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Outcomes of Intralesional Bleomycin Therapy in Low-Flow Vascular Malformations of the Head and Neck: Pain, Functional Improvement, and Patient Satisfaction from a Prospective Multi-Centre Study in Iraq

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ABSTRACT
Low-flow vascular malformations of the head and neck are congenital venous, lymphatic, and mixed lesions that cause pain, functional impairment, and psychosocial distress. Although bleomycin sclerotherapy is well established for reducing lesion volume, patient-reported outcomes such as pain relief, functional recovery, and overall satisfaction remain insufficiently documented, particularly in the Iraqi clinical setting. This prospective multi-centre study evaluated these outcomes in 20 patients with low-flow vascular malformations of the head and neck treated with intralesional bleomycin sclerotherapy across three Iraqi teaching hospitals between August 2025 and April 2026. Pain was assessed using the Visual Analog Scale or the Wong-Baker FACES scale, functional status was evaluated through clinician- and patient-reported assessment of speech, mastication, swallowing, and oral competence, and satisfaction was recorded on a five-point Likert scale four weeks after the final treatment. Pain scores decreased significantly, from a mean of 2.7 ± 2.4 at baseline to 0.9 ± 1.3 after treatment ($p < 0.001$; effect size $r = 0.71$), and 9 of the 16 patients with baseline pain (56.3%) achieved complete pain relief. All 17 patients with pre-treatment functional deficits (100%) reported meaningful improvement, and both patients with pre-treatment bleeding episodes achieved complete cessation of bleeding. The mean satisfaction score was 4.35 ± 0.99 out of 5, with all patients with pretreatment functional Impairment reporting satisfaction or high satisfaction, and no severe adverse events occurred. These findings indicate that intralesional bleomycin sclerotherapy produces clinically meaningful improvements in pain, function, and satisfaction in low-flow vascular malformations of the head and neck, supporting its role as an effective and patient-valued treatment option for these lesions.

KEYWORDS: *Bleomycin; Pain; Patient Reported Outcome Measures; Patient Satisfaction; Quality of Life; Sclerotherapy; Vascular Malformations*

1-INTRODUCTION

Low-flow VMs are a group of congenital vascular anomalies that consist of venous, lymphatic, and mixed venolymphatic lesions, which are the most common anomalies encountered in clinical practice. they occur mostly in the head and neck [1]. Unlike vascular tumor, they do not involute but stay throughout life and tend to increase in size progressively, especially during hormonal changes, trauma, or infection [2, 3]. These lesions cause several problems to the patients by multiple aspects: in addition to the aesthetic issues they cause, they may cause pain due to recurrent thrombosis and distension of the malformed vascular channels, also they affect other functions like speech, mastication, and swallowing. They also have an effect on psychosocial status, especially in patients with lesions in the aesthetic zone like lip, cheek, or tongue [4, 5].

The treatment and management of these lesions have become directed to the minimally invasive sclerotherapy in recent decades, especially those located in deep and complex anatomical sites [6, 7]. Due to the favorable mechanism of the bleomycin, which induces endothelial apoptosis and subsequent fibrosis, it produces lesion obliteration with no aggressive tissue destruction, which is seen in other agents like absolute ethanol [1, 8]. Most of the available literature on sclerotherapy with bleomycin now has been directed toward the volume reduction which is considered the primary success factor without focusing on the other subjective outcomes, which may be

more important to the patients than the volume reduction. These outcomes are pain, functional improvement such as speech and mastication [5]. These patient-reported outcomes remain underreported in the bleomycin sclerotherapy literature. This gap is especially pronounced in the Iraqi clinical context, where no prospective multi-centre study examining these outcomes has been published. This study was designed to address this gap by reporting pain reduction, functional improvement, and patient satisfaction in a prospective multi-centre cohort of 20 patients with low-flow VMs of the head and neck.

2. MATERIALS AND METHODS

2.1. Study Design and Setting

This prospective multi-centre study was conducted across three Iraqi teaching hospitals: Al-Sadr Teaching Hospital, Al-Fallujah Teaching Hospital, and Al-Najaf Al-Ashraf Teaching Hospital, between August 2025 and April 2026. All patients provided written informed consent; parental consent was obtained for minors. Ethical approval was obtained from the institutional review boards of all three participating centres.

2.2. Patients

Twenty patients diagnosed with low-flow VMs of the head and neck were enrolled using consecutive sampling. All 20 patients completed at least one treatment session and attended the four-week post-final-treatment follow-up, yielding a 100% follow-up rate. Exclusion criteria included high-flow vascular malformations, pregnancy, hypersensitivity to bleomycin, pulmonary disease, or significant systemic comorbidity.

2.3. Treatment Protocol

Intralesional bleomycin sulfate (BLEOCEL® 15, Celon Laboratories, India) was administered at a standardised concentration of 3 mg/mL, with a maximum dose of 15 mg per session and a lifetime cumulative limit of 400 mg. Sessions were separated by three to four weeks. The number of sessions per patient (range: 1–4) was determined by clinical response. Procedures were performed under local anaesthesia; conscious sedation was used for uncooperative paediatric patients.

2.4. Outcome Measures

All outcomes were assessed at baseline and at four weeks post-final treatment.

Pain. Pain intensity was assessed using the Visual Analog Scale (0–10) for adults and the Wong-Baker FACES Pain Rating Scale for paediatric patients under eight years of age. Complete pain relief was defined as a post-treatment score of zero.

Functional status. Functional improvement was evaluated through clinician- and patient-reported assessment covering speech, mastication, swallowing, oral competence, and facial symmetry. Improvement was recorded when the patient reported gain in one or more functions compared with baseline.

Patient satisfaction. Overall treatment satisfaction was assessed using a five-point Likert scale (1 = very dissatisfied; 5 = very satisfied) at the final follow-up visit.

2.5. Statistical Analysis

Descriptive statistics are reported as mean ± standard deviation for continuous variables and as frequency with percentage for categorical variables. The Shapiro–Wilk test was used to assess the distribution of continuous variables; as these were not normally distributed, non-parametric tests were applied. The Wilcoxon signed-rank test was used for comparison between baseline and post-treatment pain scores. Effect size was calculated as $r = Z/\sqrt{N}$. Ninety-five per cent confidence intervals (CIs) were calculated for the mean pain reduction (t-distribution) and for the principal proportions (Wilson method). All analyses were performed using IBM SPSS Statistics version 29. Statistical significance was set at $p < 0.05$.

3. RESULTS

3.1. Patient and Lesion Characteristics

Twenty patients were enrolled. The mean age was 23.6 ± 12.7 years (range: 4–45 years), comprising 12 females (60.0%) and 8 males (40.0%). Seven patients (35.0%) were paediatric (aged < 18 years) and 13 (65.0%) were adults. Nineteen patients (95.0%) had venous malformations and one (5.0%) had a mixed venolymphatic malformation. Lesion sites included the cheek (n = 10, 50.0%), lip (n = 9, 45.0%), tongue (n = 3, 15.0%), submandibular/parotid region (n = 3, 15.0%), and parotid space (n = 1, 5.0%). At baseline, 16 patients (80.0%) reported pain, 17 (85.0%) had a functional or aesthetic impairment, and 2 (10.0%) had recurrent bleeding episodes;

as these categories overlapped, individual patients could fall into more than one group. The mean number of treatment sessions was 2.25 ± 1.07 (range: 1–4). The baseline lesion volume showed marked right-skew (mean 3.03 ± 9.54 cm^3; median 0.56 cm^3; range 0.094–43.300 cm^3), driven by a single large outlier; the median therefore represents the central tendency of lesion size more reliably than the mean. Demographic and lesion characteristics are summarised in Table 1.

Table 1. Patient demographics, lesion characteristics, and treatment data.

Characteristic	Value	Details
Total patients	20	100% follow-up rate
Mean age (years)	23.6 ± 12.7	Range: 4–45 years
Female / Male	12 (60.0%) / 8 (40.0%)	Slight female predominance
Paediatric (< 18 years)	7 (35.0%)	Age range: 4–17 years
Adult (≥ 18 years)	13 (65.0%)	Age range: 19–45 years
Venous malformation	19 (95.0%)	Pure venous type
Mixed venolymphatic	1 (5.0%)	Venous + lymphatic
Cheek	10 (50.0%)	Most common site
Lip	9 (45.0%)	Upper and lower lip
Tongue	3 (15.0%)	Anterior and lateral
Submandibular / parotid space	3 (15.0%)	Deep fascial location
Mean baseline volume (cm^3)	3.03 ± 9.54	Median 0.56; range 0.094–43.300
Mean sessions per patient	2.25 ± 1.07	Range: 1–4 sessions

Site categories overlap; patients with lesions at more than one site are counted under each, so site counts exceed 20.

3.2. Pain Reduction

At baseline, pain scores ranged from 0 to 9 (mean 2.7 ± 2.4; median 2.0); four patients had a baseline score of zero. Post-treatment scores ranged from 0 to 5 (mean 0.9 ± 1.3; median 1.0). The mean pain reduction was 1.8 ± 1.4 points (95% CI 1.1–2.5), representing a 66.7% relative reduction from baseline. The Wilcoxon signed-rank test confirmed a statistically significant improvement ($p < 0.001$), with a large effect size ($r = 0.71$). The reduction in mean pain score is illustrated in Figure 1.

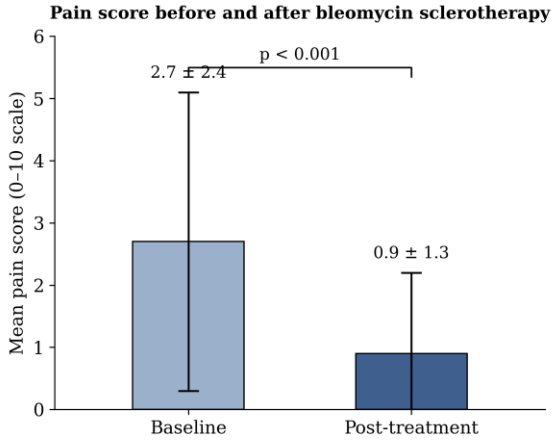

Figure 1. Mean pain score (± standard deviation) before and after intralesional bleomycin sclerotherapy. Pain decreased significantly from 2.7 ± 2.4 at baseline to 0.9 ± 1.3 post-treatment (Wilcoxon signed-rank test, $p < 0.001$; effect size $r = 0.71$; $n = 20$).

Nine of the 16 patients with baseline pain (56.3%; 95% CI 33–77%) achieved complete pain relief, all of whom had complete or near-complete lesion resolution. One patient reported no change in pain score (pre = 1, post = 1) despite complete lesion resolution on imaging, suggesting that mild residual pain may occasionally persist in the absence of detectable residual disease, possibly reflecting post-sclerotherapy fibrous tissue sensitivity. According to the site involved, lesions located in the lip had the highest complete pain relief rates (5/9, 55.6%), while the lowest rates were in submandibular and parotid lesions (0/3, 0.0%). Given the small and overlapping per-site numbers, differences across lesion sites are described descriptively and were not formally tested.

3.3. Functional Improvement

Marked functional improvement was reported by 17 patients who reported functional deficit before treatment. 3 patients of the 20 had no baseline functional issues related to their vascular malformations. Among the 17 patients with a pre-treatment functional deficit, improvement was observed in all 17 (100.0%; 95% CI 82–100%).

Improvement in aesthetics was reported by patients with lip and cheek lesions. Also, there was a reduction in palpable swelling, more comfort during mastication, and enhanced oral competence. In patients with lesions located in the tongue also reported improvement in speech and more comfortable swallowing and reduced sensation of fullness in the mouth. Two patients with bleeding episodes reported complete cessation of the bleeding at follow-up. Patients with deep submandibular and parotid lesions reported functional improvement in neck swelling reduction and improved mobility, reduced dysphagia. These patients had the lowest volumetric reduction rates.

3.4. Patient Satisfaction

In this outcome, the mean satisfaction score was 4.35 ± 0.99 (median: 5). 12 patients of 20 (60.0%) reported a score of 5 (very satisfied) and five (25.0%) reported a score of 4 (satisfied), giving a combined satisfied-or-very-satisfied rate of 17/20 (85.0%; 95% CI 64–95%). One patient (5.0%) reported a neutral score of 3, and two patients (10.0%) reported a score of 2 (dissatisfied). There were no patients who reported a score of 1. The two patients who reported the lowest score had the largest residual lesions after treatment at the follow-up visit and the lowest clinical response grades. When stratified by lesion site, mean satisfaction scores were 4.40 ± 0.84 for cheek, 4.38 ± 1.06 for lip, 4.33 ± 0.58 for tongue, and 3.67 ± 1.15 for submandibular/parotid lesions. A comprehensive summary of patient-reported outcomes is provided in Table 2, and satisfaction by lesion site is detailed in Table 3. The distribution of mean satisfaction scores across lesion sites is shown in Figure 2.

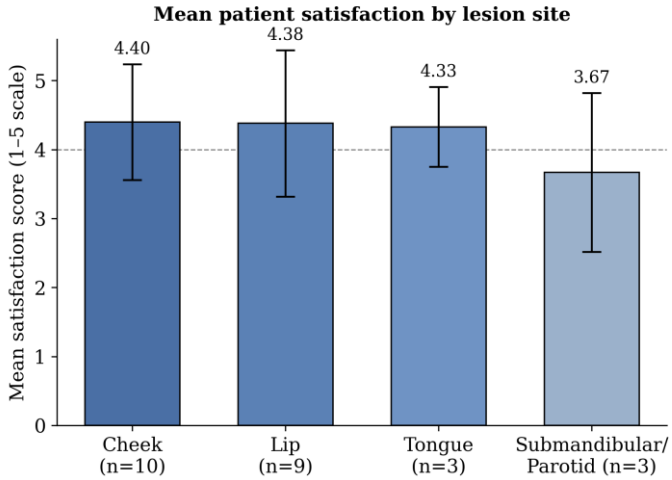

Figure 2. Mean patient satisfaction score (± standard deviation) by lesion site, measured on a five-point Likert scale. Satisfaction was lowest for deep submandibular/parotid lesions (3.67 ± 1.15) and highest for cheek lesions (4.40 ± 0.84). The dashed line denotes a satisfaction score of 4 (“satisfied”).

Table 2. Summary of patient-reported outcome measures — baseline versus post-treatment.

Outcome Measure	Baseline	Post-Treatment	p-value	Effect Size
Mean pain score (0–10)	2.7 ± 2.4	0.9 ± 1.3	< 0.001	r = 0.71
Median pain score	2.0	1.0	—	—
Complete pain relief (patients with baseline pain)	—	9/16 (56.3%)	—	—
Mean pain reduction (points)	—	1.8 ± 1.4 (95% CI 1.1–2.5)	< 0.001	—
Functional improvement (patients with baseline deficit)	—	17/17 (100.0%)	—	—
Bleeding cessation (affected patients)	—	2/2 (100.0%)	—	—
Mean satisfaction score (1–5)	—	4.35 ± 0.99	—	—
Satisfaction ≥ 4/5	—	17/20 (85.0%)	—	—
Satisfaction score 5 (very satisfied)	—	12/20 (60.0%)	—	—

Table 3. Patient satisfaction and pain relief outcomes by lesion site.

Lesion Site	n	Mean Satisfaction	Complete Pain Relief
Cheek	10	4.40 ± 0.84	4/10 (40.0%)
Lip	9	4.38 ± 1.06	5/9 (55.6%)
Tongue	3	4.33 ± 0.58	1/3 (33.3%)
Submandibular / Parotid	3	3.67 ± 1.15	0/3 (0.0%)

Site categories overlap; some patients had lesions at more than one site, so the site totals exceed 20.

4. DISCUSSION

In this study, a complete assessment of the pain reduction, functional improvement, and overall patient satisfaction, for patients with low-flow VMs in the head and neck treated with intralesional bleomycin sclerotherapy. All three outcome domains demonstrated clinically meaningful and statistically significant improvement. Pain in venous malformations arises from recurrent intralesional thrombosis caused by venous stasis within abnormal thin-walled vascular channels, from expansion of these channels during physical activity or dependent positioning, and from the pro-inflammatory cytokine environment generated by chronic localised intravascular coagulation [3, 9]. The pain relief observed across all lesion sites is explained by the mechanism of bleomycin, which induces progressive endothelial apoptosis and fibrotic obliteration of the channels. The 56.3% complete pain relief rate observed in this cohort is consistent with published reports of symptomatic improvement following bleomycin sclerotherapy in venous and lymphatic malformations [10, 11]; ethanol sclerotherapy has likewise been associated with marked symptom relief in venous malformations, albeit with greater procedural morbidity [12]. The 100% functional improvement rate among patients with pre-treatment deficits is a finding of particular clinical significance. Functional impairment — encompassing speech, swallowing, mastication, and oral competence — represents a core component of disease burden for patients with oral and perioral vascular malformations and is a primary driver of treatment-seeking behavior, particularly in younger patients [13, 14, 15]. The complete cessation of recurrent mucosal bleeding in both affected patients further underscores the functional breadth of treatment benefit achievable with bleomycin sclerotherapy. An important finding is that functional improvement was reported even in patients who achieved marked rather than complete volumetric resolution, including those with deep submandibular and parotid lesions, which indicates that complete lesion resolution is not necessary to get symptoms relief, because even partial reduction in the lesion may reduce the stimuli for pain and distension. Accordingly, in patients with complex and deep lesions, the goal of treatment should not be only complete volume reduction; functional improvement may instead represent the primary therapeutic goal.

Effective lesion response and symptom relief were obtained by the patients, as reflected in the high satisfaction rates reported here (mean 4.35/5; 85.0% satisfied or very satisfied). In addition, it is a minimally invasive procedure that spares patients the recovery period and the risk of scarring associated with surgery. The correlation between satisfaction and completeness of clinical response is consistent with the broader literature on patient-reported outcomes in functional and aesthetic interventions [5] and has direct implications for pre-treatment counselling. The lower satisfaction scores in the two patients with large, complex lesions and incomplete resolution underscore the importance of setting realistic, individualised expectations.

When the analysis is performed according to site, lesions located in the lip showed the highest complete pain relief rate (55.6%) and the most consistent functional improvement, reflecting their smaller baseline volumes and accessibility. Lesions located in deep sites such as the submandibular and parotid regions showed lower complete pain relief rates and satisfaction scores, consistent with their anatomical location, larger baseline volume, and greater complexity.

There are multiple limitations here that should be noted. First one is the sample size of 20 which limits the statistical power of subgroup analyses and restricts generalisability. Second is the follow-up period of four weeks which precludes the assessment of long-term outcome durability and recurrence. Third is the assessment of functional improvement depended on structured clinician and patient reports instead of validated instruments such as the Oral Health Impact Profile or the Patient-Reported Outcomes Measurement Information System, which would provide more strict and internationally comparable data. Studies in the future should put priority to the introducing of validated patient-reported outcome tools alongside imaging-based metrics.

5. CONCLUSIONS

Treatment of low-flow VMs of the head and neck with bleomycin sclerotherapy provides marked improvement in pain, functional status, and patient satisfaction. A mean pain reduction of 1.8 points was achieved ($p < 0.001$), functional improvement was observed in 100% of patients who presented with pre-treatment functional impairment, and 85.0% of patients reported satisfaction or high satisfaction. Bleomycin sclerotherapy is an effective and well-tolerated treatment option, supported by the data of this study. Studies with longer follow-up periods are necessary to confirm the use of bleomycin as a first-line therapy. Pre-treatment counselling should emphasise realistic, individualised outcome expectations, particularly for patients with larger or anatomically complex lesions, where functional restoration rather than complete volumetric resolution may represent the most appropriate primary treatment goal.

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Declaration

Ethical approval. Ethical approval was obtained from the institutional review boards of all three participating teaching hospitals, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Informed consent. Written informed consent was obtained from all participants; parental consent was obtained for participants under 18 years of age.

Conflicts of interest. The authors declare that they have no conflicts of interest.

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Author contributions. Both authors contributed to the study design, data collection, analysis, and interpretation, drafted and critically revised the manuscript, and approved the final version for submission.

Data availability. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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