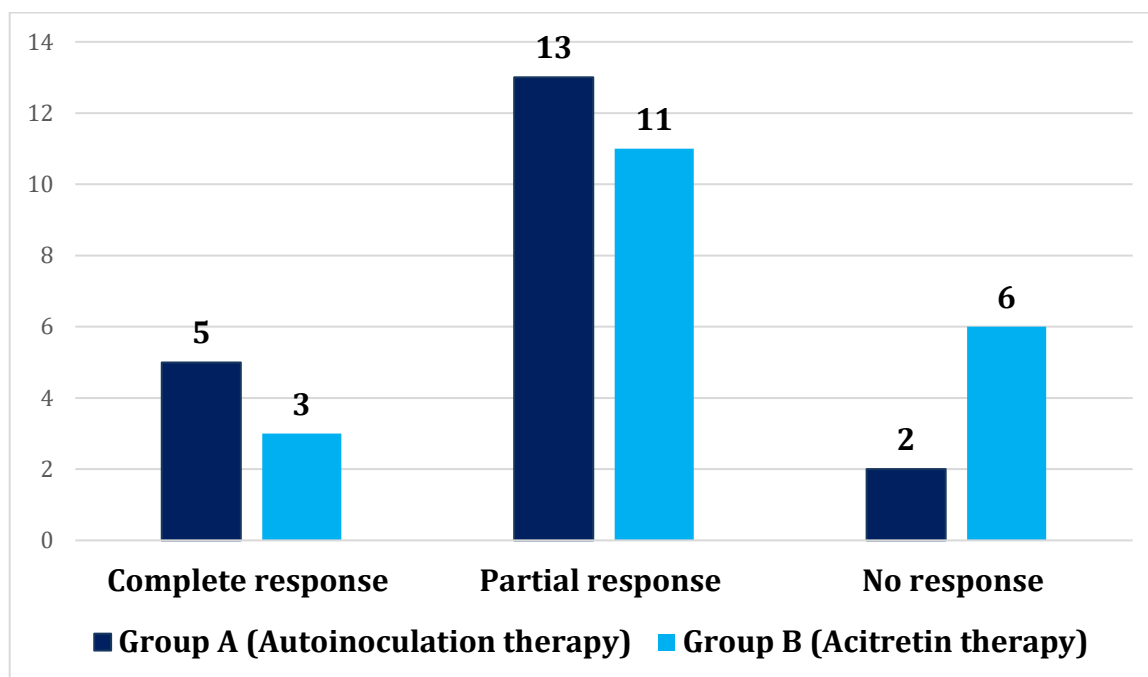


Figure-2 Comparison of incidence of complete, partial and no response (N=40)

DISCUSSION

Viral warts caused by the human papillomavirus (HPV) are common skin lesions that can be difficult to treat. Traditional therapies often fail to provide a complete cure, especially for recalcitrant warts that persist despite treatment. Two new therapies that have shown promise are autoinoculation and acitretin. The present study focused on the clinical outcomes of these two approaches in the treatment of patients with viral warts. Autoinoculation is a relatively new procedure and less invasive treatment for viral warts. The underlying theory of this approach is that a prolonged hypersensitivity reaction is triggered when the patient's immune system is exposed to HPV antigens from the wart. This immune response enables the removal of both local and distant warts.

Acitretin is a systemic retinoid that has been used to treat various dermatologic conditions including psoriasis and severe keratinization disorders. In addition, it was used to treat recalcitrant warts due to its ability to modulate cell differentiation and proliferation. Acitretin has few side effects [11]. Several studies have shown that systemic acitretin is effective in treating warts [12, 13]. The present study investigated the efficacy, safety, and outcome of acitretin in the treatment of warts.

The variations in results between this study and previous studies can be attributed to differences in the number of individuals analyzed and the types of warts studied, particularly in the context of acitretin treatment for multiple viral warts [14-16]. It has been shown to be effective in these cases. Plantar warts, which look like calluses and can grow inside, develop on the soles of the feet and can be painful, making it difficult to walk. Genitals warts caused by sexually transmitted diseases and can occur in the penis, vagina, or uterus. Some larvae are found around (periungual) or under (subungual) fingernails or toenails. Palmoplantar warts are the most common warts [19].

There are many treatment options for viral warts, including local destructive therapy and intravenous or intralesional cidofovir but these treatments are rare for complete treatment. Alternative treatments have recently been introduced, involving removal of the warts and then infiltration of the excised tissue into the skin of the warts [20].

Few studies have investigated the efficacy of autoinoculation against viral warts. A study of 48 subjects showed that autoinoculation was more effective than placebo, with complete eradication in 62.5% of cases [21, 22]. Studies have shown that 40% of autoinoculation patients achieved complete clearance, with the procedure being particularly effective in patients with less than 12 warts. Additionally, a recent study of 15 subjects showed as complete resolution in 67% after 12 weeks of

treatment [23]. A similar study conducted on 83 patients with warts infections revealed that three of 57 patients (69.5%) were completely cured when treated with autoinoculation [24].

The autoinoculation approach has proven to be cost-effective compared to current treatments. In addition, there were no reports of warts recurrence after the procedure, indicating that fewer sessions are required for complete warts removal. These warts may indicate a developed and delayed immune response to HPV with increased sensitivity.

CONCLUSION

Autoinoculation is a promising treatment for viral warts, resulting in better clinical outcomes and patient satisfaction compared to acitretin. Autoinoculation should be considered as one of the effective and safe treatment of viral warts.

REFERENCES

1. Shahid MW, Iftikhar N, Irshad M, Akhtar A, Hafeez J, Ali UA. Efficacy of Autoinoculation in Treatment of Multiple Viral Warts - A Single Arm Study. *J Coll Physicians Surg Pak* 2023; 33(02):141-144.
2. Shi L, Luo M, Zhang F, Zhang L, Wang B, Liu P, Zhang Y, Zhang H, Yang D, Zhang G, Zhou F. Photothermal therapy enhanced the effectiveness of imiquimod against refractory cutaneous warts through boosting immune responses. *J Biophotonics* 2019; 12(2):e201800149. doi: 10.1002/jbio.201800149
3. Mousa HA. Autoinoculation Therapy for the Treatment of Widespread Cutaneous Warts. *Dermatologic Surgery*. 2024 Apr 1;50(4):341-4.
4. Brown M, Williams A, Chilcott RP, Brady B, Lenn J, Evans C, Allen L, McAuley WA, Beebejaun M, Haslinger J, Beuttel C. Topically Applied therapies for the treatment of skin disease: Past Present and Future. *Pharmacological Reviews*. 2024:Pharmacol-Rev.
5. Van Doorslaer K, Li Z, Maes P et al. (2017): The papillomavirus Episteme: a major update to the papillomavirus sequence database. *Nucleic Acids Res.*, 45:499-506.
6. Lindeman J, Guimera N, Lioveras B et al. (2013): The occasional role of low-risk human papillomavirus 6, 11, 42, 44 and 70 in anogenital carcinoma defined by laser capture microdissection/PCR methodology, results from a global study. *Am J Surg Pathol.*, 37(9):1299-1310.
7. Faleiro KN, Shukla P. Role of autoinoculation in the management of cutaneous warts: A comparison study with 100% trichloroacetic acid application. *Int J Res Dermatology* 2020;6(4):537 doi: 10.18203/issn.2455-4529.intjresdermatol20.
8. Khatu S, More Y, Vankawala D, Pawar S, Gokhale N, Chavan D. Treating multiple and recalcitrant wart with autoimplantation technique. *J Dr NTR Univ Heal Sci* 2017; 6(4):247 doi:10.4103/2277-8632.221528.
9. Taneja G, Hazarika N, Bhatia R. Effectiveness of autoinoculation in viral warts: A single arm, open-label, and clinical trial. *Dermatol Ther* 2020; 33(6):e14122 doi: 10.1111/dth.14122.
10. Naheed, Asghar M, Rehman N, Afridi IU, Khalid S. Epidemiological and clinical patterns of viral warts presenting to dermatology OPD of Hayatabad Medical Complex, Peshawar. *J Pakistan Assoc Dermatologists* 2022; 32(1): 78-84.
11. Gopal V, Shenoy MM and Pinto M. Common warts revisited: a clinical study. *International Journal of Research in Dermatology*. 2017; 3: 261-6.
12. Witchey DJ, Witchey NB, Roth-Kauffman MM and Kauffman MK. Plantar warts: epidemiology, pathophysiology, and clinical management. *J Am Osteopath Assoc*. 2018; 118: 92-105.
13. Omar MA, Nofal A, Balat A, Mohamed W. Role of Acitretin in Management of Multiple Warts. *The Egyptian Journal of Hospital Medicine*. 2022 Apr 1;87(1):1153-6.

14. Nofal A, Fawzy MM, Eldeeb F, Elhawary EE. Oral isotretinoin versus acitretin in male patients with multiple recalcitrant common warts: A randomized, double-blinded placebo-control study. *Journal of Cosmetic Dermatology*. 2022 Nov;21(11):5895-901.1-8.
15. Shin DS, Han SS, Kim TL, Jang JW, Seo HM, Kim JS. Treatment of recalcitrant viral warts with combination therapy of systemic acitretin and diphenylcyclopropenone immunotherapy. *Annals of Dermatology*. 2020 Jun;32(3):243.
16. Nofal AA. Evaluation of acitretin versus oral isotretinoin in the treatment of common warts. *Zagazig University Medical Journal*. 2023 Mar 1;29(2):417-24.
17. Rijsbergen M, der Kolk NT, Hogendoorn G, Kouwenhoven S, Lemoine C, Klaassen ES, et al. A randomized controlled proof of concept trial of digoxin and furosemide in adults with cutaneous warts. *Br J Dermatol* 2019; 180(5):1058-68. doi:10.1111/bjd.17583.
18. Fasih S, Arif AB, Younas S. Pattern of skin diseases in Abbas Institute of Medical Sciences, Muzaffarabad. *Pak J Physiol* 2017; 13(4):26-9 <http://pjp.pps.org.pk/index.php/PJP/article/view/284>.
19. Abeck D, Tetsch L, Lüftl M, Biedermann T. Extragenital cutaneous warts: Clinical presentation, diagnosis and treatment. *J Dtsch Dermatol Ges* 2019; 17(6):613-34. doi: 10.1111/ddg.13878.
20. Arshad A, Younas S, Ahmed TJ, Rashid T, Nadeem M. Outcome of 20% topical zinc oxide ointment in the treatment of cutaneous warts of hands and feet. *J Fatima Jinnah Med University* 2019; 13:23-5.
21. Gulanikar AD, Bhide DS, Pethe SA. Autoimplantation therapy for recalcitrant viral warts. *Clin Dermatol Rev* 2018; 2(2):74-7. doi: 10.4103/CDR.CDR_12_17.
22. Narayanan S, Nallu K, Venu S, Chandrasekar M. A prospective clinical study on homologous autoinoculation in anogenital wart. *Int J Res Dermatol* 2019; 5(2):325-8. doi:10.18203/issn.2455-4529.IntResDermatol20190984.