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Article

Intralesional Acyclovir for Cutaneous Warts

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ABSTRACT

Cutaneous warts are a common skin problem in routine dermatological practice. There are many clinical modalities, but there are failure and recurrence. The current study aimed to evaluate the efficacy and safety of intralesional acyclovir in treating cutaneous warts. An analytic clinical trial study was conducted in Iraq/Baghdad/Al-Yarmouk Teaching Hospital from November 2021 to May 2022. The current study adopted A convenient sampling method to enroll 30 patients with cutaneous warts. The patients had intralesional acyclovir (70 mg/ml) injected into warts. The treatment was repeated at two-week intervals until complete clearance or for a maximum of 5 sessions. According to the current study's results, 30 patients were enrolled in the current study. The mean age was 23.7 (±12.7) years. Most of the patients had an age of more than 14 years. Females constituted more than half of the sample. Regarding the treatment outcome, 19 (63.3%) patients were cured, and 10 (33.3%) failed to cure. In comparison, one patient had a recurrence after being cured in three sessions. Regarding the patients who were cured, 8 (42.1%) patients were cured in two sessions, 6 (31.6%) were cured in three sessions, 2 (10.5%) were cured in one session, and 2 (10.5%) patients were cured in four sessions. In contrast, 1 (5.3%) patient was cured in five sessions. Severe pain during injection was the commonest side effect (66.6%), followed by bullous reaction (30%0), bleeding at the site of injection (20.0), and pain for a few days (16.7%). In conclusion, intralesional acyclovir was found to be effective and safe with few and transient side effects.

Keyword: Cutaneous; Patients; Bleeding.

INTRODUCTION

Warts are cutaneous and, sometimes, mucosal lesions caused by one of the several human papillomaviruses (HPV); they are the third most common skin disease encountered in practice[1]. The HPV are small 50 to 55-nm-diameter deoxyribonucleic acid (DNA) viruses that infect squamous epithelia, causing cell proliferation. They form a large group of closely related viruses, distinguished from one another based on their DNA. To date, about 100 types have been recognized and characterized[2]. Small defects of the skin are sufficient to allow the virus to infect the basal layer of the skin, which may lead to benign hyperkeratotic papillomas. Warts are very common in the general population, especially among children. The

prevalence of warts among primary schoolchildren is reported to be 22% to 33%,2,3, while the annual prevalence based on consultations in general practice is about 6%[3]. Warts represent a self-limiting condition, so that a wait-and-see approach may be justified. However, treatment is always indicated if the lesions become painful or give rise to psychological discomfort. Factors to be considered in this context include subjective disease burden, patient age, site affected, and the number and duration of lesions[4]. Initial treatment usually involves daily application of salicylic acid in liquid, film, or plaster form after soaking, cryotherapy with a second freeze-thaw cycle, bleomycin injections, laser therapy, topical immunotherapy, CO2 laser, photodynamic therapy and surgical destruction with cautery or blunt dissection. The latter option should be reserved for failures with nonscarring techniques since a plantar scar may be persistently painful. Salicylic acid (ortho-hydroxybenzoic acid) is a beta hydroxy acid agent. It is a first-line therapy that is usually chosen as it is available over the counter[2]. The viral origin of warts suggests that acyclovir, an antiviral drug with proven efficacy in DNA viruses, maybe a potential therapeutic option [5,8]. To evaluate the efficacy and safety of intralesional acyclovir in the treatment of cutaneous warts

MATERIALS AND METHODS

Study Design and Setting

A clinical therapeutic trial study was conducted in Iraq/Baghdad/Al-Yarmouk Teaching Hospital from November 2021 to May 2022.

Ethical Approval

The study has been proposed and subsequently approved by the scientific committee of the College of Medicine/ Tikrit University. Fully informed consent was obtained from the patients verbally after explaining the aim of the study thoroughly and clearly. All the information and questions were communicated to the patients precisely to avoid bias as much as possible.

Study Population

Sampling Method

The current study adopted A convenient sampling method to enroll 30 patients with cutaneous warts.

Inclusion Criteria

Patients who were presented with a common, plane, subungual warts.

Exclusion Criteria

1. Severe immunosuppression
2. Extreme age
3. Patients refusal
4. Patients received other treatment modalities within the previous month

Intervention

The patients had intralesional acyclovir (70 mg/ml) injected into warts. The treatment was repeated at two-week intervals until complete clearance or for a maximum of 5 sessions. The researcher prepared the acyclovir dose of 70 mg/ml using an acyclovir vial with a dose of 250 mg (Figure 3.1) and diluted in 3.5 ml distilled water. Before the intervention, the researcher explained the treatment modalities to the patients, including the expected side effects and their duration and severity, treatment duration, and the number of sessions. Afterward, the patients were put in a comfortable position, sitting or lying, according to the site of the warts. A proper antiseptic was used before injection. An insulin syringe with a 30 gauge needle was used for intralesional injection to the base of warts at 45 angle degrees. About

0.1-0.5 ml was injected according to the size of the warts. In some cases with large warts, more than one injection was needed. For those with multiple warts, the researcher gave them time to rest between injections. After the end of the session, the researcher communicated with the patients or relatives through mobile to ask about the side effects and gave them the date of the next session.

Data Collection

The data was obtained using a structured questionnaire that the researcher adopted after a review of similar articles with revision by the supervisor. The questionnaire included three parts:
Part one: Sociodemographic characteristics, including age, gender, and residence.
Part two: Medical history and examination included past medical history and current dermatological presentation.
Part three: Follow-up chart including the treatment outcome (no response and complete clearance). In addition to the follow-up of the side effects (bullous reaction, pain for a few days, pigmentation, blisters, bleeding, infection, allergy, scarring, or any other complications).

Statistical Analysis

The collected data were analyzed using Microsoft Excel software, version 2016, and Statistical Package for the Social Sciences, version 22. The descriptive analysis focused on frequencies and percentages. Categorical data were presented as proportions, and the chi-square test was used for the difference between the two proportions. A P-value of less than 0.05 will be considered statistically significant.

RESULTS

A total of 30 patients were enrolled in the current study. All the patients completed the recommended sessions, and the study was not dropped. The mean age was 23.7 (±12.7) years. Most of the patients had an age of more than 14 years. Females constituted more than half of the sample. As shown in table 1.

Soscidempgraphic history		N	%
Age group (years)	≤14	5	16.7
	>14	25	83.3
Gender	Male	14	46.7
	Female	16	53.3
Residency	Urban	9	30.0
	Rural	21	70.0

Table 1. Soscidempgraphic history of the patients.

Five patients had a history of chronic disease, two had diabetes, and three had hypertension, chronic obstructive lung disease, and chronic kidney disease, as shown in Figure 1.

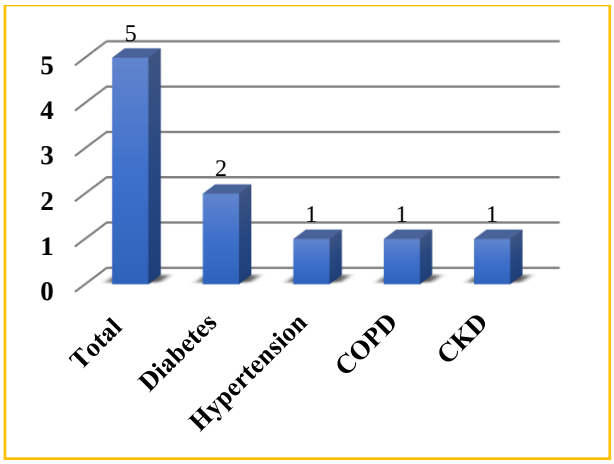

Figure 1. Distribution of the chronic disease.

Regarding the treatment outcome, 19 (63.3%) patients were cured, and 10 (33.3%) failed to cure. One patient had recurrence after being cured in three sessions, as shown in Figure 2.

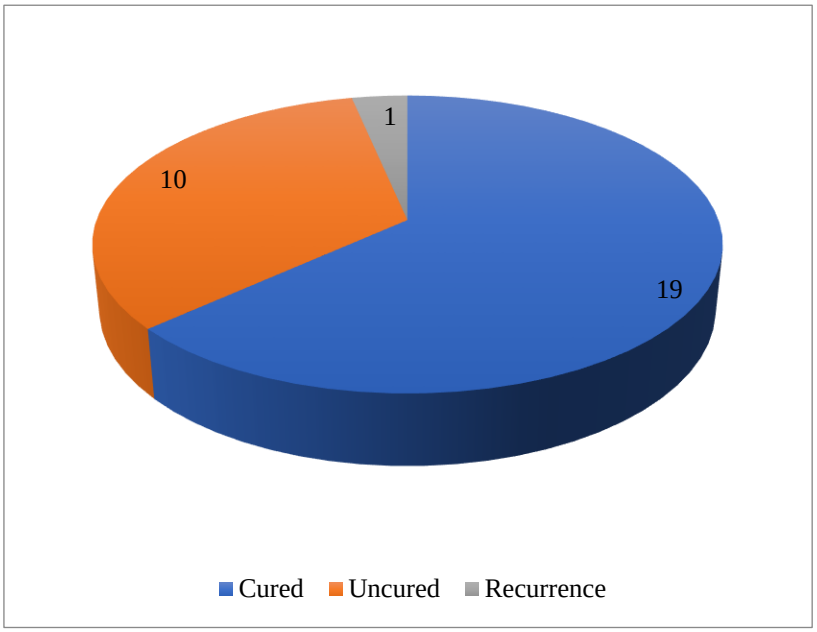

Figure 2. The outcome of the treatment

Regarding the patients who were cured, 8 (42.1%) patients were cured in two sessions, 6 (31.6%) were cured in three sessions, 2 (10.5%) were cured in one session, and 2 (10.5%) patients were cured in four sessions. At the same time, 1 (5.3%) patient was cured in five sessions. As shown in figure 3.

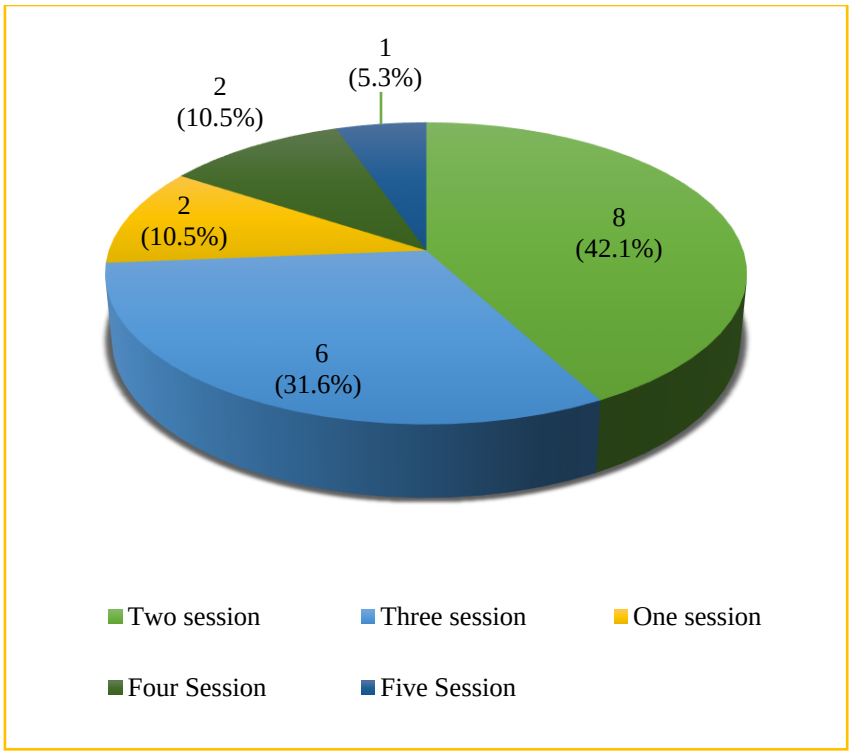

Figure 3. Distribution of patients with cure outcomes according to the number of sessions (N=19)

Most patients had common warts (80.0%). There was no significant association between the type of warts and the treatment outcome; plain warts had the lowest cured rate, as shown in Table 2.

Type	outcome			Total
	Cured	Uncured	Recurrence	
Common warts	16 (66.7)	7 (29.2)	1 (4.2)	24 (80.0)
Periungual	3 (100.0)	0 (0.0)	0 (0.0)	3 (10.0)
Plane warts	0 (0.0)	3 (100.0)	0 (0.0)	3 (10.0)
Total	19 (63.3)	10 (33.3)	1 (3.3)	30
P-value	0.093			

Table 2. Distribution of the outcome results according to the type of disease.[1]Chi-Square test

There were no significant associations between the age and gender of the patients and outcomes of treatment (Table 3).

Age and gender		Treatment outcome			P-value
		Cured N (%)	Uncured N (%)	Recurrence N (%)	
Age group (years)	<20	3 (60.0)	2 (40.0)	0 (0.0)	0.865
	≥60	16 (64.0)	8 (32.0)	1 (4.0)	
Gender	Male	7 (50.0)	6 (42.9)	1 (7.1)	0.273
	Female	12 (75.0)	4 (25.0)	0 (0.0)	

Table 3. Association between the age, gender and outcome of the treatment [1]Chi-Square test

Severe pain during injection was the most common side effect (66.6%), followed by bullous reaction (30%0), bleeding at the site of injection (20.0), and pain for a few days (16.7%), as shown in Table 4.

Complications	N	%
Severe pain during injection	20	66.6
Bullous reaction	9	30.0
Bleeding	6	20.0
Pain for a few days	5	16.7
Pigmentation	2	6.7
Blister	1	3.3
Allergy[1]	3	10.0
Others[2]	1	3.3
Infection	0	0.0
Scarring	0	0.0

Table 4. Complications of treatment. [1]patients developed itching at the injection site, lasting for a few days. [2]patient developed vasovagal attacks after injection and resolved spontaneously.

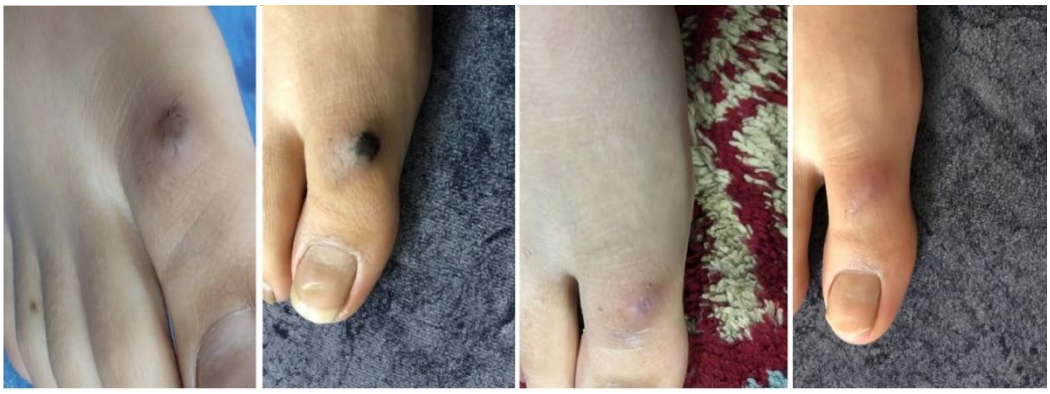

Figure 4. A 22-year-old female had one wart on the right big toe. Cured patients after four sessions

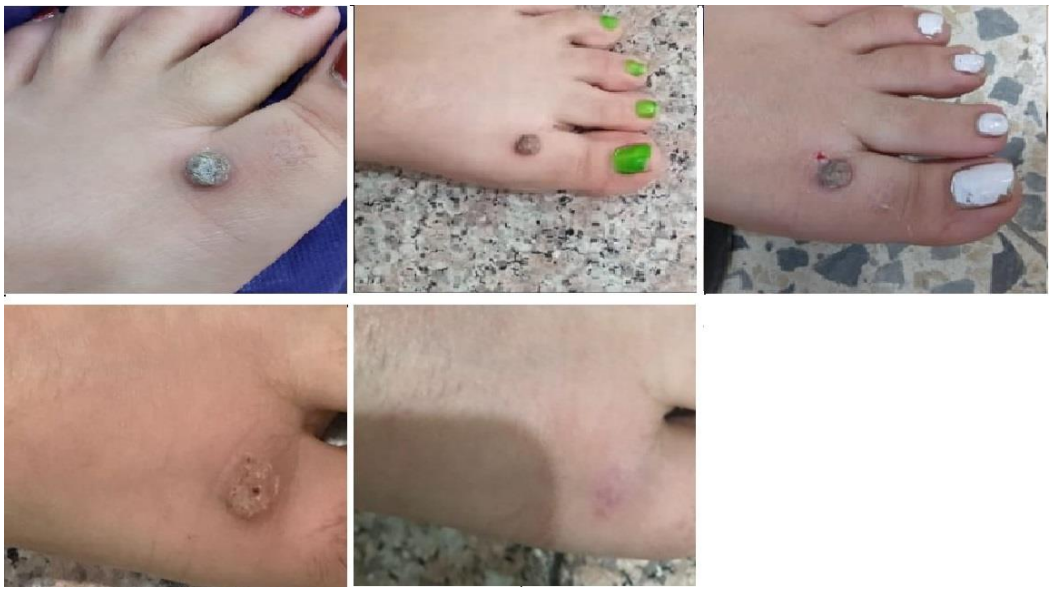

Figure 5. A 17-year-old female had one wart on the s=dorsum of the big toe. Cured patients after five sessions

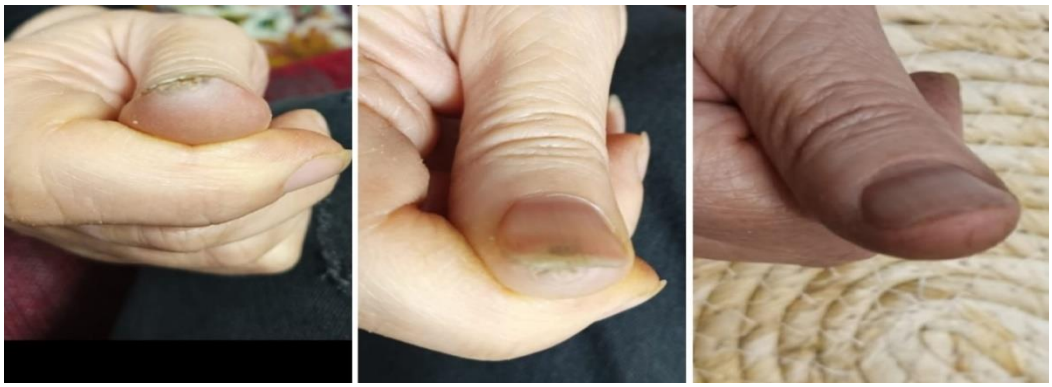

Figure 6. A 54-year-old female had one periungual wart on the right thumb. Cured patients after three sessions

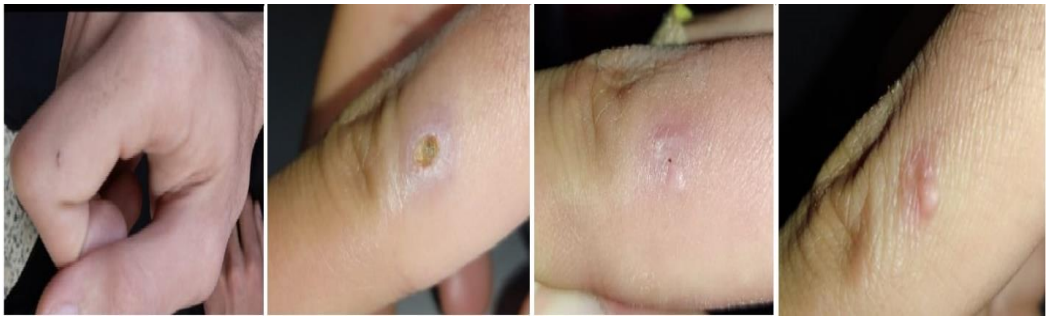

Figure 7. A 16-year-old male had one wart on the right index, cured in three sessions, then recurrence in one month

DISCUSSION

Although cutaneous warts can resolve spontaneously, these infections can persist for long periods 9. There is a very wide range of local treatments available. To our knowledge, this is the first study in Iraq to assess intralesional acyclovir's effectiveness in treating cutaneous warts[10]. The current study's first finding was that most patients had common warts (80%). In comparison, the same results were obtained in another study in Iraq in 2021, as more than half of the patients had common warts[47]. In the current study, more than half of the patients were female. The same finding was obtained in another study done in the Netherlands[11]. The main finding of the current study was that 63.3 of the patients had a complete cure. In comparison, another study done in Egypt by Ayman et al. revealed that 52.6% of the patients had complete cures [5]. In comparison to other modalities of treatment, literature research, including 23 research, was done by Christine et al. about the effectivity of Imiquimod in the treatment of cutaneous warts revealed that the combined rate of patients achieving a complete cure to therapy was 44 %, ranging from 27 to 89 %[45]. Another study in the Netherlands by Sjoerd et al. revealed that at 13 weeks, the cure rates were 39% after cryotherapy and 24% after salicylic acid topical treatment for patients with cutaneous warts[11]. In addition, bleomycin injections were associated with complete resolution in 73% of patients with cutaneous warts in another study that was done in Iran[49]. In Iraq, intralesional 5-Fluorouracil, an antimetabolite that suppresses cell division and causes cell cycle arrest, was used in the treatment of common warts and associated with a complete cure in about 60% of patients with cutaneous warts; the treatment included session every three weeks for a maximum of nine weeks[47]. Another study done in Iraq by Ihsan Mahmoud et al. to evaluate the treatment of common warts intralesional with vitamin D3 concluded that complete response was achieved in 77.7% of the patients[12]. In Italy, Intralesional cidofovir was used to treat multiple and recalcitrant cutaneous viral warts and was associated with a cure rate of 82%. Side effects

included erythema and itching during the days following the treatment (15%) and postinflammatory hyperpigmentation in their hands (20%)[13]. In the current study, 48.1% of the patients with complete cure had two sessions at two-week intervals, while the maximum duration of treatment was 2.5 months. In comparison to other options of treatment, Federica et al. revealed that the first-line therapy includes medical treatments (salicylic acid, silver nitrate, glutaraldehyde) that are useful to treat a single wart or a few and small common warts of short duration (less than 1 year). If these treatments have failed or are contraindicated, cryotherapy may be considered second-line therapy[14-16]. Severe pain during injection was the commonest side effect in the current study, followed by a bullous reaction and bleeding at the site of injection. In comparison, another study was done in Eygpt to evaluate the use of intralesional acyclovir in the treatment of cutaneous warts revealed that pain was the commonest complication during injection (89.5), followed by blistering in 52.6%, and erythema in 5.3% of the patients[17-20].

CONCLUSION

The intralesional acyclovir was found to be effective and safe with few and transient side effects.

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