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Evaluation of the Efficacy of Acitretin in the Treatment of Multiple Viral Warts: A Pilot Study

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ABSTRACT

Background: Wart treatment should be painless, safe, time-efficient, and cost-effective, according to the ideal model. **Objective:** To study patients with widespread recalcitrant warts to see if oral acitretin was clinically effective and safe. **Patients and Methods:** A total of 21 patients with multiple recalcitrant warts were studied in this study. At Zagazig University Hospitals, they were recruited from the Dermatology and Venereology Outpatient Clinic. For a maximum of four months, the patients received oral acitretin at a dose of (0.5 mg/Kg/day) until complete clearance.

Results: There were a total of 21 participants in the study. They ranged in age from 18 to 59 years old, with 11 males and 10 females; 52.4 percent, 47.6 percent respectively. Four patients (19%) showed complete response to the treatment, 12 patients (57.2%) showed partial response and 5 patients (23.8%) showed no response. With no patients stopping treatment because of side effects, the medication was found to be safe. Dry skin and cheilitis were the most common mild side effects observed. During a three-month follow-up period, there were no recurrences.

Conclusion: Patients with recalcitrant multiple warts respond favourably to the safe, effective, and well-tolerated treatment with acitretin.

Keywords: Acitretin, Recalcitrant, Treatment, Wart.

INTRODUCTION

Verrucae, or warts, affect the skin's epithelium and are thought to be the result of a human papillomavirus infection (HPV). About 7 to 10 percent of the population will develop warts at some point in their lives. Heat and moisture, such as those found in public swimming pools and locker rooms, are ideal habitats for the HPV, which is spread through direct touch or even small scratches or abrasions in the skin's stratum corneum. Autoinoculation is another method through which warts can spread locally to infect other parts of the body. Children and adults with impaired immune systems are more likely than healthy people to contract the virus and develop more severe lesions [1].

Based on DNA research and serological identification of type-specific antibodies against HPV capsid antigens, numerous HPV strains have been discovered. Papillomaviruses have over 200 distinct genotypes that are more typically associated with benign epithelial lesions [2].

HPV types 1, 2, 4, and 7 are the most common cause of warts on the hands and feet, but the genital tract is infected by more than 35 different types of HPV. HPV types 6, 11, 42, 44, and 70 are linked to low-risk anogenital warts, while HPV types 16, 18, 31, 33, 45, and 59 are most frequently linked to cervix squamous cell and adenocarcinomas [3,4].

Recalcitrant warts are those that remain throughout several months of conventional therapy despite the lack of a clear definition for the term. Plantar and periungual warts, in particular, can develop refractory in up to one-third of patients with non-genital warts. The size of the affected area, rather than the length of time the warts have been there, is what determines the recalcitrance of genital warts [5,6]. There are a variety of wart treatments available, many of which have little or no evidence to support their utility. As a rule, the best treatment should leave no scars [7].

A precise antiviral treatment for HPV is not yet available, but a few other medicines can disrupt the viral life cycle. The treatment's goals are to either kill the wart on the skin's surface or boost the immune system's ability to combat the virus [8]. Warts can be treated with a variety of methods that are both destructive and anti-mitotic, as well as immunotherapeutic. Surgical removal, cryocoagulation, electro-cautery, chemical cautery (salicylic acid 70% and trichloroacetic acid (TCA)), and laser ablations are examples of destructive therapy. Bleomycin, retinoids (tretinoin cream, isotretinoin, acitretin) and podophyllin are anti-mitotic medicines. Zinc sulfate, diphenylcyclopropenone, 5-flurouracil, and intralesional injection of an antigen are examples of immunotherapeutic drugs[9].

Warts such as epidermodysplasia verruciformis, condyloma acuminatum, and epidermodysplasia verruciformis can be treated with oral acitretin [10]. Psoriasis and other disorders of keratinization have been widely treated with acitretin because of its

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immunomodulatory, anti-proliferative, and anti-differentiative effects [11].

Acitretin medication is only successful if the right patients are chosen. In particular, pregnant women and individuals with other medical conditions, such as mood disorders and alcoholism, should avoid this medication [12]. The objective of this study was to study patients with severe recalcitrant warts to determine the effectiveness and safety of acitretin.

PATIENTS AND METHODS

A total of 21 patients with multiple recalcitrant warts were studied in this study. At Zagazig University Hospitals, they were recruited from the Dermatology and Venereology Outpatient Clinic. For a maximum of four months, the patients received oral acitretin at a dose of (0.5 mg/Kg/day) until complete clearance.

History-taking, including personal and current history, with focus on the beginning, course and duration of the disease, was required of all patients. History of systemic disorders, such as diabetes, hypertension, and hyperlipidemia, and previous treatment and family history of a comparable ailment were also included. General physical examination is part of the comprehensive clinical evaluation and a thorough dermatological exam: Each follow-up appointment was used to determine the kind, quantity, and location of warts. Clinical examination was used to make the diagnosis of warts, and participants were asked not to use any other wart treatments while they were enrolled in the trial. Adults of both sexes aged 18 or older with at least three multiple of warts were included in the research.

Exclusion of patients was done when (a) They were either pregnant, breast feeding, (b) They were suffering from significant heart, liver, and/or kidney disease, as well as endocrine and/or lipid metabolic disorders, or (c) Patients who had utilized alternative wart removal methods during the month before to the study's start date. Acitretin 25 mg was administered orally to the patients at a dose of (0.5 mg/Kg/day) until the condition was fully cleared, which could take up to four months.

Due to adverse effects including dryness or itching, patients were also instructed to apply lip balm and moisturiser to help them stick to their treatment plan. For a total of four months, fasting lipid profile and liver function tests were examined before therapy and every month during treatment. Wart size reduction and photographic comparisons were used to assess treatment response both at the beginning and on a monthly basis.

Results were judged as. (1) Complete response; returning the skin's normal identifying features after the wart had vanished, (2) Incomplete response; reduction in the size of the warts to some extent and (3) No response; There has been no reduction in the size of the warts. Adverse effects of acitretin were evaluated each visit for 4 months.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Qualitative data were represented as frequencies and relative percentages. Quantitative data were expressed as mean ± SD (Standard deviation), median, and range.

RESULTS

Twenty-one patients received oral acitretin. Their demographic data are shown in table 1**.**

Table (1): Demographic data of the patients

Parameter	N=21(%)
Gender:	
• Female	10 (47.6)
• Male	11 (52.4)
Age (years):	
• Mean ± SD	32.286 ± 13.161
• Range	18 – 59

The symptoms at the start of the study were mainly cosmetic disfigurement. Disease duration ranged from 5 to 36 months **(Table 2).**

Table (2): symptoms and disease duration

Parameters	Group
	N=21 (%)
Symptoms:	
• Cosmetic disfigurement	8 (38.1)
• Itching	2 (9.5)
• Pain	5 (23.8)
Disease duration (months):	
• Mean ± SD	10.38 ± 7.28
• Median (range)	8 (5 – 36)

The mean number of lesions was 12.38. The most common type of the warts was common warts and the most common site was the hand (Table 3).

Table (3): Disease-specific characteristics

Parameter	N=21 (%)
Number of wart:	
• Mean ± SD	12.38 ± 9.589
• Median (Range)	8 (3 – 32)
Type of wart:	
• Common	17 (81)
• Filiform	0 (0)
• Plantar	6 (28.6)
• plane	3 (14.3)
Site of wart:	
• Face and hand	1 (4.8)
• Hand	11 (52.4)
• feet	8 (38.1)
• Hand and feet	1 (4.8)
• Leg	0 (0)

Most of the patients showed partial response **(Table 4)**.

Table (4): Response to treatment

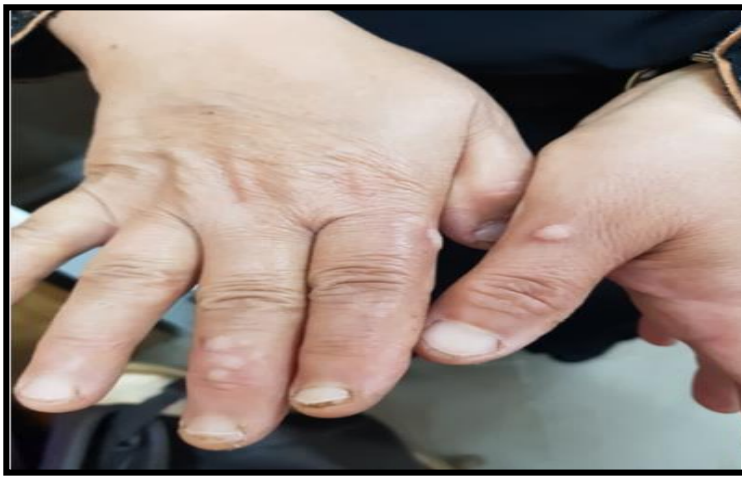
Response	N=21 (%)
Complete	4 (19)
Partial	12 (57.2)
No response	5 (23.8)

Adverse effects were tolerated by most of patients. Sixteen patients (76.2%) had no side effects **(Table 5).**

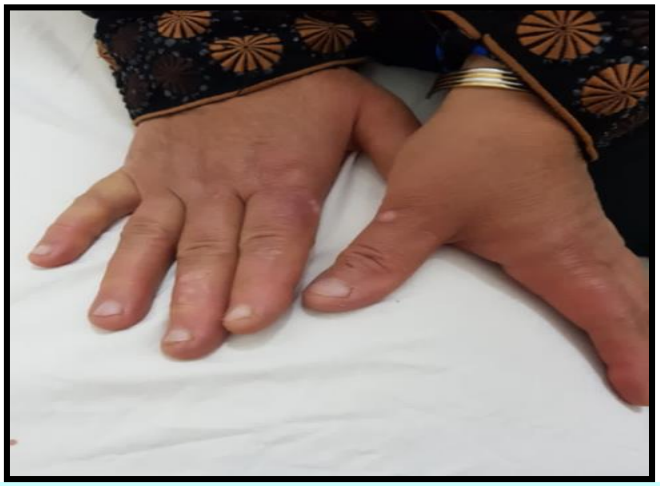
Table (5): Side effects of acitretin treatment

Response	N=21 (%)
No	16 (76.2)
GIT disturbances	0 (0)
Hypercholesterolemia	1 (4.8)
Xerosis	4 (19)

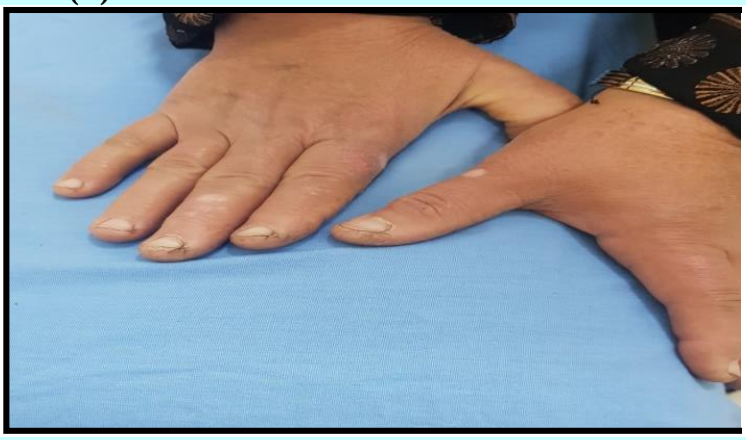
There was a period of follow up for 3 months after the end of the 4 months-treatment therapy and no patient showed relapse after the end of the treatment.



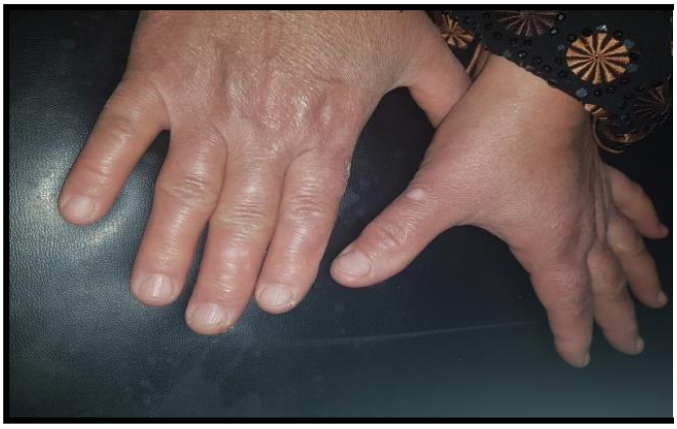
(A): Common warts before use of oral acitretin



(B): Partial response after 2 months



(C): Marked response after 3 months



(c): Complete response after 4 months

Figure (1): A 53 year-old female, with common warts on both hands, showed complete response after 4 months of oral acitretin treatment.

DISCUSSION

There are few side effects associated with acitretin, making it the most commonly prescribed systemic retinoid in dermatology [13]. Systemic acitretin has been shown to be useful in the treatment of warts in numerous investigations. The effectiveness, safety, and side effects of acitretin in the treatment of resistant extra genital warts were examined in the current study. Twenty one patients were treated by oral acitretin (0.5 mg/Kg/day) until complete clearance of warts for a maximum duration of 4 months. Treatment was successful in four patients (19 percent), partially effective in twelve patients (57 percent), and ineffective in five patients (23.8%).

Gharib *et al.* [14] have also studied how acitretin can be used to treat recalcitrant warts. Patients with several recalcitrant warts were treated with varying doses of oral acitretin. Seventy percent of patients treated with (1 mg/kg/day) for three months had their warts cleared completely, and there had been no relapses in the six months after the end of treatment. They also found that warts disappeared in 80 percent of patients who took acitretin for three months at a low dose of 0.5 mg/kg/day.

The fact that these results differ from those of the current study could be ascribed to the fact that the number of individuals analysed and the type of warts studied were different. Individual case reports in immune-competent patients have showed potential efficacy for the treatment of recalcitrant warts with acitretin [13,15,16] and immune-compromised patients [12].

In our study, no statistically significant relationship was found between the therapeutic response to acitretin therapy and the different clinical variables including; age, sex, site, type of warts, number of lesions and disease duration. This came in contrast with **Gharib *et al.*** [14] who found that the clinical reaction to warts is strongly correlated with the duration of the warts, despite the fact that this link was predicted to be the other way around.

CONCLUSION

Acitretin is an effective, safe, well-tolerated, noninvasive and inexpensive alternative systemic therapy for extensive and recalcitrant warts who are unsuitable for accepting traditional treatment methods especially on the hands and feet.

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