

Intralesional acyclovir in the treatment of cutaneous warts: A novel therapeutic approach

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Abstract

Background Warts are the cutaneous manifestations of human papilloma virus infection. Although warts resolve spontaneously, many patients seek treatment as they can be painful and may have psychosocial impact in case of multiple cutaneous warts. Acyclovir is an antiviral medication with established efficacy against DNA viruses, could become a possible revolutionary therapeutic option for warts.

Objective The purpose of this therapeutic approach is to determine the effectiveness of intralesional injection of acyclovir in the management of cutaneous warts.

Methods A total of 18 patients with warts attending DVL outpatient department were selected for the study. Depending on the size of the lesion, the patients received 0.1ml-0.3ml of intralesional acyclovir diluted with distilled water (70mg/ml) in each lesion. The procedure was repeated every two weeks till complete clearance or upto a total of four sessions. Adverse effects were documented, and the study participants were monitored on a monthly basis for three months following the final injection to look for any relapse.

Results All 18 patients completed the study by 8weeks duration. Complete clearance was observed in 9 patients (50%), with an excellent response in 5 patients (27.7%), good response in two patients (11.11%), and no response in 2 patients (11.11%).

Conclusion Intralesional acyclovir can be an efficient therapeutic tool for solitary cutaneous warts, but it provides no added benefit for distant warts. It can be beneficial modality in patients seeking for quick response.

Key words

Warts; Acyclovir; Novel, Intralesional.

Introduction

Warts are benign epidermal proliferation caused by human papilloma virus targeting basal keratinocytes. Management is quite challenging

due to unpredictable clinical course. Various treatment modalities are available for management of warts, but no single therapy is yet approved or completely effective. We attempted intralesional acyclovir injection in treatment of warts because of its activity on HPV infected keratinocytes by decreasing viral DNA replication. Mode of administration by intralesional route was chosen to deliver higher concentration of the drug into the wart and to minimize systemic side effects associated with oral acyclovir.

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Table 1

Grade 4= Complete clearance (VAS=100%)	Complete disappearance of treated warts and skin texture at the site is restored to normal
Grade 3= Excellent response (VAS=75-99%)	Reduction in size and number of treated warts, few residual warts still visible
Grade 2= Good response (VAS=50-74%)	Some reduction in size only but no decrease in number of warts
Grade 1= Poor response (VAS≤ 50%)	No significant change in size and number of warts

This study includes 18 patients with warts treated with intralesional acyclovir (70mg/ml). Till date, only single study is available in the literature, documenting the use of acyclovir for this indication.

Methods

The current study was a prospective uncontrolled interventional study conducted from June 2021 to June 2022 in the outpatient dermatology department of a tertiary care centre after obtaining approval from the institutional ethical committee. The present study comprised 18 people who had been clinically diagnosed with warts. Exclusion criteria were children under the age of 12, pregnant and lactating women, any signs of immunosuppression, any local/systemic infection, and any hypersensitivity to acyclovir.

All patients who took part in the current study gave informed consent. Age, gender, wart duration, wart location, number of warts, location of warts, and past treatment history were all documented.

Depending upon the size of the lesion, the patients received 0.1ml - 0.3ml of intralesional acyclovir diluted with distilled water (70mg/ml), at the base of each wart. Before treatment and at each follow-up appointment, clinical pictures were taken. The reduction in the size and number of warts classified the response to treatment into four grades based on the Visual Analogue Scale (VAS) score (**Table 1**). Documentation of adverse effects was done, and

patients were monitored on a monthly basis for three months following the final injection for detection of any relapse.

Results

The study was successfully completed by all 18 patients. The ages of the individuals spanned between 14 to 40 years old, with a mean age of 25±4.5 years. The study included patients with diverse types of warts. The most common type was common wart, followed by palmoplantar warts. The average number of warts per person was 2.44±2.55, with a maximum of 8 warts. Warts lasted an average of 7.45±5.92 months, with the least period of one month and a highest of 14 months (**Table 2**).

By the end of the study period (8 weeks, 4 doses of injection), 9 (50%) of the patients had completely cleared their warts. Five (27.77%) patients had grade 1, complete clearance of

Table 2

<i>Parameters</i>	<i>Number of patients (n)</i>
Age	
Less than 20 yrs.	4(22.22%)
20-30yrs	8(44.44%)
30-40yrs	6(33.33%)
Sex	
Females	6(33.33%)
Males	12(66.66%)
Duration of warts	
Less than 6months	13(72.22%)
6-12months	2(11.11%)
More than 12months	3(16.67%)
Type	
Common	11(61.11%)
Palmar	4(22.22%)
Plantar	3(16.67%)



Figure 1 (a) shows clinical picture of patient prior to the treatment. (b) shows clinical picture of patient after evaluating the outcome of previous 3 injections. Some residual warts are seen, a VAS score of 75-99%.

warts by the fourth week (after analysing the effectiveness of the prior two injections). By the sixth week (after analysing the effectiveness of last three injections), three more patients (5+3), for a total of eight (44.44%), had complete clearance of warts, and five (27.77%) patients had a VAS score of 75%-99% (**Figure 1**). By the eighth week (after analysing the effectiveness of previous four injections), 9 (50%) patients achieved total clearance of warts (**Figure 2A, 2C**), and two (11.11%) patients had a VAS score of 50-74%. By the end of 8 weeks, two (11.11%) patients did not show any response. After a few days, several individuals developed haemorrhagic eschar, which eventually desquamated and left normal skin

markings (**Figure 2b**). In our study (n=18), all patients (100%) complained of pain during injection. Haemorrhagic eschar was noted in 14 patients (77.77%), blister formation in 10 patients (55.55%) and secondary infection in 2 patients (11.11%).

Discussion

The invention of antiviral medication targeting HPV is incredibly challenging. Papillomaviruses, unlike herpes viruses, do not encode kinases, polymerases, or proteases. HPV uses variety of host-cell enzymes, particularly host-cell DNA polymerase, for virus replication. As a result, synthesizing antiviral medicines that are specifically integrated into HPV DNA might be exemptionally challenging.⁴

Acyclovir is an analogue of purine nucleoside that selectively inhibits herpes virus. This specificity and selectivity is attributable to the capability of such viruses to encode for a viral thymidine kinase. Thus, potentiating phosphorylation of acyclovir to its intermediate form acyclovir monophosphate. Cellular enzymes convert this to acyclovir triphosphate, which is then integrated into viral DNA. This causes viral DNA chain termination finally leading to decreased viral replication.²

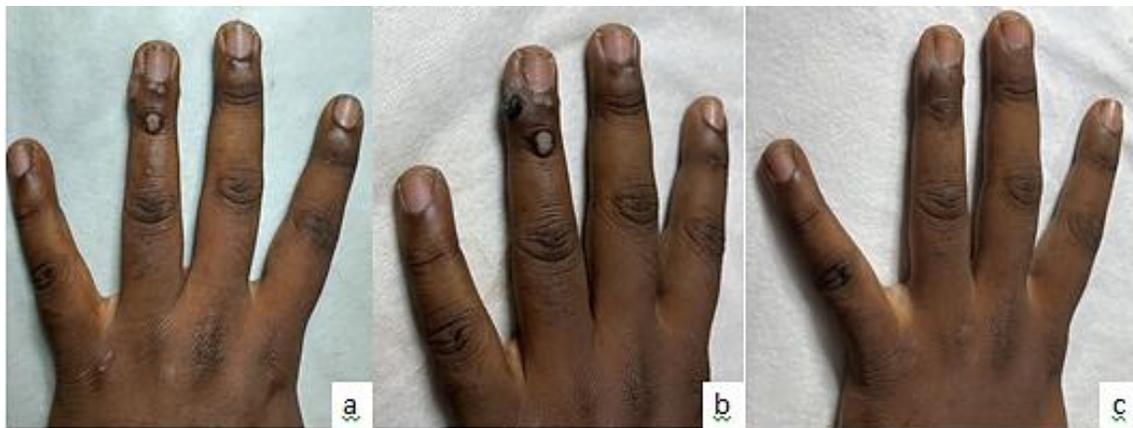


Figure 2 (a) shows clinical picture of patient prior to the treatment. (b) haemorrhagic eschar. (c) shows clinical picture of patient after evaluating the outcome of previous 4 injections, a VAS score of 100%.

In our study 9 patients (50%) showed complete response. In a study conducted by Elsayed A *et al.*¹ on the treatment of warts with intralesional acyclovir, complete clearance of cutaneous warts was achieved in 52.6% of patients, a partial clearance in 36.8%, and no response was observed in 10.5% of study participants. In a single case report, Bauer *et al.* (1982) documented clearance of refractory plantar warts after topical administration of acyclovir cream.³ Pechman *et al.* (1983) demonstrated the therapeutic efficacy of acyclovir ointment in a patient with recalcitrant plantar warts.⁴

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Elsayed A *et al.*¹ reported injection pain in 93.8% of the patients and blistering occurring in about 50% of the patients.

Treating warts with conventional ablative modalities may be associated with recurrence as these procedures lack specificity for viral infected cells. Recurrence can occur as a result of latent HPV reactivation in the neighbouring healthy skin that has not been treated. Our study aims to spotlight the use of intralesional acyclovir, an antiviral drug with specific action against DNA virus to overcome the recurrence rate and can be beneficial modality in patients seeking for quick response.

A review of the available literature reveals only

one study on the efficacy and safety profile of intralesional injection of acyclovir in the management of cutaneous warts; thus, our study is another such attempt to assess the effectiveness of injection acyclovir in the management of cutaneous warts, thus filling a gap in the existing literature.

Limitations The limitation of the current study was small sample size (n=18), and patients were not followed up on beyond 8 weeks of the study period, thus the rate of wart recurrence could not be thoroughly explored. Hence, larger sample size trials with a longer follow-up time are needed to further investigate the effectiveness of intralesional acyclovir for therapeutic cure of cutaneous warts.

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