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Efficacy and Safety of Intralesional 5-Flurouracil in Treatment of Warts

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ABSTRACT

Background: Warts are common benign skin lesions caused by human papillomavirus (HPV), with varying clinical presentations based on the type of HPV and site of infection. Treatment options aim to eliminate the infected epidermis, but pain, side effects, and cost influence treatment choice. 5-Fluorouracil (5-FU), an antimetabolite, has been explored as a potential treatment, with intralesional administration offering improved efficacy over topical application. **Objective:** This study aimed to evaluate the efficacy and safety of intralesional 5-FU in the treatment of warts. **Methods:** A cross-sectional observational study was conducted between January and June 2024, enrolling 85 patients from the Dermatology Department at Pakistan Emirates Military Hospital. Intralesional 5-FU (0.1 ml/cm², 50 mg/ml) was administered biweekly, with a maximum of six injections. Patients were monitored fortnightly for two months' post-treatment. Clinical improvement was assessed based on predefined efficacy grades: excellent (75–100% improvement), good (50–74% improvement), satisfactory (25–49% improvement), and poor (<25% improvement). Data analysis was performed using IBM-SPSS 21.0, with statistical significance set at $p \leq 0.05$. **Results:** Of the 85 patients, 64 (75.3%) exhibited an excellent response, primarily after the second and third injections. Eleven patients (12.9%) showed a good response, six (7.1%) had a satisfactory response, and four (4.7%) demonstrated poor improvement. The treatment was well tolerated, with minor adverse effects such as erythema and oedema, and no cases of necrosis or scarring. **Conclusion:** Intralesional 5-FU demonstrated significant efficacy in wart treatment, with a favourable safety profile. These findings support its use as an effective alternative for managing recalcitrant warts, warranting further research to optimize treatment protocols.

INTRODUCTION

Warts or verrucae represent prevalent, benign skin lesions resulting from human papillomavirus infection [1]. They constitute a common dermatological condition, with an incidence of approximately 33% among children aged 6 to 12 years and around 3.5% among adults [2]. The clinical presentation of warts exhibits variability, influenced in part by the specific type of HPV involved and the site of infection [3]. The term 'warts' encompasses various wart types and occasionally encompasses wart-like conditions not associated with HPV infection, such as seborrheic keratosis. Warts are categorized based on their locations and morphologies as (I) Common wart, (II) Plantar wart, (III) Plane wart, and (IV) Genital wart (condyloma accuminatum) [4].

The common treatment methods for warts focus on eliminating the virus-infected epidermis. These methods encompass various approaches such as topical applications like salicylic acid [5], 3-glutaraldehyde [6], and retinoic acid [7], as well as procedures like electrocoagulation [8], cryotherapy [9], and the utilization of CO_2 lasers [10]. Pain associated with treatment, side effects, and cost can significantly influence the selection of a therapeutic approach [11].

Furthermore, 5-Fluorouracil (5-FU) serves as an antimetabolite utilized either independently or in conjunction with other chemotherapeutic compounds in the treatment of solid tumors. Classified as a pyrimidine analogue, its structural composition enables disruption of nucleoside metabolism. Incorporation into RNA's single helix and DNA's double helix ensues, leading to cell cytotoxicity and eventual cell death [12, 13].

In addition, 5-Fluorouracil (FU) functions as an antimetabolite, impeding cell division and inducing cell cycle arrest [14]. While topical 5-FU is employed in wart treatment, its efficacy is limited [15]. Intralesional administration of 5-FU allows for increased drug concentrations within the lesion, as demonstrated in prior studies highlighting its effectiveness in treating warts [16]. Therefore, this study aims to assess the

efficacy and safety of intralesional 5-fluorouracil in treating warts.

METHODOLOGY

Between January 2024 and June 2024, a cross-sectional observational study enrolled 85 wart patients from the Dermatology Department at Pakistan Emirates Military Hospital. The study aimed to include a total of 85 patients to evaluate the efficacy and safety of intralesional 5-fluorouracil by estimating a proportion or apparent prevalence with a specific precision, considering an estimated true proportion of 0.33, a desired precision of 10%, and a confidence level of 0.95, given a population size of 85 patients over six months. All patients provided written informed consent, and ethical clearance was obtained from the appropriate hospital authorities. Eligible participants, aged ≥12 years, of either sex, diagnosed clinically with warts on anybody site, were enrolled. Exclusion criteria included patients with more than five warts, pregnant or lactating women, and individuals with vascular, cardiovascular, renal, or hepatic conditions.

Intralesional injections of 0.1ml/cm² of 5-FU (50mg/ml) were administered at the base of each wart after the area was cleansed with isopropyl alcohol. Injections were repeated biweekly, up to a maximum of six injections. Patients were monitored fortnightly for up to two months following the final injection, and evaluation was based on clinical improvement. Efficacy was assessed across four grades: excellent (75–100% improvement), good (50–74% improvement), satisfactory (25–49% improvement), and poor (<25% improvement).

Statistical Analysis

The data were verified, coded, and analyzed using IBM-SPSS 21.0 (IBM SPSS Inc., Chicago, IL, USA). Descriptive statistics, including means, standard deviations, medians, ranges, and percentages, were calculated. The chi-square test was employed to compare frequency distribution differences among efficacy grades versus sex. A significance level of $p \leq 0.05$ was considered statistically significant.

RESULTS

Table 1 presents the demographic and clinical characteristics of all 85 patients included in the study. The mean age of the participants was 30.7 years (±10.3). The majority of the patients were female (59, 69.4%), while males accounted for 26 (30.6%). The average duration of warts was 7.1 months (±2.7). Regarding the site of involvement, warts were most commonly found on the feet (39, 45.9%), followed by the hands (29, 34.1%) and the genital region (17, 20.0%).

Table 1

Demographic and clinical characteristics of all the patients (n = 85).

Variables	Categories	n (%)
Age	mean ± S.D	30.7 ± 10.3
Sex	Male	26 (30.6)
	Female	59 (69.4)
Duration of warts (months)	mean ± S.D	7.1 ± 2.7
Site of Involvement	Genital	17 (20.0)
	Hand	29 (34.1)
	Feet	39 (45.9)

Table 2 summarizes the efficacy of 5-fluorouracil treatment across follow-up visits for the 85 patients included in the study. A total of 64 patients (75.3%) demonstrated an excellent response (75–100% improvement), with the majority achieving significant improvement after the second (34 patients) and third (29 patients) injections. Eleven patients (12.9%) showed a good response (50–74% improvement), with improvements observed mainly after the third (3 patients), fourth (4 patients), and fifth (4 patients) injections. Six patients (7.1%) experienced a satisfactory response (25–49% improvement), with one patient improving after the fifth injection and five after the sixth. Four patients (4.7%) showed a poor response (<25% improvement), with no significant progress throughout the treatment course.

Table 2

Efficacy of 5-fluorouracil treatment on follow up visits (n = 85).

Responses	No of Pts	1st inj.	2nd inj.	3rd inj.	4th inj.	5th inj.	6th inj.
Excellent (75-100% improvement)	64		8	34	29	14	
Good (50-74% improvement)	11				3	4	4
Satisfactory (25-49% improvement)	6					1	5
Poor (<25% improvement)	4						4

DISCUSSION

Warts affecting the palmoplantar region and genital area pose a significant therapeutic challenge, necessitating ongoing research into effective treatment options. 5-Fluorouracil (5-FU), an antimetabolite, inhibits cell division and induces cell cycle arrest, making it a potential treatment for warts [17]. Historically, topical 5-FU was explored as a treatment, with most studies conducted in the 1970s and 1980s. However, the efficacy of this approach was limited due to variations in study design and methodology, leading to the general consensus that topical 5-FU was not highly effective [18].

Intralesional administration of 5-FU offers distinct advantages over topical application. The typical

intralesional dose for wart treatment ranges between 2–6 mg, which is significantly lower than the systemic therapeutic dose (less than 1/150th), thereby minimizing systemic adverse effects [19]. This mode of administration ensures direct drug delivery to the affected tissue, enhancing efficacy while reducing systemic toxicity.

Several studies have demonstrated the effectiveness of intralesional 5-FU in wart treatment [19]. reported an overall response rate of 82.3%, with 64.7% of patients achieving complete resolution and 17.6% showing partial improvement. Successfully utilized intralesional 5-FU for treating condylomata acuminata [18]. The findings of the present study align with these results, as 70% of patients exhibited an excellent response. Similarly, a study by Iscimen et al [19]. investigating the use of intralesional 5-FU for common plantar warts found a complete clearance rate of 70%.

A study conducted by Srivastava et al. further supports the efficacy of intralesional 5-FU in wart treatment. Their findings indicated a complete response in 95.38% of patients, demonstrating that intralesional 5-FU is both an effective and safe therapeutic option for palmoplantar warts [20]. Adverse effects associated with intralesional 5-FU were generally mild, with erythema and oedema being the most commonly reported. Importantly, no cases of necrosis or scarring were observed, highlighting the favorable safety profile of this treatment approach [19].

CONCLUSION

Intralesional 5-fluorouracil is a highly effective, safe, and cost-efficient alternative for the treatment of warts, demonstrating particularly strong efficacy in the management of genital warts.

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