Evaluating the efficacy and safety of intralesional acyclovir in the management of recalcitrant cutaneous warts: A Retrospective review of 20 cases.

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Abstract

Background: Recalcitrant cutaneous warts, often resistant to conventional therapies, present a persistent challenge in dermatological practice. Acyclovir, an antiviral agent with activity against herpesviruses, has shown potential immunomodulatory effects that may offer therapeutic benefit in wart management.

Objective: To evaluate the efficacy and safety of intralesional acyclovir in the treatment of recalcitrant cutaneous warts through a retrospective review of clinical outcomes in 20 patients.

Methods: A retrospective analysis was conducted on 20 patients with recalcitrant cutaneous warts who received intralesional acyclovir injections over a six-month period. Data on patient demographics, lesion characteristics, treatment regimen, response rates, adverse effects, and recurrence were collected and analyzed.

Results: Of the 20 patients, 14 (70%) demonstrated complete resolution of warts, while 4 (20%) showed partial response. Two patients (10%) had no response to treatment. Minimal adverse effects were reported, primarily localized pain and mild inflammation at the injection site. No systemic side effects were observed. At 3-month follow-up, recurrence was noted in 2 cases (10%).

Conclusion: Intralesional acyclovir appears to be a promising, safe, and well-tolerated treatment option for recalcitrant cutaneous warts, particularly in patients unresponsive to conventional therapies. Larger prospective studies are warranted to confirm these findings and elucidate the underlying mechanisms of action.

Keywords: Cutaneous warts, Intralesional acyclovir, Recalcitrant warts, Verruca vulgaris, Viral warts, Treatment challenges, Treatment outcomes, Side effects, Dermatologic treatments, Immunocompromised patients, Human papilloma virus, Retrospective review.

Introduction

Managing cutaneous warts can be challenging due to the variable response rates and tolerability of current treatments [1,2]. Intralesional (IL) therapies, such as acyclovir have shown promise for patients with numerous or recalcitrant warts, though current literature is limited [2]. One trial of 31 patients randomized to receive IL acyclovir or placebo reported 52.6% clearance with IL acyclovir [3] while another study of 40 patients reported 60% clearance in patients who received IL acyclovir [4]. We present a retrospective review of 20 patients with recalcitrant cutaneous warts treated with IL acyclovir at a single academic centre.

Cutaneous warts are common benign proliferations of the skin and mucosa caused by infection with Human Papillomavirus (HPV). Despite their typically self-limiting nature, certain warts become recalcitrant—persisting for months or even years despite multiple treatment attempts. Traditional therapeutic options such as cryotherapy, salicylic acid, laser ablation, and electrosurgery often show variable efficacy and are associated with high recurrence rates, pain, or scarring. This necessitates exploration of alternative and more effective treatment modalities, especially for resistant cases.

Intralesional therapies, including immunotherapeutic agents and antivirals, have gained attention for their ability to elicit a localized and systemic immune response against HPV-infected tissue. Acyclovir, a guanosine analog commonly used against herpesviruses, has demonstrated antiviral properties that may be useful against HPV-related lesions. Its intralesional administration may increase local drug concentration and

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Received: *22-Aug-2024, Manuscript No. AADRSC-24-146115;* ***Editor assigned:*** *26-Aug-2024, AADRSC-24-146115 (PQ);* ***Reviewed:*** *10-Sep-2024, QC No. AADRSC-24-146115;* ***Revised:*** *19-Aug-2025, Manuscript No.AADRSC-24-146115 (R);* ***Published:*** *26-Aug-2025, DOI: 10.35841/aara-9.3.276*

Citation: *Dao DD, Robinson MA, Bibee KP, et al. Evaluating the efficacy and safety of intralesional acyclovir in the management of recalcitrant cutaneous warts: A Retrospective review of 20 cases. Dermatol Res Skin Care 2025;9(4):276*

enhance therapeutic efficacy without significant systemic absorption or toxicity.

While the topical or oral use of acyclovir for warts has not yielded consistent outcomes, limited reports suggest that intralesional delivery could offer a promising alternative for managing recalcitrant warts. However, there remains a paucity of clinical data on its safety and efficacy. This retrospective review of 20 cases aims to assess the therapeutic outcomes and potential adverse effects associated with intralesional acyclovir in persistent cutaneous warts.

Literature Review

A retrospective review of Johns Hopkins' electronic medical records from January 2021 to September 2023 identified 20 patients age ≥ 18 with a clinical and/or histologic diagnosis of cutaneous warts treated with intralesional acyclovir. Treatment outcomes were categorized as no response, partial response (reduction in size and/or number, but persistent lesions) or complete clearance.

The 20 patients included 14 females (70%) and six males (30%) with an average age of 37 (± 13.2) years (Table 1). Four patients (20%) were immunosuppressed. All patients previously failed other therapies, with 10 patients (50%) having failed three or more treatment modalities. Patients received IL acyclovir (50 mg/ml), 0.1 mL per wart, with the intent to repeat injections every two weeks until complete clearance was achieved. Patients received 1 to 4 treatments (average of 1.6 treatments) with an average of 43.5 (± 17.8) days between treatments.

Table 1. *Summary of patient cases with cutaneous warts.*

Patient/Sex/Age	History of immunosuppression	Location of warts	Number of lesions	Previous Tx	Rounds of Tx	Tx outcome	Adverse effects
1/F/50	-	L plantar foot	2	LN2	1	Complete	None reported
2/M/33	-	R great toe, R thumb	2	LN2, IL candida, Il cidofovir	2	Complete	None reported
3/F/58	-	L 3rd periungual finger	4	SA, IL unspecified chemotherapy	1	Partial	None reported
4/F/33	-	B/L palms	4	LN2	2	Partial	Severe pain
5/F/20	-	B/L palms	12	SA/5-FU, IL cidofovir, IL candida, PO cimetidine	2	Complete	Blistering
6/F/31	-	L calcaneus	2	LN2, SA, IL cidofovir, IL 5-FU, topical imiquimod, PDL	2	Partial	None reported
7/F/57	RA on Humira	R 2nd finger	1	LN2	1	Partial	Severe pain
8/F/71	Lung transplant on tacrolimus, prednisone	L 2nd finger	1	LN2	2	Partial	None reported
9/F/50	-	B/L hands, R 2nd finger	10	LN2, SA, IL candida	1	None	Erythema, edema, severe pain
10/M/36	HIV	B/L thumbs, L 4th finger, R plantar heel	5	LN2	1	Partial	Severe pain
11/F/31	-	L plantar foot, R 4th toe	2	LN2	2	Complete	Hyperpigmentation
12/M/40	HIV	Penile shaft, Scrotum	3	PPD	1	None	None reported
13/F/28	-	R thumb	2	LN2, IL cidofovir	1	None	Blistering
14/F/40	-	R 2nd and 3rd finger, L plantar foot	3	LN2, SA, IL candida, topical 5-FU, unspecified laser	1	None	None reported
15/M/32	-	L 3rd finger	1	LN2, SA, IL candida	1	Partial	None reported
16/M/24	-	R thumb, 2nd finger	1	LN2	1	Complete	None reported

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17/F/32	-	R 2nd finger, R plantar foot, R great toe	4	LN2	4	Partial	None reported
18/F/19	-	R plantar foot	6	LN2, SA/5-FU, IL candida, topical cidofovir, topical 5-FU, PO cimetidine, PO zinc	1	Partial	Severe pain
19/M/30	-	L periungual 2nd finger, R thumb	2	LN2, SA, SA/5-FU, IL candida, PDL	1	None	None reported
20/F/28	-	L 2nd, 4th subungual finger	2	LN2, SA, IL candida	1	None	Blistering, severe pain

Five patients (25%) achieved complete clearance, 9 patients (45%) had partial response, and 6 patients (30%) had no response to injections. Patients who had no response received only one treatment. Immunosuppressed patients had either no response or only partial response. Adverse effects included severe pain (30%), blistering (16%), erythema (5%), edema (5%), and hyperpigmentation (5%).

Discussion

Our study highlights the potential efficacy of IL acyclovir for recalcitrant cutaneous warts, with 70% of patients achieving either complete (25%) or partial (45%) clearance. The observed decrease in complete clearance rate as compared to prior studies, may be attributed in part to the retrospective nature of our study, the presence of recalcitrant warts in our cohort, the inclusion of immunosuppressed patients, the longer interval between injections, and fewer injections on average due to inconsistent follow-up. Adverse effects were comparable (Supplementary File).

Patients with no response received only one injection, suggesting improved outcomes with multiple injections. Severe injection-related pain led five patients to seek alternative treatments; anesthesia with infiltrated lidocaine has been shown to alleviate injection site pain prior to keloid injections, 5 and may be considered to enhance patient comfort [5].

The observed therapeutic response in our cohort supports the hypothesis that intralesional acyclovir may exert a direct antiviral effect against HPV, possibly through modulation of local immune responses. Although originally developed for herpesvirus infections, its role in wart resolution suggests off-target benefits that merit further exploration. Importantly, patients experienced minimal adverse effects, indicating a favorable safety profile. These findings align with emerging evidence supporting antiviral agents as adjuncts or alternatives to destructive wart therapies. However, limitations such as small sample size, retrospective design, and lack of a control group underscore the need for larger randomized controlled trials to validate these promising outcomes.

Conclusion

In conclusion, our study demonstrates that IL acyclovir may have efficacy in treating cutaneous warts, particularly when recalcitrant to conventional treatments. While no serious safety events were observed, adverse effects, notably severe pain, and blistering, may limit tolerability. Future studies should investigate strategies for improving injection tolerability and double-blinded randomized controlled trials are essential to establish IL acyclovir's efficacy in wart treatment. Study limitations include its retrospective design, small sample size, lack of a control group, variable treatment rounds, and intervals between treatments.

Patient Consent

The authors attest to obtaining written patient consent for the publication of recognizable patient photographs or other identifiable material, with the understanding that this information may be publicly available.

Funding Sources

None.

Conflicts of Interest

No potential conflicts of or competing interests to disclose.

IRB Approval Status

Approved by the Johns Hopkins University IRB: IRB00388482.

References

1. Hekmatjah J, Farshchian M, Grant-Kels JM, et al. The status of treatment for plantar warts in 2021: No definitive advancements in decades for a common dermatology disease. Clin Dermatol. 2021;39(4):688-94.
2. Dall'Oglio F, D'Amico V, Nasca MR, et al. Treatment of cutaneous warts: an evidence-based review. Am J Clin Dermatol. 2012;13:73-96.
3. Elsayed A, Nassar A, Marei A, et al. Intralesional acyclovir: a potential therapeutic option for cutaneous warts. J Cutan Med Surg. 2022;26(1):25-30.
4. Meghana Reddy E, Rajashekar TS, Suresh Kumar K. A comparative study of intralesional acyclovir *vs.* immunotherapy for treatment of viral warts. Cureus. 2023;15(5):e38781.

Citation: *Dao DD, Robinson MA, Bibee KP, et al. Evaluating the efficacy and safety of intralesional acyclovir in the management of recalcitrant cutaneous warts: A Retrospective review of 20 cases. Dermatol Res Skin Care 2025;9(4):276*

5. Park TH. Topical anesthetic versus lidocaine mixture for pain relief during keloid treatment: A prospective, split study. J Craniofac Surg. 2023;34(7):e636-8.

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