Case Report

Efficacy of Nd: YAG laser photocoagulation versus sclerotherapy in the treatment of oral vascular malformations (A Randomized controlled clinical trial)

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ABSTRACT

Background: Treatment of vascular malformations (VMs) is a challenging endeavor for oral and maxillofacial surgeons regarding maintaining aesthetic integrity and functionality. Bleomycin sclerotherapy has been described as effective, & Nd:YAG laser appears to be one of the promising therapeutic options.Aim: To assess the efficacy of Nd:YAG laser photocoagulation versus bleomycin sclerotherapy in the treatment of oral venous VMs. Materials and methods: Twenty-two patients with oral low-flow venous VMs participated in a randomized clinical trial. Patients were randomly allocated into Nd:YAG laser & bleomycin sclerotherapy groups. The patients were assessed for the clinical healing response & post-operative complications. Statistical analysis was performed, and significance was set at the 5% level.Results: The Nd-YAG laser group showed early significant improvement in the clinical healing response over the bleomycin group. Pain was significantly higher in the bleomycin groups on the first postoperative day but decreased later. No significant differences were found in postoperative complications except for the bleeding incidence, where it was significantly higher in the bleomycin group.Conclusion: Nd-YAG laser photocoagulation and bleomycin sclerotherapy efficiently treat oral venous VMs with minimum postoperative complications and no recurrence. Nd-YAG laser demonstrates significantly faster clinical healing responses, as well as causes significantly less pain, no bleeding, and has better acceptance by the patients. while bleomycin sclerotherapy is better in the case of esthetically visible venous VMs when the risk of scarring is present

Key Words : Nd:YAG laser, Photocoagulation ,Sclerotherapy, Bleomycin , low-flow vascular malformations.

Received: 10 October 2025, **Accepted**: 14 October 2025

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ISSN: 2090-097X, ,September 2025, Vol. 16, No. 4

INTRODUCTION

Vascular anomalies are a diverse group of vascular pathological lesions that can affect vessels throughout the human body. They present a wide range of clinical manifestations, have varying prognoses, and offer several therapeutic options.[1] Approximately 60% of vascular anomalies are located in the soft tissues of the head and neck.[2] The most recent update of the International Society for the Study of Vascular Anomalies (ISSVA) classification in 2025 categorizes vascular anomalies into three primary groups: vascular tumors, vascular malformations (VMs) and Potentially Unique Vascular Anomalies (PUVA).[3] VMs are divided into fast flow, slow flow and developmental anomalies of named vessels. Based on the linked blood vessel of the lesion, the slow flow VMs are divided into capillary, lymphatic, venous, and combined malformations.[4] The ISSVA classification distinctly differentiates vascular tumors (hemangiomas), which are true vaso-proliferative neoplasms, from VMs, which are non-neoplastic lesions regarded as congenital anomalies in embryonic vascular morphogenesis, exhibiting limited postnatal endothelial mitotic activity; this

DOI: 10.21608/omx.2025.426809.1313

distinction is crucial for precise diagnosis, effective treatment, and enhanced outcomes. [3,5] Distinct treatment options have been developed to treat VMs trying to improve patients' quality of life, including injection sclerotherapy, Light Amplification by Stimulated Remission of Radiation (LASER) therapy, embolization, cryotherapy, medical therapy (beta-blockers, cortisone), surgical resection and a combination of these modalities has been used to treat VMs.[6,7] Sclerotherapy has been established as the first-line management for the majority of head and neck venous and lymphatic malformations. A variety of sclerosing agents are utilized to treat the low-flow vascular malformations; despite this, it is yet unknown whether one is the most effective and safest. [8] Bleomycin was recognized as an effective sclerosant agent for the treatment of VMs. Bleomycin is an anticancer drug that has been shown to be useful as well in the treatment of VMs. It prevents DNA synthesis, which results in cell death with little edema or inflammation. This effect may be due to its mechanism of destroying endothelial cells through apoptosis rather than necrosis. [9,10] LASER therapy has emerged as a revolutionary tool that delivers estimated aesthetics outcomes and has been identified as one of the most advanced innovations in the modalities of the treatments of VMs, owing to its photocoagulation, selective photo-thermolysis and photo ablation characteristics. [11] A variety of laser devices have been used in clinical settings to treat VMs. They have been shown to be safe, non-invasive and efficient in treating mucosal intraoral and cutaneous low flow VMs with varying wavelengths, settings, and application techniques[12-14] The Neodymium Yttrium Aluminum Garnet (Nd: YAG) laser is considered an attractive therapeutic alternative with promising outcomes in VM treatment. It is selectively absorbed by hemoglobin and poorly absorbed in water, with a 1064 nm wavelength and a 5–6 mm penetration depth. As it penetrates deeper through tissue, the Nd:YAG laser causes strong coagulative activity and hemostasis. [14-16] To our knowledge, there is no study published comparing the efficacy of Nd:YAG laser thermo-photocoagulation versus bleomycin sclerotherapy in the treatment of oral venous VMs. Thus, our main aim here was to assess and compare the efficacy of Nd: YAG laser thermo-photocoagulation versus bleomycin sclerotherapy in the treatment of oral venous VMs in terms of clinical healing response and postoperative complications assessment parameters.

The present study was designed to test the hypothesis that there is no difference in the clinical healing response and postoperative complications assessment parameters between Nd:YAG laser thermo-photocoagulation versus the bleomycin sclerotherapy in the treatment of oral venous VMs .

PATIENTS AND METHODS

Study Design

Our study was designed as a prospective, randomized controlled clinical trial on 22 patients with oral venous low flow VMs in accordance with the CONSORT guidelines for reporting randomized clinical trials [17], and the work was carried out in accordance with the ethical standards of the modified Helsinki Declaration for human clinical studies [18], between October 2023 and May 2025, The study received ethical approval from the Research Ethics Committee of Alexandria University's Faculty of Dentistry (Approval NO: 0770-09/2023-IORG 0008839). The National Institutes of Health Clinical Trials Registry in the United States has this study registered (NCT05099081). All participants provided written informed consent, and patients were selected from the maxillofacial department outpatient clinic of Faculty of Dentistry, Alexandria University. A 5% alpha error and 80% research power were used to estimate the sample size. The percentage of patients who demonstrated an area reduction based on the Vlachakis criteria was 100% for the laser group and 66.7% for the liquid bleomycin sclerotherapy group [9,16]. To account for any potential loss to follow-up, the sample size was expanded from the minimal calculated sample size of ten patients per group to eleven patients per group. Number of groups × number of patients per group (2 × 11) = 22 is the overall sample size. G*power 3.0.10 [19] was used to calculate the sample size, which was based on Rosner's method [20].

Study and control groups

Adult patients suffering from low flow oral venous VMs with a size less than 4cm, with no previous treatment for it, and medically free patients of both genders were included in our study. Subjects were excluded if they had syndrome-related vascular lesions, extensive lesions and patients with high-flow Oral VMs or any pulmonary disease. Eligible patient sample (n= 22) was allocated randomly in equal proportions by simple randomization [21] using computerized random number generator [22] with an allocation ratio of 1:1 according to the treatment modality used for the treatment of oral venous VMs into study and control groups. The study is positive controlled were both groups received treatment and each group of patients received a single treatment. Study group were 11 patients treated by Nd:YAG laser photocoagulation and control group were 11 patients treated by bleomycin sclerotherapy.

Methodology

A.Preoperative Assessment

All patients provided a comprehensive preoperative history, which included their principal complaint, medical and dental histories, and any associated symptoms resulting from having VMs, such as pain, bleeding, discomfort when eating and speaking, or a poor appearance of the lip or tongue. VMs were examined to assess the extent, the location, the size, the consistency, and if there was any discomfort upon palpation. To serve as a baseline for comparison following therapies, images of the VMs were obtained during the initial session. Each patient had a Doppler ultrasound (Philips Hd5 Ultrasound System © Koninklijke Philips N.V. Amsterdam, Netherlands.www.philips.com.) to confirm the diagnosis and assess the lesion's size, flow, and extension.

B.Operative Phase.

1-Nd:YAG laser transmucosal thermo-photo-coagulation group [15,16,23] (Fig.1)

Figure 1. Nd:YAG laser transmucosal thermo-photo-coagulation. A) Preoperative view of the venous low-flow VM in the labial vestibule of the upper lip. B) Nd:YAG laser (1084 nm) application in a non-contact mode, 4 watts, 2-3 mm away and perpendicular to the surface of the lesion. C) Immediate postoperative view after laser application showing the polka dot pattern appearance. D) 1-week postoperative view showing the ulceration formation E) 1-month post-operative view showing moderate disappearance of the lesion. F) Immediate postoperative view after the second session of laser application showing clinical signs of shrinking and whitening G) 1-week postoperative view after the second laser session showing proper healing and mild ulcer formation H) Excellent improvement and complete disappearance of the VM.

Before beginning work, all researchers using lasers and patients were required to wear safety glasses to prevent reflected laser beam from damaging the retina, cornea, and lens. Only essential people were allowed access to the treatment area, and the laser equipment was kept in a specially marked clinic that had a warning sign. Then a local anesthesia was given according to the lesions' locations. (4% alexadricaine, Alexandria Company for Pharmaceuticals and Chemical Industries ,EGYPT.)The technique used was a transmucosal thermo-photocoagulation technique (non-contact mode) with an Nd:YAG laser of a 1064 nm wavelength (Fotona LightWalker® AT-S laser system-FOTONA, Texas, USA. https://www.fotona.com.) operating in a continuous mode, and the output power of the laser beam was selected at 4 W using a flexible 300 µm fiber-optic Nd:YAG handpiece (R21-C3, 300 µm fiber-optic handpiece, FOTONA, Texas, USA.) After activation of the fiber-optic tip, the handpiece of the laser system was maintained perpendicular to the surface of the lesion and was set to be 2-3 mm away from the lesion's surface. The treatment was started at the edges of the lesion and moved towards the center in a multiple-spot manner, with each spot spaced at least two to three millimeters apart to avoid overlap and thermal concentration at the same spot (polka dot pattern). The fiber was not kept on the same spot for longer than five seconds. The lesion was irradiated until clinical signs of shrinking and whitening manifested. After each of several irradiated spots, the lesion was swabbed with moist gauze embedded in a cold saline solution to minimize deep thermal injury. Every part of the venous VM received laser energy until the lesion became firm and turned light grey. The occurrence of blanching was a sign of photocoagulation immediately following the laser therapy. Pictures were taken immediately after the laser session to compare the treatment outcomes. The sessions were repeated every four weeks until no more intervention was needed.

2-Intralesional Bleomycin sclerotherapy group [9,24] (Fig.2)

Figure 2: Intralesional Bleomycin Sclerotherapy A) Bleomycin Injection 15 IU, vial used. B) Bleomycin solution preparation procedure C) Preoperative view of the venous low-flow VM in the floor of the mouth. D) Intralesional injection of bleomycin after confirming the presence of the needle inside the VM. E) 1-week postoperative view showing the ulceration formation F) The second session of intralesional bleomycin injection after 1 month of the first injection G) 1-week postoperative view showing moderate shrinkage of the VM. H) 2-month postoperative view before the third injection. I) 2 weeks after the third injection. J) Excellent improvement and complete disappearance of the VM.

Each patient received a local anesthesia according to the VMs' locations. After that the reconstituted bleomycin solution (Bleocip Bleomycin Injection 15 IU, Vial, Cipla, Mumbai, India) was freshly prepared by dissolving 15 mg of the powdered form of bleomycin in 15 ml of normal saline (every 1 IU of bleomycin corresponds to 1 mg/ml of bleomycin). The required dose was calculated according to the lesion size and patient weight on each visit within the range of the maximum recommended dose for adults, 15 mg per session. Then the reconstituted bleomycin solution was used immediately after preparation using a 3 ml/24-gauge sterile syringe under complete aseptic techniques. Intralesional bleomycin sclerotherapy injection was done after confirming the presence of the needle inside the vascular lesion. The sclerosing agent was injected intralesionally into the mucosa at several locations, initially at the lesion's periphery and then in the middle, until blanching was noticed. After injection, pressure was applied using gauze for 3-5 minutes to prevent the reflux of bleomycin and to achieve hemostasis. Pictures were also taken immediately after the injection to compare the treatment outcomes. Injections were repeated every four weeks until no more intervention was needed.

C.Early Postoperative Care

Anti-inflammatory and Anti-edematous tablets were prescribed for all patients three times daily for three days. All patients were instructed to apply cold fomentations on the first day, in addition to avoiding hot or hard-textured foods for the first three days following the intervention.

D.Follow-up phase

The follow-up plan included clinical evaluation for the following clinical assessment parameters up to one year after interventions:

1-Clinical healing response

The primary outcome was the clinical healing of VMs in response to the two interventions. At 1, 2, 4, 8, 12, 24 weeks after intervention, the lesion's area was measured to determine its change in size. At each time point, the area reduction percentage was then recorded. (16) The area reduction was evaluated using the Vlachakis criteria [25] and was categorized as follows: when the vascular lesion has completely disappeared or there is a complete response showing a 90–100% reduction in area, this indicates excellent improvement. A 50–89% reduction in area is a good improvement. A 20–49% area reduction is a moderate improvement. A reduction of 0–19% in area is inadequate and elicits no response.

2-Postoperative complications

Pain: The score of pain intensity was evaluated at the first, second, and fifth days after each intervention. Every patient was asked to rate their degree of pain or discomfort using the Numeric Rating Scale (NRS-11). This verified test gauges' pain on a scale of 0 to 10, with 0 denoting no pain or oral symptoms, 1–3 light pain, 4–6 moderate pain, 7–9 severe pain, and 10 the worst pain conceivable. [26]

Edema: Edema was subjectively assessed and categorized as no edema, mild, moderate, and severe on the first, third, and seventh day. [27]

Presence of any other complications:

Based on clinical observations, the presence of any additional complications, such as ulceration, bleeding, ecchymosis, infections, scarring, or recurrence were noted up to one year after interventions.[27,28]

Statistical analysis

The data was entered into the computer and analyzed using IBM SPSS software package version 20.0 (IBM Corporation, Armonk, NY, 2011). Categorical data were represented by numbers and percentages. The chi-square test was employed to compare the two groups. Alternatively, Fisher's exact or Monte Carlo adjustment was used when the expected count for over 20% of the cells was less than 5. The normality of continuous data was assessed using the Shapiro-Wilk test. The quantitative data was expressed using the mean, median, standard deviation, interquartile range, and range (minimum and maximum). The Student t-test for normally distributed quantitative variables was used to compare two groups. Furthermore, the Post Hoc Test (Dunn's) was utilized for pairwise comparisons, and the Friedman test was utilized for comparisons involving more than two periods and categories. The significance of the results was evaluated at the 5% level.

Results

Our study included twenty-two adult patients with oral venous low flow VMs, 13 of whom were male (59.1%) and 9 of whom were female (40.9%) with age ranging from 18 -56 years old with a mean of 34.59 ± 11.07 years presented with oral venous VMs were enrolled in our study. Patients were gathered from Alexandria University's Faculty of Dentistry's maxillofacial outpatient clinic. Two groups of eleven patients each were randomly assigned: The Nd-YAG laser group and the bleomycin sclerotherapy group. The demographic data for both groups was recorded and tabulated. (Table 1)

Table (1):Compares the two groups under study based on demographic data and the number of sessions.

FSR	Grade	Description
No	S0	No sensation
	S1	Deep cutaneous pain
	S2	Some superficial pain and touch
	S2+	Superficial pain and touch plus hyperesthesia
Yes	S3	Superficial pain and touch without hyperesthesia and static 2-point discrimination >15 mm
		Indicates useful sensory function
	S3+	Same as S3 with good stimulus localization and static 2-point discrimination of 7-15 mm
		Indicates useful sensory function
	S4	Same as S3 and static 2-point discrimination of 2-6 mm
		Indicates complete sensory recovery

IQR: Inter quartile range SD: Standard deviation
t: Student t-test

%2: Chi square test FE: Fisher Exact
MC: Monte Carlo test

p: p value for comparing between the two studied groups*: Statistically significant at p ≤ 0.05

The buccal mucosa and the tongue were the most common sites for the venous VMs in the present study with a total of 14 lesions, 7 (31.8%) lesions each. The majority of the lesions sized less than 2 cms which were 17 (77.3%). The required number of sessions for the lesions to be completely eliminated were fewer in the laser group (1, 2 or 3 sessions) than the bleomycin group (2, 3 or 4 sessions). With a p-value of 0.049, the difference in the number of sessions needed between both of the groups was statistically significant. (Table 1)

1.Clinical healing response

Regarding the clinical healing response according to the Vlachakis criteria, it was shown that the Nd-YAG Laser group had a statistically significant improvement of healing than the bleomycin group on the 1st, 2nd, 4th and 8th weeks with p-values of 0.022,0.035,0.001and 0.003, respectively. However, when comparing the healing between the 2 groups on the 12^{th} and 24^{th} weeks, the results were statistically insignificant. (Table 2a),

Table (2a):Comparison of the clinical healing response between the two groups under study.

Clinical healing response	Nd-YAG Laser (n = 11)	Bleomycin (n = 11)	χ2	p
1 week				
Excellent	4 (36.4%)	0 (0.0%)	7.255*	MCp= 0.022*
Good	4 (36.4%)	2 (18.2%)		
Moderate	3 (27.3%)	9 (81.8%)		
Poor	0 (0.0%)	0 (0.0%)		
2 week				
Excellent	4 (36.4%)	0 (0.0%)	6.068*	MCp= 0.035*
Good	4 (36.4%)	3 (27.3%)		
Moderate	3 (27.3%)	8 (72.7%)		
Poor	0 (0.0%)	0 (0.0%)		
4 week				
Excellent	8 (72.7%)	0 (0.0%)	14.098*	MCp >0.001*
Good	2 (18.2%)	10 (90.9%)		
Moderate	1 (9.1%)	1 (9.1%)		
Poor	0 (0.0%)	0 (0.0%)		
8 week				
Excellent	9 (81.8%)	2 (18.2%)	8.909*	0.003*
Good	2 (18.2%)	9 (81.8%)		
Moderate	0 (0.0%)	0 (0.0%)		
Poor	0 (0.0%)	0 (0.0%)		
12 week				
Excellent	11 (100.0%)	8 (72.7%)	3.474	FEp= 0.214
Good	0 (0.0%)	3 (27.3%)		
Moderate	0 (0.0%)	0 (0.0%)		
Poor	0 (0.0%)	0 (0.0%)		
24 week				
Excellent	11 (100.0%)	11 (100.0%)	–	–
Good	0 (0.0%)	0 (0.0%)		
Moderate	0 (0.0%)	0 (0.0%)		
Poor	0 (0.0%)	0 (0.0%)		

(Fig. 3). When comparing the clinical healing response within each group, both groups began to show statistically significant improvement in healing results after 8 weeks when compared to the 1st week results. This significant improvement continued till the 24th week. (Table 2b)

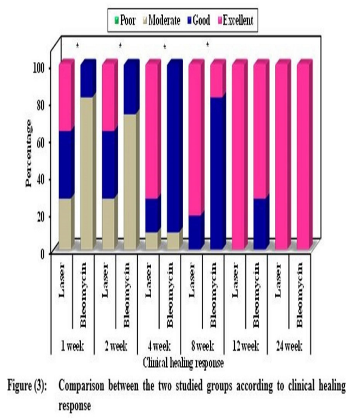

Figure 3. Comparison between the two studied groups according to clinical healing response

Table (2b):Comparison of the clinical healing response among each group during the different studied periods

Clinical healing response	1 week	2 week	4 week	8 week	12 week	24 week
Nd-YAG Laser (n = 11)						
Excellent	4 (36.4%)	4 (36.4%)	8 (72.7%)	9 (81.8%)	11 (100.0%)	11 (100.0%)
Good	4 (36.4%)	4 (36.4%)	2 (18.2%)	2 (18.2%)	0 (0.0%)	0 (0.0%)
Moderate	3 (27.3%)	3 (27.3%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Poor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
p0		1.000	0.077	0.026*	0.009*	0.009*
Bleomycin (n = 11)						
Excellent	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (18.2%)	8 (72.7%)	11 (100.0%)
Good	2 (18.2%)	3 (27.3%)	10 (90.9%)	9 (81.8%)	3 (27.3%)	0 (0.0%)
Moderate	9 (81.8%)	8 (72.7%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Poor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
p0		0.820	0.053	0.004*	<0.001*	<0.001*

2.Postoperative complications

a.Pain

Pain was evaluated according to the Numeric Rating Scale (NRS-11). There were statistically significantly higher pain levels in the bleomycin group compared to the Nd-Yag laser group only on the 1st postoperative day with p -value of 0.024. However, later on the 2nd and 5th days, pain was statistically insignificant between the 2 groups and all patients had no pain by the 5th day in both groups. (Table 3a), (Fig.4)

Table (3a): Comparison of the Pain Intensity (NRS-11) between the two groups under study.

Pain (NRS-11)	Nd-YAG Laser (n = 11)	Bleomycin (n = 11)	χ2	p
1st day				
No pain /oral symptoms (0)	5 (45.5%)	0 (0.0%)	6.832*	MCp= 0.024*
Mild pain (1–3 grade)	4 (36.4%)	9 (81.8%)		
Moderate pain (4–6 grade)	2 (18.2%)	2 (18.2%)		
Severe pain (7–9 grade)	0 (0.0%)	0 (0.0%)		
Worst imaginable pain (10)	0 (0.0%)	0 (0.0%)		
2nd day				
No pain /oral symptoms (0)	7 (63.6%)	7 (63.6%)	0.000	FEp= 1.000
Mild pain (1–3 grade)	4 (36.4%)	4 (36.4%)		
Moderate pain (4–6 grade)	0 (0.0%)	0 (0.0%)		
Severe pain (7–9 grade)	0 (0.0%)	0 (0.0%)		
Worst imaginable pain (10)	0 (0.0%)	0 (0.0%)		
5th day				
No pain /oral symptoms (0)	11 (100.0%)	11 (100.0%)	–	–
Mild pain (1–3 grade)	0 (0.0%)	0 (0.0%)		
Moderate pain (4–6 grade)	0 (0.0%)	0 (0.0%)		
Severe pain (7–9 grade)	0 (0.0%)	0 (0.0%)		
Worst imaginable pain (10)	0 (0.0%)	0 (0.0%)		

%2: Chi square test FE: Fisher Exact MC: Monte Carlo
p: p value for comparing between the two studied groups

*: Statistically significant at p ≤ 0.05

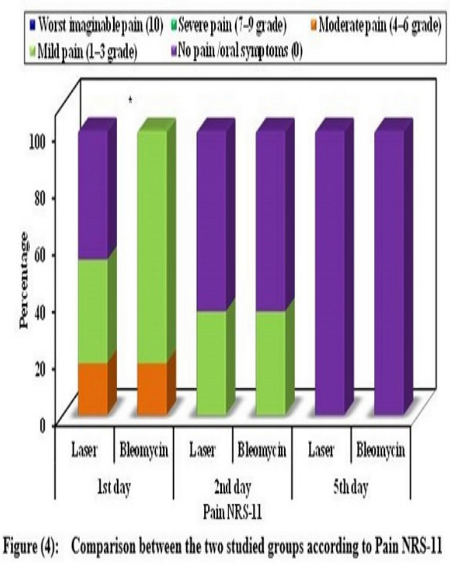

Figure 4. Comparison between the two studied groups according to Pain NRS-11

Concerning the pain within each group, only the results between the 1st day and the 5th day showed a statistically significant decrease in pain level. (Table 3b)

Table (3b):Comparison of the Pain Intensity (NRS-11) among each group during the different studied periods

Pain (NRS-11)	1st day	2nd day	5th day
Nd-YAG Laser (n = 11)			
No pain /oral symptoms (0)	5 (45.5%)	7 (63.6%)	11 (100.0%)
Mild pain (1–3 grade)	4 (36.4%)	4 (36.4%)	0 (0.0%)
Moderate pain (4–6 grade)	2 (18.2%)	0 (0.0%)	0 (0.0%)
Severe pain (7–9 grade)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Worst imaginable pain (10)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sig. bet. periods.	p1=0.286,p2=0.033*,p3=0.286		
Bleomycin (n = 11)			
No pain /oral symptoms (0)	0 (0.0%)	7 (63.6%)	11 (100.0%)
Mild pain (1–3 grade)	9 (81.8%)	4 (36.4%)	0 (0.0%)
Moderate pain (4–6 grade)	2 (18.2%)	0 (0.0%)	0 (0.0%)
Severe pain (7–9 grade)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Worst imaginable pain (10)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sig. bet. periods.	p1=0.008*,p2<0.001*,p3=0.286		

Fr: Friedman test, Sig. bet. periods were done using Post Hoc Test (Dunn's)
p1: p value for comparing between 1st day and 2nd day
p2: p value for comparing between 1st day and 5th day
p3: p value for comparing between 2nd day and 5th day
*: Statistically significant at p ≤ 0.05

b.Edema:

Despite that the bleomycin group experienced more edema than the Nd-YAG laser group, the differences were statistically insignificant throughout the follow up with p-values of 0.068,0.362, and 1.000 respectively. (Table 4a), (Fig.5) However,

Table (4a): Comparison of the two studied groups based on edema severity.

Edema	Nd-YAG Laser (n = 11)	Bleomycin (n = 11)	χ2	p
1st day				
No	5 (45.5%)	0 (0.0%)	6.403	MCp= 0.068
Mild	4 (36.4%)	8 (72.7%)		
Moderate	2 (18.2%)	3 (27.3%)		
3rd day				
No	8 (72.7%)	6 (54.5%)	2.432	MCp= 0.362
Mild	2 (18.2%)	5 (45.5%)		
Moderate	1 (9.1%)	0 (0.0%)		
7th day				
No	10 (90.9%)	11 (100.0%)	1.048	FEp= 1.000
Mild	1 (9.1%)	0 (0.0%)		
Moderate	0 (0.0%)	0 (0.0%)		

%2: Chi square test FE: Fisher Exact MC: Monte Carlo

p: p value for comparing between the two studied groups

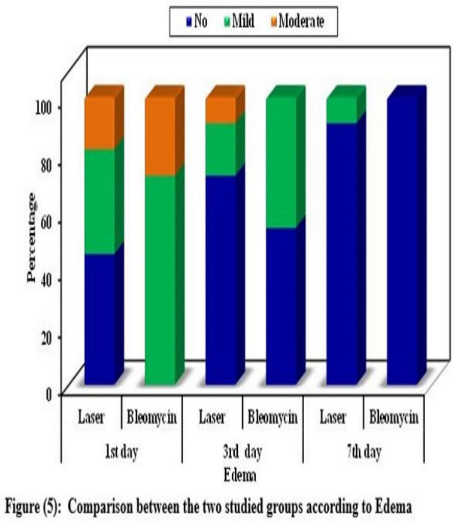

Figure 5. Comparison between the two studied groups according to edema

within each group the decrease in edema was statistically significant, between the 1st and 3rd as well as between the 1st and 7th day in the bleomycin group, while only significant between the 1st and 7th day in the Nd-YAG laser group. (Table 4b)

Table (4b): Comparison of the edema severity among each group during the different

Edema	1st day	3rd day	7th day
Nd-YAG Laser (n = 11)			
No	5 (45.5%)	8 (72.7%)	10 (90.9%)
Mild	4 (36.4%)	2 (18.2%)	1 (9.1%)
Moderate	2 (18.2%)	1 (9.1%)	0 (0.0%)
Sig. bet. periods.	p1=0.241,p2=0.043*,p3=0.394		
Bleomycin (n = 11)			
No	0 (0.0%)	6 (54.5%)	11 (100.0%)
Mild	8 (72.7%)	5 (45.5%)	0 (0.0%)
Moderate	3 (27.3%)	0 (0.0%)	0 (0.0%)
Sig. bet. periods.	p1=0.011*,p2<0.001*,p3=0.201		

Fr: Friedman test, Sig. bet. periods was done using Post Hoc Test (Dunn's)
p1: p value for comparing between 1st day and 3rd day
p2: p value for comparing between 1st day and 7th day
p3: p value for comparing between 3rd day and 7th day
*: Statistically significant at p ≤ 0.05

C.Presence of any other complications

Concerning any other postoperative complications, such as ulceration, bleeding, ecchymosis, infections, scarring or recurrance, although ulceration was the most evident complication in both groups, the difference between them was actually not statistically significant. With the exception of the bleeding incidence, which was statistically significantly greater in the bleomycin group than in the laser group (p =0.035), the remaining complications did not exhibit a difference in significance between the two groups. (Table 5)

Table (5):Comparison of the two groups under study based on additional complications.

	Total Sample (n = 22)	Nd-YAG Laser (n = 11)	Bleomycin (n = 11)	Test of Sig.	p
Ulcer-ation	21 (95.5%)	10 (90.9%)	11 (100.0%)	c2=1.048	FEp=1.000
Ecchy-mosis	1 (4.5%)	1 (9.1%)	0 (0.0%)	c2=1.048	FEp=1.000
Infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	–
Scarring	3 (13.6%)	3 (27.3%)	0 (0.0%)	c2=3.474	FEp=0.214
Bleed-ing	5 (22.7%)	0 (0.0%)	5 (45.5%)	c2=6.471*	FEp=0.035*
Recur-rence	0 (0.0%)	0 (0.0%)	0 (0.0%)	–	–

IQR: Inter quartile range SD: Standard deviation
t: Student t-test
%2: Chi square test FE: Fisher Exact
MC: Monte Carlo test
p: p value for comparing between the two studied groups
*: Statistically significant at p ≤ 0.05

DISCUSSION

Various management strategies are now implemented for the treatment of oral venous VMs. However, comparing different treatment options in this field may be scarce. Bleomycin sclerotherapy and laser therapy are two of the mainstays of venous VMs management. Therefore, our study aimed to assess and compare the efficacy of Nd: YAG laser thermo-photocoagulation versus bleomycin sclerotherapy in the treatment of oral venous VMs. In our study, the Nd: YAG laser (1046 nm) was chosen in particular because it is weakly absorbed by water and selectively absorbed by hemoglobin, Hemoglobin absorbs the photon energy and produces a high temperature locally, which causes thermo-photocoagulation, hemostasis and lesion shrinking. The selective destruction of lesional vessels is the Nd-YAG laser's mode of action. [29]. In addition to, it has penetrating capacity to reach the deep vessels of VMs. This was also confirmed by Bastos JT et al.[30]. The application of Nd: YAG laser in transmucosal non-contact irradiation mode, was found to have great outcomes on all the patients in our study. This may be attributed to its penetration capacity to the deeper layers of the tissue efficiently targeting the VMs. This is unlike the other types of lasers that have poorer penetration power. This confirms with Chang CJ et al who stated that although KTP Laser and Nd: YAG laser were used by many studies for the treatment of venous VMs, it was found that the wavelengths of Nd: YAG laser is double that of KTP laser, and that it's more powerfully absorbed by the oxyhemoglobin and the deoxyhemoglobin within the blood vessels. [31] Moreover, this technique was convenient for all the patients in the Nd: YAG laser group who were relieved to hear that the technique was superficial and non-invasive.In our study, it was decided to use intralesional bleomycin sclerotherapy, as the clinical research has looked closely at liquid bleomycin's efficacy in sclerotherapy for low-flow VMs. An advantage of this method is its inherent ability to cause a non-specific inflammatory response,a scleroembolic effect, and an endothelial-to-mesenchymal transition that remove the entire vascular network supplying the lesion, indicating the potential for regenerative somatic growth to replace the vascular anomaly.[32] In consistent with Muir et al [33] study who suggested that using intralesional bleomycin injections as a first-line treatment for lymphatic and venous malformations,as well as hemangiomas, rather than invasive surgery and concluded that bleomycin has a high sclerosing effect on the endothelium of vascular anomalies, positive therapeutic outcomes and lack of significant side effects. In the present study, the maximum dose of bleomycin each session was 15 mg, and the dosage was adjusted according to the patient's weight and the size of the lesion on basis of the work of Muir et al [33] to keep the dose at the safe range that prevent the occurrence of pulmonary fibrosis. The majority of cases in the present study were males (59.1%), with the remaining 40.9% being female. This is consistent with the higher male prevalence in the findings of Armogida et al [16] and Jan et al [34]. In contrast to prior studies where the female ratio was higher than the male ratio (9,19,35,36 The clinical healing response results from the current investigation revealed a statistically significant overall improvement in the clinical healing response through the follow up periods within each group with excellent clinical healing response at the end of the study duration which prove the efficacy of both modalities in the treatment of oral venous VMs. when comparing the results of both groups, it was found that the patients in the transmucosal thermo-photocoagulation Nd-YAG Laser group had a statistically significant improvement of healing earlier than the intralesional bleomycin sclerotherapy group patients on the 1st, 2nd, 4th and 8th weeks follow up while the difference between the two groups at the 12th and 24th weeks was insignificant. In addition, there was a difference in the required number of sessions for the lesions to be completely eliminated that was statistically significantly fewer in the Nd-YAG laser group than the bleomycin group. This may be attributed to the wavelength of 1064 nm of the Nd:YAG laser offers the benefit of deeper penetration and more absorption by oxyhaemoglobin and deoxyhaemoglobin without interacting with the surface layers. Since the lesion contracted in both horizontal and vertical directions, therefore, shortly after irradiation, its thickness decreased. In addition, it was found in our study results that small lesions were healed completely after one session without any recurrence at the follow-up period because the laser beam reached deep within the lesion causing immediate shrinking of the VMs. This is consistent with the findings of Takamaru et al [15] and Armogida et al. [16] Furthermore, the sclerosing effect of bleomycin relies on disrupting the proliferation of vascular endothelial cells by cutting the DNA chain during the S phase of the cell cycle, which inhibits DNA synthesis. Moreover, bleomycin causes irreversible damage to endothelial cells, causing a non-specific inflammatory response that encourages blockage and sclerosis of blood vessels. As a result, the mechanism of action for intra-lesional bleomycin sclerotherapy is distinct and may require a longer time to take effect.[35] Concerning postoperative pain, the NRS-11 scale employed during postoperative patient follow-up indicates that the pain intensity was significantly higher in the bleomycin group than in Nd-Yag laser group only on the 1st postoperative day (p= 0.024) However, pain was statistically insignificant between the two groups on days two and five, and by the fifth day, there was no pain felt by any of the patients in either group. The Nd:YAG laser group's lower NRS scores on the first postoperative day could be explained by using the output of the laser beam's settings at a selected power (4 W) with a polka dot technique and cooling during laser application, which resulted in no or little pain. This is in line with the results of Medeiros et al. [36] and Armogida et al. [16]. While Asai et al. [37]performed a clinical study to assess the efficacy of photocoagulation using an Nd:YAG laser for treating VMs in the oral region with an 8–15 W output. They reported that 11 of 69 (15.9%) patients experienced pain more frequently in larger lesions (>15 mm) than those with smaller lesions, while symptoms disappeared within 1 week. Moreover, the local inflammatory reaction after sclerotherapy may have contributed to the greater rate of pain scores in the bleomycin sclerotherapy group. This data is consistent with the findings of Brandão et al.[32]. In contrast to the findings of a study conducted by Arafat et al.[38] to assess the safety and clinical outcomes of intralesional injections of bleomycin in the treatment of pediatric patients with venous VMs, they reported no pain during or after injections. In terms of postoperative edema during the first week after the treatments, it was noted that the bleomycin group patients experienced transient localized edema more than the Nd-YAG laser group patients; however, the differences showed no significant change, and all the cases in both groups showed proper resolution of the transient edema and excellent healing. This may be due to the inflammation induced by the injected bleomycin especially in large sized lesions. These clinical findings are confirmed by the findings of Bhardwajet al [35]and Arafat et al. [38] Regarding the cause of postoperative transient edema in the Nd: YAG laser group may be due to heat produced by the laser radiation causes blood vessels to photocoagulate and trigger an inflammatory cascade, which increases the amount of fluid in the treated area. Whereas, in our study, low laser beam output (4 W) with using polka dot technique was selected in addition to the cooling used during laser irradiation. The heat accumulation inside the tissues was kept to the minimum that decreased the chance of postoperative edema in the Nd-YAG laser group. This is inconsistent with the findings of Takamaru et al.[15] who use a laser beam output of 10 W and demonstrated that 47% of the cases showed moderate to severe postoperative swelling they believed that tissue damage from prolonged Nd: YAG laser irradiation was the most likely cause of moderate to severe postoperative swelling. Furthermore, the large size and deep location of the VMs lesions may cause significant swelling when using NdYAG laser at higher outputs as documented by Asai et al.[37] Based on our findings, it can be stated that the two groups do not differ statistically significantly concerning other postoperative complications, such as ulceration, ecchymosis, infections, or scarring, except for the bleeding incidence, where it increased significantly in the bleomycin group compared to the Nd-YAG laser group, especially in large-sized lesions (> 3 cm). This can also attributed to the high affinity of the Nd:YAG laser to hemoglobin therefore, the damage to the surrounding tissue is avoided by selectively targeting and photocoagulating hemoglobin while releasing heat during the procedure, thus preventing bleeding and reducing complications related to adjacent tissues. This agrees with a study by Vesnaver A & Dovs DA [39], a study by Bekhor PS [40], and Armogida et al. [16]. None of the lesions showed recurrence over the course one year of the follow up period after the treatment with Nd:YAG transmucosal thermo-photocoagulation or bleomycin sclerotherapy. This could be because of the proper laser beam parameters, low energy level, and the long wavelength of the selected Nd-YAG laser (1064 nm) which makes it possible to target even the deep and large venous VMs for a longer period of time, resulting in its resolution without increasing the risk of complications or scarring. This also agrees with Takamaru et al [15] who stated that none of the cases showed recurrence of VMs one-year after using a single non-contact Nd: YAG irradiation. In addition to that the lack of reccurance in the intralesional bleomycin sclerotherapy may be due to the irreversible effect of bleomycin as a sclerosing agent. By comparing both modalities, Nd-YAG transmucosal thermo-photocoagulation is an excellent, non-invasive, safe, convenient and rapid treatment modality for the treatment of oral venous VMs. All patients showed high satisfaction from the outcomes achieved. Moreover, efficient and rapid healing was easily achieved with few or no pain, absence of bleeding and no recurrence. However, the laser machine is more expensive and needs higher learning skills to adjust the proper laser beam parameters, as well as, the risk of minimal scaring if large VMs or using improper parameters makes it critical to use it in esthetic area. Likewise, intralesional bleomycin sclerotherapy serves as an effective, feasible, safe and minimally invasive treatment modality for oral venous VMs with minimal transient complication rate. The advantage of absence of scarring makes it superior in case of VMs present in esthetic area however, the risk of bleeding makes it crucial to be chosen in large sized VMs. It can be concluded that Nd-YAG laser photocoagulation and bleomycin sclerotherapy efficiently treat oral venous VMs with minimum postoperative complications& no recurrence. Nd-YAG laser demonstrates significantly faster clinical healing responses, as well as causes significantly less pain, no bleeding and has better acceptance by the patients than intralesional bleomycin sclerotherapy while sclerotherapy is better in case of esthetically visible venous VMs when a risk of scarring is present. One of the study's limitations was that neither the patients nor the operators were blinded due to the recognizable nature of both techniques. Additionally, the size and locations of the venous VM are not specified, which would allow for a more thorough comparison. It is advised that future studies choose particular VM areas of comparable sizes. Also, it is recommended to assess the long-term efficacy or the recurrence rate, which is known to be high in these VMs since our mean follow-up of one year was also rather short.

DECLARATIONS: The authors declare that they have no competing interests.

Acknowledgements We appreciate Dr. Ali Sheta's assistance with the oral VMs' ultrasonographic examination.

Funding No company or organization is

providing any financial assistance.
Data availability Upon request, the corresponding author will provide all of the data used in this work.
Conflict of interest: No conflicting interests are disclosed by the authors.

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