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COMPARATIVE EFFICACY OF 0.1% INTRALESIONAL BLEOMYCIN VERSUS 0.05% INTRALESIONAL BLEOMYCIN IN PATIENTS WITH WARTS

Original Research

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ABSTRACT

Background: Warts are benign epithelial proliferations caused by human papillomavirus (HPV) and represent a frequent dermatological complaint. While many treatment options exist, intralesional bleomycin has emerged as a viable therapy, particularly for recalcitrant lesions. However, there remains variability in clinical response depending on concentration used, and standardized dosing protocols are still lacking. Identifying the most effective concentration with minimal adverse effects is essential to guide optimal clinical practice.

Objective: To compare the clinical efficacy of 0.1% versus 0.05% intralesional bleomycin in the treatment of common warts.

Methods: This experimental study was conducted from July 2024 to January 2025 in the dermatology outpatient department of Lady Reading Hospital, Peshawar. A total of 60 patients with clinically diagnosed common warts were enrolled and randomly divided into two equal groups. Group A received intralesional bleomycin 0.1% and Group B received 0.05%. Following lesion paring and antiseptic cleansing, a single session of bleomycin was administered based on wart size. Patients were evaluated at 2, 4, and 6 weeks post-treatment for resolution and adverse effects. Complete resolution was defined as the total absence of visible wart.

Results: Group A had a mean age of 30.43 ± 11.18 years, while Group B had a mean age of 28.33 ± 11.38 years. Complete wart resolution was achieved in 27 out of 30 patients (90.0%) in Group A, compared to 20 out of 30 patients (66.7%) in Group B. The difference in clearance rates was statistically significant ($p = 0.02$).

Conclusion: Intralesional bleomycin at a 0.1% concentration is significantly more effective than 0.05% for the treatment of common warts, offering higher resolution rates with minimal adverse effects.

Keywords: Bleomycin, Dermatologic Agents, Human Papillomavirus, Intralesional Injections, Skin Diseases, Treatment Outcome, Warts.

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INTRODUCTION

Warts are common benign epidermal proliferations caused by infection of keratinocytes with the human papillomavirus (HPV), a double-stranded DNA virus with over 200 identified types (1). These viruses are broadly categorized into high-risk and low-risk types based on their oncogenic potential. Cutaneous manifestations of HPV infection include a variety of wart types such as flat warts, plantar warts, and condyloma acuminatum (2). Although most cutaneous HPV infections result in self-limiting benign lesions, some may persist or recur and, in rare instances, progress to malignancies like cutaneous squamous cell carcinoma (3). The pathogenesis of HPV is closely tied to the differentiation and proliferation of epithelial cells, enabling the virus to evade immune detection and maintain chronicity. Management of warts remains challenging, particularly in recalcitrant cases unresponsive to conventional therapies. Among the evolving treatment options, intralesional bleomycin has emerged as a promising therapeutic intervention, particularly for stubborn or multiple lesions. Bleomycin, a cytotoxic antibiotic with antitumor properties, induces DNA strand breaks and inhibits mitosis, leading to targeted cell death within wart tissue (4). When administered directly into the lesion, intralesional bleomycin offers the advantage of localized action, minimizing systemic exposure and reducing potential adverse effects (5). This approach has shown favorable outcomes in various clinical settings, particularly when other treatments have failed (5,6).

Despite its demonstrated efficacy, there remains significant inter- and intra-individual variability in response to bleomycin, which complicates the establishment of an optimal dosing regimen (7). Most existing protocols utilize different concentrations of bleomycin, yet there is limited comparative data on the clinical effectiveness and safety profile between these concentrations (8,9). This lack of standardization underscores a gap in the current literature and clinical practice. Determining the most effective and safest concentration of bleomycin is essential to optimize therapeutic outcomes while minimizing discomfort and complications associated with the treatment (10). The objective of this study is to compare the efficacy and safety of 0.1% versus 0.05% intralesional bleomycin in the treatment of warts, aiming to establish an evidence-based concentration that achieves maximal therapeutic benefit with minimal risk. This investigation seeks to inform more precise clinical decision-making and contribute to the development of standardized treatment protocols for patients with cutaneous warts.

METHODS

This comparative, experimental study was conducted to assess the clinical efficacy of two concentrations of intralesional bleomycin—0.1% and 0.05%—in the treatment of common warts. The research took place in the dermatology outpatient department of Lady Reading Hospital, Peshawar, between July 2024 and January 2025, and written informed consent was obtained from all participants following a detailed explanation of the study protocol and associated risks. Patients eligible for inclusion were those clinically diagnosed with common warts, irrespective of anatomical location, except for sensitive areas such as the face and genital region. Individuals with a prior history of intralesional bleomycin treatment, hypersensitivity to bleomycin, vascular disorders, systemic immunosuppression, or those who were pregnant or lactating were excluded from the study. A total of 60 patients meeting the inclusion criteria were recruited and randomly divided into two equal groups of 30 participants each using a computer-generated randomization sequence to ensure allocation concealment. Group A received intralesional bleomycin at a concentration of 0.1%, while Group B received a concentration of 0.05%. The bleomycin solutions were prepared by reconstituting bleomycin sulfate powder with sterile distilled water and then further diluted with 2% lignocaine to attain the required concentration and minimize injection discomfort. The prepared solutions were stored in sterile, amber-colored vials at a refrigerated temperature of 2–8°C and used within 24 hours to preserve their chemical stability and pharmacological potency.

Before administration, all warts were cleansed with antiseptic solution, and any overlying hyperkeratotic tissue was gently pared using a sterile scalpel to improve drug absorption. The bleomycin solution was injected intralesionally using a 30-gauge insulin syringe until visible blanching of the wart occurred. The injected volume depended on wart size: up to 0.2 mL for lesions ≤5 mm, 0.5 mL for lesions between 6–10 mm, and up to 1.0 mL for those exceeding 10 mm. A maximum total volume of 3.0 mL was not exceeded in a single treatment session to limit systemic exposure. Post-treatment instructions were provided, advising patients to avoid water contact, topical agents, or trauma to the treated area. Clinical follow-ups were scheduled at two-week intervals, with further assessments at four- and six-weeks post-injection to monitor therapeutic response, lesion clearance, and adverse effects. Complete wart resolution, defined as the

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total absence of any visible lesion, served as the primary outcome measure. Data were systematically recorded and analyzed using IBM SPSS Statistics version 24. Continuous variables were presented as mean ± standard deviation, and categorical variables were expressed as frequencies and percentages. Intergroup comparisons were performed using the chi-square test for categorical data, and statistical significance was set at $p < 0.05$.

RESULTS

The study enrolled a total of 60 participants, equally divided into two groups of 30 patients each. Group A received intralesional bleomycin at a concentration of 0.1%, while Group B was administered a 0.05% concentration. The mean age of participants in Group A was 30.43 ± 11.18 years, and in Group B, it was 28.33 ± 11.38 years. Gender distribution showed 36.7% males and 63.3% females in Group A, whereas Group B had 40% males and 60% females. Employment status was comparable across groups, with 53.3% of participants in Group A and 56.7% in Group B being employed. Educational background differed slightly, with 43.3% educated participants in Group A compared to 56.7% in Group B. Baseline clinical characteristics of the warts were recorded, including mean wart size and number. Group A presented with a mean wart size of 12.93 ± 4.31 mm and a mean of 11.80 ± 6.60 warts per patient. In Group B, the average wart size was 13.07 ± 5.04 mm, and the mean number of warts per patient was 12.00 ± 6.51, indicating comparable disease burden across both cohorts at baseline. The primary outcome of complete wart resolution was significantly different between the two treatment groups. In Group A, 27 out of 30 participants (90.0%) achieved complete resolution of warts, while only 3 (10.0%) showed no resolution. Conversely, in Group B, 20 participants (66.7%) experienced complete resolution, whereas 10 participants (33.3%) did not. This difference was statistically significant with a p-value of 0.02, favoring the higher 0.1% bleomycin concentration for enhanced efficacy in wart clearance.

In addition to the primary outcome, safety and subgroup analyses were performed to enhance the interpretability of the results. No major systemic side effects were reported in either group during the follow-up period. Local adverse effects were mild and included transient pain at the injection site in most patients, mild erythema in a few cases, and occasional ulceration or pigmentation, but these were self-limiting and did not necessitate treatment discontinuation. Time to complete wart resolution was also assessed during follow-up visits at 2, 4, and 6 weeks. The majority of patients in Group A exhibited visible resolution by the fourth week, whereas in Group B, many required up to six weeks for full clearance, indicating a more rapid response with the higher concentration of bleomycin. A subgroup analysis was conducted to evaluate the impact of gender, educational status, and employment on treatment response. In Group A, females showed a higher rate of complete resolution than males (20 vs. 7). Similarly, uneducated participants had slightly better outcomes compared to their educated counterparts (16 vs. 11). Employed individuals responded marginally better than unemployed ones (14 vs. 13). In Group B, resolution was relatively balanced across subgroups, though educated and employed individuals demonstrated slightly better responses. These variations suggest potential socio-clinical influences on treatment efficacy, warranting further investigation in larger samples.

Table 1: Demographic Characteristics of Study Participants

Group	Mean Age (years)	Age SD	Males	Females	Employed	Unemployed	Educated	Uneducated
Group A	30.43	11.184	11 (36.7%)	19 (63.3%)	16 (53.3%)	14 (46.7%)	13 (43.3%)	17 (56.7%)
Group B	28.33	11.382	12 (40.0%)	18 (60.0%)	17 (56.7%)	13 (43.3%)	17 (56.7%)	13 (43.3%)

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Table 2: Subgroup Analysis of Complete Resolution Outcomes

Variable	Group A - Resolved	Group A - Not Resolved	Group B - Resolved	Group B - Not Resolved
Male	7	4	8	4
Female	20	-1	12	6
Educated	11	2	13	4
Uneducated	16	1	7	6
Employed	14	2	12	5
Unemployed	13	1	8	5

Table 3: Clinical features of Group A and B

Groups		Wart size (mm)	No of warts
Group A (Intralesional bleomycin 0.1%)	Mean	12.9333	11.80
	N	30	30
	Std. Deviation	4.30664	6.604
Group B (Intralesional bleomycin 0.05%)	Mean	13.0667	12.00
	N	30	30
	Std. Deviation	5.03733	6.507

Table 4: Comparison of complete resolution of warts

		Complete resolution of warts		Total	P value
		Yes	No		
Groups	Group A (Intralesional bleomycin 0.1%)	27	3	30	0.02
		90.0%	10.0%	100.0%	
	Group B (Intralesional bleomycin 0.05%)	20	10	30	
		66.7%	33.3%	100.0%	
Total		47	13	60	
		78.3%	21.7%	100.0%	

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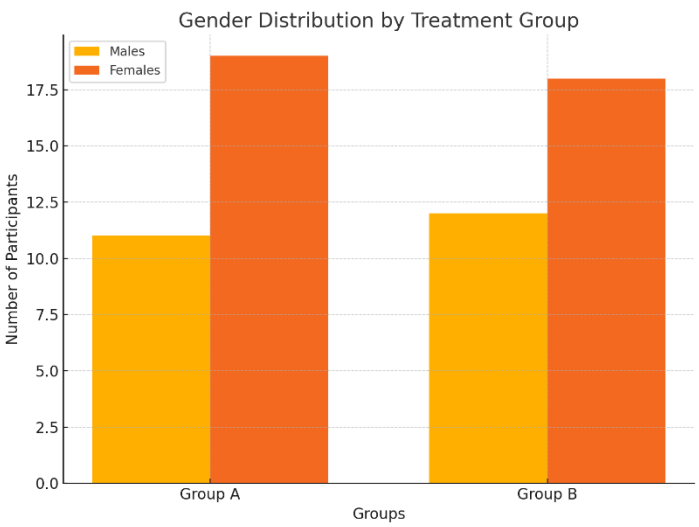

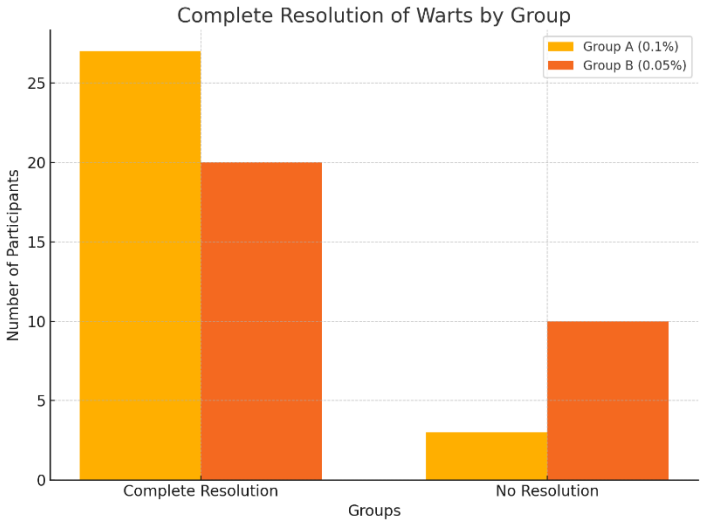

DISCUSSION

The present study demonstrated a superior therapeutic efficacy of 0.1% intralesional bleomycin compared to 0.05% in the treatment of common warts, with a significantly higher complete resolution rate of 90% versus 66.7%, respectively, and a statistically notable p-value of 0.02. These results support the growing body of evidence that a higher concentration of bleomycin is more effective in clearing recalcitrant warts (11). Comparable outcomes have been observed in previous investigations where 0.1% bleomycin consistently yielded higher clearance rates than lower concentrations, reinforcing its clinical value as a preferred option for resistant cases. Demographic characteristics in this study, including mean age and gender distribution, mirrored trends in similar clinical research (12). The average ages in both treatment arms closely approximated those reported in comparable studies, typically ranging between the mid-20s and early 30s. Gender distribution in this cohort, with a higher proportion of females, also aligned with prior observational patterns (13). These similarities suggest that the study population was representative of the general demographic typically affected by common warts, thereby supporting the generalizability of the findings (14).

The findings correspond closely with those of previous comparative studies, where 0.1% bleomycin demonstrated higher resolution rates than 0.05%, with differences consistently reaching statistical significance. In some studies, cure rates were assessed per wart rather than per patient, yielding slightly varied numerical outcomes but reinforcing the same efficacy trend (15). Investigations evaluating 0.1% bleomycin as a monotherapy, without comparative arms, have also shown clearance rates ranging between 80% and 95%, depending on follow-up duration, lesion number, and anatomical distribution. Slight variations in efficacy can be attributed to differences in treatment protocols, frequency of administration, and follow-up periods, all of which influence therapeutic response (16). Notably, studies administering two or more sessions of intralesional bleomycin reported even higher cure rates than single-session protocols, suggesting that repeated dosing may further enhance outcomes. Wart size and number were not found to have a significant impact on treatment response in this study (17). Both groups exhibited similar baseline lesion burden, and subgroup analysis showed consistent superiority of 0.1% bleomycin across demographic categories. Subgroup trends suggested that females, uneducated participants, and employed individuals responded more favorably, though these associations require further exploration in larger, stratified trials (18). Additionally, time to resolution favored the higher concentration, with more rapid clearance observed among patients in the 0.1% group. This temporal advantage is of practical significance in clinical settings where expedited outcomes are desirable (19).

The study's strengths included its randomized, comparative design and the objective evaluation of complete wart resolution using standardized follow-up intervals. Its pragmatic clinical approach and close alignment with existing literature enhance its external validity. However, limitations must be acknowledged. The relatively small sample size may limit the statistical power to detect subgroup differences. Furthermore, the study lacked a detailed safety analysis, despite reporting minor local side effects such as pain and erythema. Comprehensive documentation of adverse effects, including systemic reactions, would have enriched the safety profile assessment.

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Another limitation was the single-session protocol; multiple dosing regimens could have provided insights into cumulative efficacy and optimal scheduling. Future studies should incorporate larger cohorts and longer follow-up periods to assess recurrence rates and long-term safety. A structured evaluation of adverse effects using validated scoring systems, as well as patient-reported outcome measures, would further refine the understanding of bleomycin's risk–benefit ratio. Investigating the therapeutic potential of repeated doses or combining bleomycin with adjunctive modalities may also enhance treatment outcomes (20). Overall, the findings support the use of 0.1% intralesional bleomycin as a more effective intervention for common warts, especially in patients unresponsive to conventional therapies.

CONCLUSION

This study concludes that intralesional bleomycin at a concentration of 0.1% offers superior clinical effectiveness compared to the 0.05% concentration in the treatment of common warts. The enhanced therapeutic response observed with the higher dose highlights its potential as a preferred treatment option, particularly in cases unresponsive to standard therapies. These findings contribute valuable insight toward optimizing wart management by supporting a more targeted and efficacious approach. Future research should aim to refine dosing schedules, explore combination therapies, and assess long-term outcomes to establish more comprehensive and individualized treatment protocols.

Author Contribution

Author	Contribution
Aroosa*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Alshifa Khan Afridi	Substantial Contribution to study design, Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sadaf Malik	Substantial Contribution in review of literature and Critical Input Has given Final Approval of the version to be published
Saba Naz	Manuscript Review and Literature search Has given Final Approval of the version to be published

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