

Original Article

Role of Foam Sclerotherapy with Injection Ethanolamine Oleate for the Treatment of Venous Malformation in Head-Neck Region

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Abstract:

Background: Venous malformations (VMs) are a variety of low flow vascular malformations, which are developmental error of morphogenesis of veins where veins are dysplastic lined by quiescent or normal endothelium. Although surgical extirpation is the standard method for the treatment of vascular malformations, this procedure often leads to significant loss of motor function, nerve damage, or massive bleeding in patients which may endanger the life. Therefore, sclerotherapy has now been accepted as a less invasive alternative and good results have been obtained.

Objectives: This study was conducted to evaluate the clinical outcomes after Foam sclerotherapy with injection Ethanolamine Oleate (EO) for the treatment of VMs in head-neck region.

Methods: This quasi-experimental study was conducted in the Department of Otolaryngology-Head & Neck Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU). Forty-three patients with venous malformation in head neck region that had the inclusion criteria were enrolled as a study sample. The patients were diagnosed mostly clinically & confirmed by demonstrating non-pulsatile blood flow and venous space using Duplex ultrasound. The sclerosing solution 5% Ethanolamine Oleate (EO) was used in this study. Sclerofoam was produced using the Tessari method in 4:1 air to liquid ratio, the foam had been used within 60-90 seconds. Results of the study were categorized as excellent, good, fair and poor. Ethical clearance was obtained from the Institutional Review Board (IRB) of BSMMU.

Results: Among 43 patients 34(79.1%) patients underwent single session and 9(20.9%) were two sessions. All the lesions were responded to EO. Response to sclerotherapy

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categorized as excellent were in two third 29 (67.4%) patients and 14 (32.6%) had good response. No sessions resulted in poor responses. No complications occurred following any procedures. All of the sessions were performed as a day case basis without anesthesia.

Conclusions: Foam sclerotherapy with injection EO appears to be safe and effective for the treatment of VMs in the head and neck region and should be considered when treating these complex lesions.

Key words: Ethanolamine oleate, Venous malformations, Sclerotherapy

Introduction:

Vascular malformations are congenital lesions of the vascular or lymphatic system which occurs due to an erroneous vascular development during embryogenesis. Vascular malformations can be classified into high and low flow malformations. Arteriovenous malformations (AVMs) are high flow; capillary malformations (CMs), lymphatic malformations(LMs), and venous malformations (VMs) are low flow lesions. The greatest proportion of low-flow malformations is located in the head and neck region^{1,2}.

Venous malformation is one of the most common benign vascular lesions, with approximately 40% of cases appearing in the head and neck. They can affect a patient's appearance and functionality and even cause life-threatening bleeding or respiratory tract obstruction. The lesions can be present within muscles, adipose tissue and sometimes are difficult to delineate^{3,4}.

The vast majority of these malformations are sporadic and more commonly occur in the tongue, mouth, face, neck, airway tract and muscle. Venous malformation is not only disfiguring but is also usually associated with complications such as pain, ulcers, bleeding, and the compression or invasion of adjacent structures. These complications may have severe impact on speech, swallowing, and respiratory function and may even lead to death due to bleeding and suffocation^{4,5}.

Pain is common with venous malformations in the upper face and is largely secondary to

these static malformed venous pools leading to spontaneous thrombosis and resultant phlebitic syndrome in the area of thrombosis. In addition, the expression of matrix metalloproteinase-9 was recently found to be increased in intramuscular venous malformations, suggesting that venous malformations have the capability for invasive growth and angiogenesis while expanding slowly due to the increase in hydrostatic pressure. Progesterone receptors are highly expressed in venous malformations, which might be one of the reasons for the rapid increase in the number of lesions when hormonal levels change^{6,7}.

There are various kinds of treatment methods for venous malformation, including sclerotherapy, surgical therapy, combined surgical therapy & sclerotherapy, embolization and laser therapy. Such various modes of treatment actually reflect the fact that no single modality is entirely satisfactory for the treatment of all VMs. Surgical therapy can cure the disease, but may not possible in all cases, for example, large diffuse VMs. Surgery is not also possible in difficult approachable sites, such as oropharynx, mediastinum, esophagus, etc. Moreover, surgical therapy is costly, risky, time consuming and causes psychological embarrassment to the patients and their parents and it needs to hospital stay. The laser therapy is also costly and inadequate for all except the thinnest lesions. Embolization requires technical sophistications and is not feasible in all

cases. In such situation, sclerotherapy may be quite helpful. There are numbers of sclerosant for the treatment of VMs, such as: 5% ethanolamine oleate, absolute ethanol (100% ethanol), 1 and 3% sodium tetradecyle sulfate, ethibloc, polidocanol. No perfect sclerosant exists, and those compounds yielding better results often have higher rates of side effects and complications. Ethanolamine oleate has an established role as a sclerosant for lesions elsewhere in the body, most notably for esophageal varices requiring sclerotherapy, for which it is the only agent with Food and Drug Administration (FDA) approval. Recently, administration of new sclerosing foam has been introduced by Cabrerra Garrido, predominantly for the treatment of varicose veins of lower extremities and appeared to have the advantage of causing more severe damage on the intima compared with the liquid form⁸. However, few studies have been reported on the use of sclerosing foam for the treatment of symptomatic VMs. This current study presents a single center experience using ethanolamine oleate for such lesions⁸⁻¹¹.

Methods:

A quasi experimental study was performed in the Department of Otolaryngology- Head & Neck Surgery at Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka from January 2018 to July 2019. A total of 43 patients with 43 venous malformations (22 male, 21 female; age range 11-62 years, the mean age was 26.1±12.2 years) were included in the study (Table 1). Diagnosed cases of venous malformation (VMs) in head-neck region with size up to 3 cm in greatest diameter were the inclusion criteria. Postoperative patients with recurrent and residual venous malformations were also included. The patients were diagnosed mostly clinically and confirmed by

demonstrating non-pulsatile blood flow and venous space using duplex ultrasound. Magnetic resonance imaging sequences was also reviewed to document the location, extension and size of VM in few patients. Photographs of the lesion were taken.

The sclerosing solution 5% ethanolamine oleate (EO) was used in this study. The volume injected and the total number of sessions was depended on the size and distribution of the VMs and weight of patients. However, the maximum dose of injected sclerosants was not exceeding 0.4ml/kg per session. The sclerosing foam was produced by Tessari's method using EO with the liquid-to-air ratio of 1:4. After the treatment session, compression dressing was applied for promoting endosclerosis. The compression was maintained for 30- 60 minutes. The patients were allowed to go home after injection, observed on 3rd and 7th day and advised to report if any complications arise. Categorization was as follows.

| | |
|-----------|---|
| Excellent | Lesions with no remaining visible abnormality |
| Good | Lesions that was visibly smaller and subjectively less than half their original sizes. |
| Fair | Lesions that was visibly smaller and subjectively greater than half their original sizes. |
| Poor | No change of lesion. |

Patients asked whether they satisfied with sclerotherapy as follows: very satisfied, satisfied, dissatisfied, or neither. Markedly improved" and improved" were defined as a good response", and very satisfied" and satisfied" were defined as satisfaction". Photographs also were taken during each follow up to document the effects of injections. In doubtful cases present or absent of lesions was confirmed by doppler USG.

Results:

Result was calculated and expressed in tables.

Table-I :
Age of the patients (n=43)

| Age (in year) | No. of patients | Percentage |
|-----------------|-----------------|------------|
| 11-20 | 18 | 41.9 |
| 21-30 | 14 | 32.6 |
| 31-40 | 5 | 11.6 |
| 41-50 | 4 | 9.3 |
| >50 | 2 | 4.7 |
| Mean \pm SD | 26.1 | \pm 12.2 |
| Range (min-max) | 11.0 | -62.0 |

Table-II :
Cases according to presenting complaints (n=43)

| Presenting complaints | No. of patients | Percentage |
|-----------------------|-----------------|------------|
| Pain | 7 | 16.3 |
| Swelling | 42 | 97.7 |
| Bleeding | 15 | 34.9 |
| Discomfort | 5 | 11.6 |
| Cosmetic problem | 4 | 9.3 |

Table-III :
Cases according to size of lesion (n=43)

| Size (cm) | No. of patients | Percentage |
|-----------------|-----------------|------------|
| <1 | 3 | 7.0 |
| 1-2 | 25 | 58.1 |
| >2 | 15 | 34.9 |
| Mean \pm SD | 2.0 | \pm 0.8 |
| Range (min-max) | 0.5 | -3.0 |

Table IV :
Location of lesion (n=43)

| Location | No of patients | Percentage |
|---------------------------|----------------|------------|
| Buccal mucosa | 8 | 18.6 |
| Lower alveolus | 1 | 2.3 |
| Lateral margin of tongue | 13 | 30.2 |
| Dorsum of tongue | 6 | 14.0 |
| Ventral surface of tongue | 4 | 9.3 |
| Inner aspect of lip | 4 | 9.3 |
| Angle of mouth | 4 | 9.3 |
| Face | 1 | 2.3 |
| Root of the neck | 1 | 2.3 |
| Hand palate | 1 | 2.3 |

Table-V :
Cases according to compressibility, color and temperature (n=43)

| | No. of patient | Percentage |
|--------------------|----------------|------------|
| Compressibility | 43 | 100.0 |
| Bluish color | 43 | 100.0 |
| Normal temperature | 43 | 100.0 |

Table-VI :
Association between size and number of treatment sessions (n=43)

| Size (cm) | Number of treatment sessions | | | | P value |
|-------------|------------------------------|------|-----------------------------|------|---------------------|
| | One treatment session (n=34) | | Two treatment session (n=9) | | |
| | n | % | n | % | |
| \leq 2 cm | 24 | 70.6 | 4 | 44.4 | 0.143 ^{ns} |
| >2 cm | 10 | 29.4 | 5 | 55.6 | |

NS= Not significant

P value reached from chi square test

Table-VII :
Treatment outcome (n=43)

| Treatment outcome | No. of | Percentage |
|--------------------|--------|------------|
| | | patients |
| Regression | | |
| Good | 14 | 32.6 |
| Excellent | 29 | 67.4 |
| Recurrent bleeding | | |
| Present | 0 | 0.0 |
| Absent | 43 | 100.0 |

Discussion:

The venous malformations are congenital anomalies of vein, which are the common vascular anomalies. These lesions grow in proportion with body growth. They create physical and psychological embarrassment to the patient and as well as to their guardians. They may cause life-threatening complications also. There are many treatment modalities of Venous Malformations such as elastic supporting stockings, embolisation, LASER, surgery, sclerotherapy. Among them, though surgery can cure the disease but sometime surgical treatment is not possible in large diffuse venous malformations and in unapproachable sites. Surgery has some morbidity and mortality also. It is costly and time consuming for both patients and surgeons. Elastic supporting stocking has doubtful response, LASER treatment is costly and not effective in all cases, embolisation needs technical sophistication. The natural involution of untreated venous malformation has not been documented. So, there is a research for an agent who is either alternative to surgery or helpful to surgery. In this situation sclerotherapy with a suitable agent can solve this problems. There are many sclerosants, like Ethanolamine Oleate, Absolute Ethanol, Ethiblock, Polidocanol of which Ethanolamine Oleate is potent, has

minimal side effects, cost effective and easily available in our country. Ethanol causes extensive tissue damage if it is extravasated¹² but ethanolamine has no such effect. Ethibloc and polidocanol are not available in Bangladesh. We chose to use ethanolamine oleate because of its availability and its ability to produce vascular block by necrosis of vascular endothelium as well as blood vessel walls.¹² Ethanolamine oleate is a mild sclerotherapeutic agent, therefore, it does not cause any harmful side effects to other tissues if extravasated.¹² Although ethanolamine oleate can cause serious complications such as haemolysis and renal failure, in therapeutic doses it is highly diluted in the circulation and is inactivated by serum albumin and globulin.^{13,14} It may cause some hypersensitivity reactions.¹² EO is also used in country like Japan, Korea, Italy and USA for sclerotherapy of venous malformation with success. Encouraged with the experience of others^{12,13} we have also used Ethanolamine Oleate intralesional among our study population. During the study period, from January 2018 to July 2019 forty-three patients with venous malformations were seen by the investigator directly or referred by others. In doubtful cases, diagnosis was confirmed by Doppler ultrasonography. Ages of the patients were ranged from 11 to 62 years. The mean age was found 26.1, SD was ± 12.2 years. In literature the incidence of Venous Malformations is same in both male and females (Cohen BA, 1987) and in our study male: female ratio was 1.05:1 which is also almost same. The cause of arriving at the hospital was mainly complications such as swelling, bleeding, pain and some had cosmetic issue. Our study shows majority 42(97.7%) patients had swelling followed by 15(34.9%) had bleeding, 7(16.3%) had pain, 5(11.6%) had discomfort and 4(9.3%) had cosmetic problem.

Among the study population 42(97.7%) had good sign of nutrition. Mean pulse was 82.2 ± 4.6 beats/min, mean SBP was 111.9 ± 3.9 mmHg, mean DBP was 71.6 ± 3.7 mmHg and mean respiratory rate was 16.6 ± 1.0 breaths/min. The study was performed on 43 patients with 43 lesions. Majority 13(30.2%) patients had lateral margin of tongue followed by 8(18.6%) had buccal mucosa, 6(14.0%) had dorsum of tongue, 4(9.3%) had ventral surface of tongue, 4(9.3%) had inner aspect of lip and 4(9.3%) had angle of mouth. The site of lesion did not affect the outcome of sclerotherapy. There were no sexual variations of responses observed in our study. All the patients were freshly enrolled. They did not have any history of previous surgery, sclerotherapy or any other intervention which might reflect the outcome of sclerotherapy.

The dose of injection Ethanolamine Oleate varies from 0.5ml to 16ml depending upon the site and size of lesion and weight of patients. According to surface area we use maximum 0.4 – 1ml per sq. cm area. In case of small lesions like 1cm in diameter and if there is no underlying bones and cartilage 50mg (1ml) of intra-lesional injection Ethanolamine Oleate was given. But lesions over bones and cartilage e.g. lesions over hard palate, relatively small amount (.4ml per square cm) of injection were pushed in a single session due to fear of sloughed out. Patients were followed up after 8 weeks, when single session cover the whole lesion. For large diffuse lesions where a single session can't cover the whole lesion due to relatively low body weight, second session was performed after 21 days interval and results were evaluated after 8 weeks of last injection session. Only one session of injection was required for total regression of three fourth (70.6%) lesions, among them

24 had had size ≤ 2 cm and 10 had > 2 cm, nine other needed two sessions of which five had > 2 cm. But this difference was not statistically significant ($p > 0.05$). Maximum two sessions were performed depending upon site and size of lesion and weight of patients. All of the patients had response to Ethanolamine Oleate, which correlates the result of others¹²⁻¹⁴. Doppler USG confirmed the result in doubtful cases. All patients observed swelling after injections, which also correlates with others^{15,16}.

No complications occurred following any procedures. No recurrent bleeding was seen after the treatment. Alexander MD et al. did a study on 2014 at Department of Radiology, Santa Clara Valley Medical Center, San Jose, California, USA which also shows no complication following sclerotherapy. Side effects noted were epithelial sloughs out which healed spontaneously. Epithelial sloughed out occurs seems to be due to over dose of injection in relation to size of lesion, which is avoidable. No other side effects except epithelial sloughed out experienced in our study. One study shows 86% excellent response¹⁶, another study shows 75% excellent response¹³ and our study shows 67.4% excellent response. With the above findings, our study shows that the foam sclerotherapy with ethanolamine oleate for the treatment of venous malformations is an effective one.

Conclusion:

Foam sclerotherapy in venous malformations of head and neck can be safely performed using Ethanolamine Oleate. The advantage of foam sclerosant includes the possibilities of reducing the amount of necessary sclerosing solutions as well as the concentration with an acceptably low rate of adverse events. Treatment with this agent is well tolerated and caused no complications in this study. Using the proposed protocol, foam sclerotherapy is an effective treatment

method of venous malformations of head and neck region, promoting the remission or reduction in size of these lesions.

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