ORIGINAL ARTICLE

# EFFECTIVENESS OF ORAL ISOTRETINOIN VERSUS TOPICAL TRETINOIN 0.05% IN THE MANAGEMENT OF FACIAL PLANE WARTS

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**Background:** Facial plane warts present a therapeutic challenge due to limited treatment options. Electrocautery and cryotherapy, though effective, carry risks of scarring and pigmentation. Laser therapy is often inaccessible in resource-limited settings. While both topical tretinoin and oral isotretinoin have shown satisfactory outcomes, no standard treatment exists. Dermatologists are cautious with oral isotretinoin due to the absence of clear guidelines. This trial aimed to compare the efficacy of oral isotretinoin versus topical tretinoin 0.05% in treating facial plane warts. **Methods:** Approved by the hospital's ethics board, this randomized control trial began in January 2023 at Khyber Teaching Hospital. Clinically diagnosed patients with facial and neck plane warts were enrolled. A total of 106 participants were randomized into two groups. Group A received topical tretinoin 0.05%, while Group B was administered oral isotretinoin at 0.5 mg/kg. Treatment response was assessed at 1 and 3 months. Complete lesion clearance marked treatment success, with monthly follow-up for 3 months to assess recurrence. **Results:** Among 106 patients (61 males, 45 females), 30 (56.6%) in Group A and 42 (79.2%) in Group B achieved complete clearance ($p$=0.0125). Recurrence occurred in 4 participants per group (13.3% in A; 9.3% in B, $p$=0.612). **Conclusion:** Oral isotretinoin proved significantly more effective than topical tretinoin 0.05% in treating facial plane warts, with a comparable recurrence rate.

**Keywords:** Facial warts; Plane warts; Isotretinoin; Verruca plana; Tretinoin

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## INTRODUCTION

Plane warts, also known as Verruca Plana are a type of cutaneous warts that can develop on any part of the body. They predominantly develop on the face, neck, dorsum of hands, arms and legs.[1] Verruca Plana frequently affects young adults and children and the common strains of human Papillomavirus that manifest as verruca plana are type 3, 10 and 28. Clinically, they present as small flat asymptomatic papules and are often multiple.[2]

The involvement of face leads to a cosmetic nuisance and the risk of spread due to their contagious nature is an additional concern. Multiple treatment modalities have been utilized in managing plane warts with variable efficacy. Electrosurgery, cryotherapy, Lasers, intralesional as well as topical medications constitute the therapeutic arsenal.[3,4]

Treatment of warts involving the face is no less than a challenge, as treatments like cryotherapy and electrosurgery, due to the risk of potential scarring and pigmentation, are generally avoided, particularly if the lesions are multiple. Recently LASERS have gained popularity in treating facial warts but lack of their availability in most hospitals makes them less accessible for many.[5] Moreover, home remedies like Aloe vera, garlic, Apple vinegar, duct tape and orange peel have all been tried in treatment of warts producing variable results.[6] Topical retinoids are one of the commonly prescribed treatments for facial flat plane warts particularly in children. Oral isotretinoin has also been tried in the treatment of flat warts and the results are satisfactory.[7]The adverse effect profile of both topical and oral retinoids has been well established due to their widespread use in dermatological practice. Retinoids exhibit a multiplex of biological effects including regulation of proliferation and differentiation of keratinocytes. They are known to suppress the replication of Human Papillomavirus (HPV) and can produce apoptosis in cells infected by HPV.[8]

Oral Isotretinoin proved successful in 69% of the cases of plane warts in a study, in comparison to 38% of those treated with topical Isotretinoin.[7]There is no specific treatment for the management of facial warts according to literature. Despite the high prevalence plane warts in our area, no randomized controlled trial has been conducted. Most dermatologists are hesitant while prescribing oral isotretinoin as first line therapy as

no clear guidelines exist. The purpose of the study was to establish the superiority of oral Isotretinoin in managing the cases of facial plane warts over topical tretinoin cream 0.05%. Thereby encouraging the researchers and physicians to prescribe oral Isotretinoin in suitable cases of facial plane warts as the first line therapy.

## MATERIAL AND METHODS

This randomized control trial was conducted between January and December 2023 after getting approval from hospital's ethical review board. The study was done at Khyber Teaching Hospital Peshawar and principles of declaration of Helsinki were strictly adhered throughout the research. Patients having flat warts involving the face and neck attending our dermatology outpatient were inducted as study participants. Subjects that met the inclusion criteria of this clinical trial were enrolled. Pregnant and lactating females along with those who have received any previous treatment in the last 3 months were excluded from this research. Sample size was calculated for a two-sample t-test with two-sided $\alpha = 0.05$ and 80% power. Assuming a standardized effect size (Cohen's d) of 0.55, the required sample was 52 participants per arm (104 total); allowing for minimal loss to follow-up produced a final planned enrollment of 106 participants. 106 participants were randomly allocated into 2 groups A and B, 53 in each group, by block randomization. Randomization was performed using permuted block randomization with variable block sizes (4 and 6) and an allocation ratio of 1:1. A reproducible randomization list was created by the study statistician using a computer random number generator.

Sequentially numbered, opaque, sealed envelopes containing group assignments were prepared and used for allocation concealment; envelopes were opened only after participant eligibility and informed consent were confirmed. This approach ensured equal group sizes (53 participants per arm, total N = 106) while reducing the risk of allocation predictability Written consent was taken from the patients/parents and the possible side effects of the retinoids were explained in detail. Only those married females were enrolled who agreed to strictly adhere to dual methods of contraception. Topical tretinoin 0.05 mg was applied onto the surface of facial warts daily at night in group A for 3 months. Oral Isotretinoin 0.5 mg/kg body weight was given to those in group B. Response to treatment was observed initially after 1 month and later after 3 months. Treatment was stopped after 3 months and declared successful if all the lesions have disappeared by the end of 3 months. The participants who showed complete clearance were then followed up monthly for an additional 3 months to document the recurrences.

Patient's hospital ID, name, age, gender, duration of lesions, lesion count and previous treatment received if any were all documented. The outcome variable, i.e., clearance of warts was noted after 3 months and the recurrences were recorded at the end of 6 months.

The Statistical Package for Social Sciences (SPSS) version 24 was used to interpret the research results. Quantitative variables like age and duration of illness were computed by using the mean and standard deviation while gender and efficacy were estimated in terms of frequencies and percentages.

Stratification was used to control the confounding variables like age, gender, and duration of warts. Chi-square test was used to examine the efficacy within groups. P-value of lower than or equivalent to 0.05 was considered as significant.

## RESULTS

In our study, a total of 106 patients participated, which were divided by block randomization into group A and group B. Subjects of this study had ages from 14–53 years and the average age was 19.34±6.557 years. Most participants i.e.,78 (73.58%) was between the age of 14–20. 19.98±7.086 years was the average age of participants in group A and in group B it was 18.70±5.979 years. Out of 106 research subjects, 61 (57.54%) were males and 45 (42.45) were females. Mean duration of disease was 9.49±4.719 months, i.e., in group A 9.53±5.060 months and in group B 9.45±4.401 months. Efficacy-wise, 30 (56.60%) participants from group A had a successful response while in group B, the warts were completely removed in 42 (79.24) patients. $p$=0.01253 (Table 1)

Four patients from both successfully treated groups, i.e., 13.3% from group A and 9.3% from group B encountered recurrence. $p$=0.612

Stratification was done for gender, number of years, total time of illness till treatment and lesion count. (Table 2).

**Table-1: Efficacy (n=106)**

| Efficacy | Group A | Group B | *p*-value |
|---|---|---|---|
| Yes | 30 (56.60) | 42 | 0.01253 |
| No | 23 | 11 | |

**Table-2: Stratification of efficacy with respect to gender, age, duration and number of Lesions**

| | | Efficacy | Group A (n=53) | Group B (n=53) | *p*-Value |
|---|---|---|---|---|---|
| **Gender** | Male | yes | 16 | 26 | 0.0688 |
| | | no | 12 | 7 | |
| | Female | yes | 14 | 16 | 0.0896 |
| | | no | 11 | 4 | |
| **Age in years** | 42,8,3,36,13,4 14-20 | yes | 25 | 32 | 0.003 |
| | | no | 17 | 4 | |
| | 21-30 | yes | 4 | 8 | 0.603 |
| | | no | 4 | 5 | |
| | >30 | yes | 1 | 2 | |
| | | no | 2 | 2 | |
| **Duration of Disease** | ≤6 months | yes | 10 | 15 | 0.032 |
| | | no | 8 | 2 | |
| | >6 months | yes | 20 | 27 | 0.111 |
| | | no | 15 | 9 | |
| **Number of lesions** | ≤10 | yes | 8 | 13 | 0.006 |
| | | no | 3 | 3 | |
| | >10 | yes | 22 | 29 | 0.015 |
| | | no | 20 | 8 | |

## DISCUSSION

In this clinical trial, the results after 3 months has determined that oral Isotretinoin cleared facial plane warts in significantly higher number of patients when compared with topical tretinoin 0.05% cream. And a total of 8 patients, i.e., 4 patients from each group, experienced a recrudescence of the lesions.

Singh *et al*. concluded in their research that 8 (26.93%) patients treated with topical 0.05 % tretinoin showed good response while in 13 (48.15%) patients, the response was excellent.[9] Topical administration of a natural retinoid obtained from fish liver oil was found efficacious in treating recalcitrant warts on the back of a hand in a female patient.[10]

Adapalene a third-generation retinoid, produced excellent results in 26 (59.09%) children with common and plane warts and satisfactory improvement in 11 (25%) cases, as mentioned by Gupta et al. In 7 (15.9%) cases the treatment failed to produce any improvement. 13.64% (6) patients developed mild side effects, including dryness and itching.[11]

Nooruldin *et al* inducted 40 subjects in their clinical study to determine the efficacy of isotretinoin in warts. 37.5 % (15) cases having plane warts have exhibited complete remission when treated with oral Isotretinoin for three months.[12] Topical tretinoin 0.05% led to complete clearance of lesions in 84.6% of cases in case-control research in comparison to control group that depicted clearance in 32% of the cases.[13]

Nofal *et al* assessed the role of retinoids in the treatment of warts and concluded that both oral acitretin and isotretinoin are efficacious and safe.[14] In a comparative trial by Akram *et al* efficacy of topical 0.05% tretinoin cream was compared with 5% KOH in the management of facial warts. They reported that 0.05% tretinoin cream produced desired outcome in 28% of the cases.[15]

In a case report by Białecka *et al* oral isotretinoin was found successful in management recalcitrant warts.[16] Kosumi *et al* presented two case reports and reviewed the literature on treatment of disseminated warts, in immune compromised patients by systemic retinoid. Oral retinoids have shown promising results.[17]

Pasmatzi *et al* in a case report while treating an immunocompetent person, having resistant and widely distributed common warts, noticed complete disappearance of lesions after 6 weeks of treatment with oral Isotretinoin (1 mg/kg/day). The patient was followed up for 2 years and no recurrence was reported.[18]Fourteen immunocompetent patients with resistant warts have shown good response when treated with oral isotretinoin as reported in a case series.[19]

Topical isotretinoin gel has achieved complete remission in 38% of the cases having plane warts while oral isotretinoin was found effective in 69% as established in a clinical trial. Also 5 (31%) patients treated with topical gel formulation and 6(46%) patients with oral Isotretinoin showed partial improvement.[7] Olguin-García MG *et al* compared isotretinoin with placebo in managing facial warts and found it superior to placebo and cheilitis was the only documented side effect.[20]

## CONCLUSION

This study proved the effectiveness of oral isotretinoin in managing the cases of verruca plana involving the face, when compared with topical 0.05% tretinoin cream. So, it is recommended to use oral Isotretinoin as the primary option in suitable patients, especially males as they don't carry the risk of teratogenicity.

## AUTHORS CONTRIBUTION

HG: Conceptualization, data collection, data analysis. and interpretation, literature search, write. ZK: Concept, literature review, Data Analysis, interpretation, proof reading, supervision. ZBJ: Literature review, data analysis, interpretation

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