

# Treatment of venous malformations with ethanolamine oleate: a descriptive study of 83 cases

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Published online: 3 February 2011  
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## Abstract

**Purpose** To evaluate the outcome and complications of sclerotherapy with injection ethanolamine oleate for the treatment of venous malformations (VMs).

**Methods** Eighty-three patients' (39 males and 44 females) age ranging from 3 months to 21 years with 85 lesions were followed clinically for about 1 year following treatment with injection of ethanolamine oleate. The cases were enrolled between January 2006 and December 2009. The amount of ethanolamine oleate per treatment session ranged from 0.50 to 10 ml, and maximum dose was 0.40 ml per kg body weight. All patients were evaluated after 8 weeks of last injection session. All of the treatment sessions were performed on a day-case basis.

**Results** Eighty-five lesions have under gone 201 sclerotherapy sessions with 39 requiring one, 27 requiring two and 19 lesions requiring more than two sessions. Sclerotherapy with ethanolamine oleate provided complete resolution of symptoms in 79 lesions and significant improvement of 6 lesions. There is no recurrence of studied patients. All patients experienced pain and swelling to a variable degree for short duration. Skin sloughed out in four patients which were healed spontaneously. No other complications were observed in our study.

**Conclusion** The treatment of VMs with injection ethanolamine oleate is safe and effective.

**Keywords** Venous malformation · Cavernous hemangioma · Sclerotherapy · Ethanolamine oleate

## Introduction

Venous malformations (VMs) are low flow vascular malformations that can cause significant clinical problems and some times difficult to treat. Although they are present at birth, but may not be significantly evident [1]. They never regress, but even may expand and can present as single or multiple lesions in any location of body-like face, oral cavity, tongue, limbs, trunk, pharynx, genitalia, urinary bladder, brain, spinal cord, liver, lungs, skeletal muscles and bones. There is no sex preponderance [1]. The incidence of VM is 1–4% [2]. They can be cosmetically inconsequential or tragically distorting. VMs are mislabeled both in medical parlance and literature as cavernous hemangioma. History and physical examination usually confirm diagnosis of VM [1].

At present, various therapeutic options for venous malformation are

1. Sclerotherapy
2. Surgical therapy
3. Combined surgical therapy and sclerotherapy
4. Embolisation
5. 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

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VMs. Surgery is not also possible in difficult approachable sites, such as oropharynx, mediastinum, esophagus, etc. Surgical therapy is costly, risky, time-consuming and causes psychological embarrassment to the patients and their parents and it needs hospital stay. The laser therapy is costly and also inadequate for all except the thinnest lesions [3]. Embolisation requires technical sophistications [4], and is not feasible in all cases. In such situation, sclerotherapy may be quite helpful. Surgery may be needed to remove the residual fibrosis and phleboliths. There are numbers of sclerosant for the treatment of VMs, such as:

1. 5% ethanolamine oleate [5–9],
2. absolute ethanol [100% ethanol] [10, 11],
3. 1 and 3% sodium tetradecyle sulfate [4, 10],
4. ethibloc [12]
5. polidocanol [13].

Among these agents, ethanolamine oleate is one of the safe agent and easily available in Bangladesh.

## Methods

A prospective case study was performed between January 2006 and December 2009 in Bangabandhu Sheikh Mujib Medical University, Gonoshasthya Somaj Vittik Medical College, ZH Sikder Women's Medical College and in some private clinics of Dhaka City in Bangladesh. All patients up to 21 years of age with clinical VMs were studied. Post-operative patients with recurrent and residual disease of VMs were also included. Patients with a history of previous infections on VMs were excluded to avoid confusion.

Patients were diagnosed clinically. Doppler ultrasonography was done in some cases for documentation and academic purpose. Plain X-ray of relevant part done in few cases to see the effects of VMs.

After proper counseling and written informed consent from the guardians, all the patients were treated with intralesional injection of ethanolamine oleate on a day-case basis.

The maximum dose of ethanolamine oleate was 0.4 ml (20 mg)/kg [5, 6] of body weight ranges from 0.5 to 15 ml per session. The dose was adjusted according to the site and size of lesions and weight of patients. Injections were pushed directly into the lesion (intravascular or extravascular) with 25G/26G needle (Fig. 1) until slight elevation of lesion was noted [5, 6]. The patients were allowed to go home few hours after injection and observed on third and seventh day and advised to report if any complications arise. In case of small lesions in relation to body weight, which can cover in a single session, follow-up was given after 8 weeks of last session to evaluate the effect of ethanolamine oleate. If initial

procedure cannot cover the whole lesion in that case, patients were advised to attend after 3-week interval for second and subsequent procedures and follow-up given after 8 weeks of last session. For large diffuse lesions, more than two sessions were needed and in one patient we gave nine injection sessions.

## Results

A total of 83 patients with 85 lesions were studied. Thirty-nine patients were males and 44 females. Male female ratio was almost 1:1. The patients were aged from 3 months to 21 years. Mean age was 15.1 years, SD was  $\pm 1.13$  (Table 1).

Out of 85 lesions, 49 (57.65%) were presented at birth. Rest 36 (42.35%) appeared after birth.

The lesions were variegated in size and shape. The lesions appeared as focal, diffuse, serpentine or cystic, etc. The most common site of occurrence was the cranio-facial area 45 (53%). VMs also involved the head, axilla, trunk, limb genitalia and perineum (Table 2).

Among the 85 lesions, 33 were treated with oral steroid for at least 3 months, 7 were treated with intralesional steroid, 3 treated surgically, but recur after 6–8 months, 1 was treated previously with the injection ethanolamine oleate, but recurred after 6 years and 41 had no history of treatment. In all of these cases, steroid was non-responsive (Table 3).

The amount and frequency of injection of ethanolamine oleate were decided depending on the site and size of lesion and body weight of the patients. The surface area of the lesions varied from 1 to 132 sq. cm. Mean surface area was  $14 \pm 1.29$  sq. cm. The amount of the drug varied from 0.5 to 15 ml (mean  $5.03 \pm 0.73$  ml) per session. All of the procedures were performed on a day-case basis without anesthesia, except two patients with lesions in the oral cavity, who were treated under general anesthesia.



**Fig. 1** Procedure of injecting ethanolamine oleate

**Table 1** Age distribution of the patients

Age group (years)	No. of patients, <i>n</i> (%) ( <i>N</i> = 85)
1	15 (18)
1–4	16 (19)
4–14	29 (35)
15–21	23 (28)

**Table 2** Distribution of lesions in various sites of the body

Sites	No. of lesions, <i>n</i> ( <i>N</i> = 85)
Face	18
Oral cavity with lip	19
Tongue	4
Head	4
Neck	7
Trunk	15
Limb	16
Perinium	2

**Table 3** History of previous treatment of venous malformations

Past history of treatment	No. of lesions, <i>n</i> ( <i>N</i> = 85)
Oral steroid (prednisolone)	33
Parenteral steroid (triamcinolone)	7
Sclerotherapy (ethanolamine oleate)	1
Surgery	3
No treatment	41

Eighty-five lesions have under gone 201 sclerotherapy sessions with 39 requiring 1, 27 requiring 2 and 19 lesions requiring more than 2 sessions, rest needed multiple injection sessions, highest being 9 injection sessions and mean was 2.41.

All of lesions respond to injection of ethanolamine oleate sclerotherapy. Positive response was determined by regression of the lesion (reduction of size, fading of blue

color, flattening of the lesion and/or scarring). Figures 2, 3, 4, 5 show the response of ethanolamine oleate injection.

Responses of ethanolamine oleate were evaluated after 8 weeks of last injection session.

Response of ethanolamine oleate were graded in four groups

Excellent	Complete regression
Good response	>50% regression
Poor response	<50% regression
No response	No regression

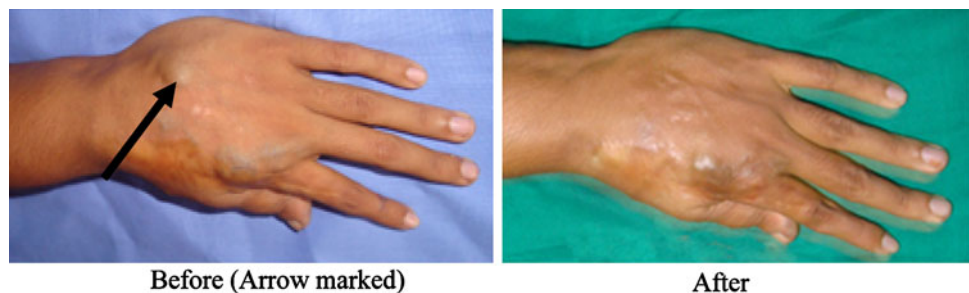
Among the 85 lesions, 79 had complete cure of disease. Rest 6 lesions (which were diffuse) had significant improvement of disease and palliation of symptoms (Table 4). All patients experienced pain and swelling to a variable degree for 3–7 days. Only symptomatic treatment was given to them.

Skin necrosis occurred in four patients, in two cases full thickness in a small area and in two cases—partial thickness skin loss was observed. All four lesions were healed spontaneously. No other side effect observed in the study. The site of lesion did not have any relation in the outcome of sclerotherapy. There were no age and sexual variations of responses observed in our study. In three cases, there were firm to hard non-compressible small amount of residual fibrous tissue observed which were asymptomatic and patients were satisfied. All of the patients were followed up at least 1 year after 8 weeks of initial evaluation, i.e. 14 months after last injection. There was no recurrence during the study period.

**Discussion**

Sclerotherapy with injection of ethanolamine oleate is an effective mode treatment of VMs. There are various sclerosing agents other than ethanolamine oleate like ethanol, ethibloc, polidocanol, etc. Ethanol causes extensive tissue damage if extravasated [14], but ethanolamine

**Fig. 2** VMs on dorsal aspect of hand before and after sclerotherapy



**Fig. 3** VMs on lower lip and tongue before and after sclerotherapy



**Fig. 4** VMs on volar aspect of left forearm—before and after 8 weeks of single injection



**Fig. 5** VMs on lower lip before and after sclerotherapy (procedure not yet completed)

**Table 4** Response of treatment

Response	No of patients, <i>n</i> (%) ( <i>N</i> = 85)
Cure	79 (93)
Good response	6 (7)
Poor response	0
No response	0

has no such effect. Ethibloc, polidocanol, etc. are not available in Bangladesh. We have chosen to use ethanolamine oleate because of its availability and its ability

to produce vascular block by necrosis of vascular endothelium as well as vessel wall [5, 15]. There were also studies with ethanolamine oleate in Bangladesh [5, 6]. Though ethanolamine oleate can cause serious systemic hazards, such as hemolysis, renal shutdown, but in therapeutic dose it is highly diluted in circulation. In circulation, serum albumin and globulin inactivates diluted ethanolamine oleate [16, 17] and serious systemic hazards, such as hemolysis and/or renal shut down cannot occur in therapeutic dose. It may cause some hypersensitivity reactions like any other drugs [15], but we did not face any such situations. It is used as a sclerotherapeutic agent for the treatment of VM in many countries like Korea [18], UK [19], USA [20], Japan [5, 21] and Brazil [8]. It is also used for the other disease like renal cyst [22], hydrocele [23] and bleeding peptic ulcer [24]. Ethanolamine oleate is commonly used for the treatment of esophageal varices [25, 26]. All of our patients had excellent and good response to ethanolamine oleate, which correlates the result of others [3, 5, 10, 11, 18–21]. All patients observed swelling after injections similar to the other studies [13]. Complications, such as epithelial sloughs in our four patients were healed spontaneously. No other side effects were observed in our study and the rate of complication did not differ from that of other studies [19]. Although there is no report of recurrence in literatures and we have also no recurrence during our studied period, but we found a recurrent case after 6 years of sclerotherapy with ethanolamine oleate. Probably, there were some residual lesions which were not evident at that time, but became evident later with aging at her 21 years of age. Other six patients with six lesions those showed significant improvement were satisfied and refused further treatment. The results of the present and other studies show that sclerotherapy with ethanolamine oleate for the treatment of VMs is an effective one.

## Conclusion

Sclerotherapy with ethanolamine oleate is effective for the treatment of VMs with acceptable safety margin, but often sclerotherapy has to be repeated. However, long-term

effects and the results of sclerotherapy with injection of ethanolamine oleate should be evaluated in a longer period of follow-up.

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