Sarah Arafat / Afr.J.Bio.Sc. 6 (5) (2024). 9015-9025 **ISSN: 2663-2187**

https://doi.org/ 10.48047/AFJBS.6.5.2024. 9015-9025

African Journal of Biological Sciences

Pros and Cons of Ethanol-amine Oleate Sclerosing Agent in Management of Maxillofacial Low Flow Vascular Malformations

Sarah Arafat [1], Abdelbadia Abdallah Abdelmabood [2], Wesam Mohamed [3], Gamal El-Tagy [4], Amr El-Swify [5]

1. Assistant Lecturer, Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Misr University for Science and Technology, Egypt.
2. Professor, Oral and Maxillofacial Surgery Department, Faculty of Dental Medicine, Al- Zagazig University, Al-Zagazig, Egypt.
3. Professor, Pediatric Surgery Department, Cairo University Specialized Pediatric Hospital (CUSPH), Faculty of Medicine, Cairo University, Cairo, Egypt.
4. Professor, Pediatric Surgery Department, Cairo University Specialized Pediatric Hospital (CUSPH), Faculty of Medicine, Cairo University, Cairo, Egypt.
5. Professor, Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Suez Canal University, Ismailia, Egypt.

Abstract

Maxillofacial vascular malformations are congenital anomalies that cause many functional and esthetic complications. Intralesional sclerotherapy is currently their gold standard treatment option.

There are many sclerosing agents available with various advantages and disadvantages; Ethanol-amine Oleate is among the most commonly used sclerosing agents. The aim of this review article is to provide a clear understanding of usage, pros and cons of Ethanol-amine oleate sclerosing agent in management of low flow maxillofacial vascular malformations.

Key Words: Ethanol-amine Oleate, sclerosing, maxillofacial, Low Flow, vascular malformations

Corresponding Author: Sarah Arafat
E-mail: sarah2000arafat@gmail.com
ORCID 0000-0003-4786-1695
Postal Code: 21571

Article History:
Volume 6, Issue 5, 2024
Received: 15 May 2024
Accepted: 02 Jun 2024
doi: 10.48047/AFJBS.6.5.2024. 9015-9025

Maxillofacial vascular malformations are congenital anomalies that cause many functional and esthetic complications; vascular malformations are classified into high flow and low flow; venous malformations are the most common type of low flow vascular malformations. Intralesional injection sclerotherapy is currently the gold standard treatment for vascular malformations. Ethanol-amine Oleate (EO) 5% is an organic chemical compound, consisting of Ethanol- amine (primary amine & primary ethanol alcohol) as a basic substance, with oleic acid and benzyl alcohol 2% as a preservative. Its common brand name is Ethamolin®. It is prepared as 50 mg per 1 mL of sterile aqueous solution; and it is available in 2 mL and 5 mL ampules. It has an alkaline pH range: 8 – 9. It is mainly metabolized mainly by the liver, rather than the kidneys.(1)

Ethanol-amine Oleate sclerosing agent is FDA approved and has been used for years to treat oesophageal varices, caused by liver disease that results in severe bleeding from the esophagus into the throat. (2)

Masaki et al(3)conducted their early experimental study in 1990 to understand the pharmacological effect of EO on endothelium of blood vessels in animals. The authors observed by electron microscope that when EO was injected into blood vessels, it destroyed the endothelium of blood vessels; causing occlusion of those blood vessels within few minutes. The authors assumed from this animal experiment that when EO causes acute irritation, inflammatory reaction of the vascular endothelium, thrombus organization, sclerosis of blood vessels, and eventually collapse and disappearance of oesophageal varices or varicose veins.

Johann et al (4) conducted the first clinical trial in 2005 to evaluate the effectiveness of EO sclerosing agent in 30 patients having oral hemangiomas and vascular malformations. The authors reported that all lesions responded with complete clinical resolution, and concluded that EO is an effective sclerosing agent for treatment of oral vascular anomalies.

Similarly, Alexander et al (5) in 2014 conducted their study to evaluate EO injection of venous malformations in the head and neck region. The authors concluded that effectiveness and safety of EO exceeds other sclerosing agents in venous malformations of the head and neck.

Later, Kato et al (6) conducted a cohort study of 15 patients having oral vascular anomalies of size smaller than 2 cm, injected with undiluted 5% EO in one session. The authors confirmed effectiveness and safety of EO sclerosing agent.

According to the available literature, EO 5% sclerosing agent is safe and effective treatment of venous malformations, because of its low toxicity, availability, and cheap price compared to other sclerosing agents. Itis a mild sclerosing agent due to its lower concentration; with has less frequent and less harmful side effects than Ethanol 95% sclerosing agent. On the other hand, Ethanol sclerosing agent causes excessive tissue damage and peripheral nerve injury if extravasated, EO 5% does not deeply invade tissues and vascular walls; thereby, reducing the potential damage to adjacent soft tissues and nerves in the head and neck region. [7]

On the other hand, EO sclerosing agent is also used in maxillofacial surgery for intra-articular injection of TMJ superior joint space every 2-3 weeks to treat joint hypermobility and recurrent dislocation; however, it carries the risk of TMJ ankylosis. [8] Also, EO sclerotherapy is used in treatment of maxillofacial peripheral giant cell granulomas [9]

Ethanol-amine Oleate 5% is available in 5 mL vials (EPICO, Egypt) that should be kept away from light. (Fig. 1) Its safe dose is 0.4 mL /Kg, and its maximum dose is 20 mL\ session; given at 1 or 2 weeks interval; the dose should be adjusted in each treatment session according to vascular lesion size and patient body weight, the number of injections is decided according to the clinical response of each vascular lesion. [10]

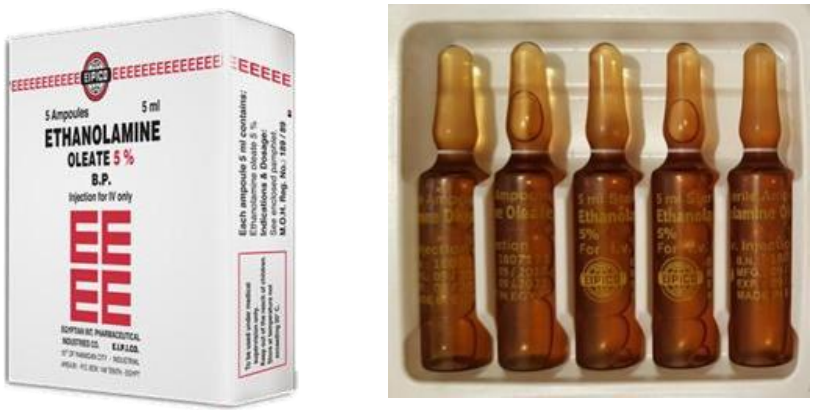

Fig. 1: Ethanol-amine Oleate 5% ampules ***

*** Ethanol-amine Oleate, EPICO, Egypt

Fernandes et al [(11)] and Kato et al [(12)] recommended using 5 % EO sclerosing agent undiluted, as it is more effective and requires fewer sessions. However, it has to be clarified that in the previously mentioned studies were conducted on adult patients and the size of facial vascular anomalies was smaller than 2 cm, which required smaller dose of undiluted EO 5% to be injected. This is an important factor to consider during judging the absence of adverse effects with fewer sessions to achieve quick successful results. Sclerotherapy with undiluted EO 5% of vascular anomalies larger than 2 cm size will necessitate a larger dose of EO to be injected, and in pediatric patients with lower body weight, this would definitely result in more adverse effects, as the safe pediatric dose of EO 5% is 0.4 mL \Kg.

On the other hand, Ragab et al in their study emphasized that 5% EO has to be diluted with sterile normal saline or distilled water, in a ratio 1:4 when used in facial lesions to avoid ulceration and\or facial nerve injury. [(13)]

Duffy et al in their study suggested that EO complications are caused by its high alkaline PH (range: 8 – 9). The high dose of local anaesthesia required with EO sclerosing agent increases the risk of systemic toxicity in children due to physiologic differences and weight between children and adults. Because the maximum recommended dose of any drug is based on the patient body weight. Therefore, EO intralesional sclerotherapy in children is recommended to be performed under GA to reduce risk of systemic toxicity of local anaesthesia, and to monitor vital signs during the procedure [(14)]

Regarding systemic complications of EO, Macroscopic haemoglobinuria (MH) is a common serious systemic complication following sclerotherapy using EO for venous malformation. Fujiki et al in their study catheter was inserted to monitor urine output and MH in all patients prior and after sclerotherapy; the authors recommended that MH should be closely monitored during sclerotherapy. [(15)]

Moreover, Lee et al [(16)] emphasized that pulmonary edema, which had been reported to be induced by oleic acid in animal lung ,can also develop in the human body with intravascular injection of EO sclerosing agent.

Although data available in literature suggest that EO can be used safely in case of intravascular administration below its safe dose of 0.5ml/kg; the product manufacturer [*][Glaxo Pharmaceuticals] had reported anaphylactic shock in 3 patients after EO sclerotherapy injection of varicose veins, with a dose less than 0.5ml/kg. [(17)]

Although all cases of anaphylaxis have been reported only with sclerotherapy of oesophageal varices and varicose veins, this life-threatening complication of EO must be kept in mind during intralesional injections of venous malformations; and it should be managed by emergency IM injection of Epinephrine 0.25 mg into Vastus Lateralis muscle of thigh (00.25 mg for pediatrics & 0.5 mg for adults of 1:10,000 Epinephrine), not given IV; as it will reach, stimulate the myocardium and can cause ventricular fibrillation. (18)

In our recent study in 2021 conducted on 15 children suffering from maxillofacial venous malformations, EO was injected at 2 weeks interval, post-operative pain, swelling, and elevation of body temperature occurred in all cases on the first post-operative day; scarring occurred in only 2 cases in the lower lip. (19)

Finally, the authors recommended that intralesional sclerotherapy only for intra-oral vascular malformations to avoid post-operative pain, facial ulceration and scarring. In addition, GA is recommended to avoid pain during intralesional injection, the potential risk of toxicity of excessive amount of local anaesthesia that would be required, and to allow monitoring of all vital signs during and the treatment procedure.

Declaration:

This review article is a part of the PhD thesis of the first author, in Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Suez Canal University in Egypt, entitled "Comparative Study between Bleomycin and Ethanol-amine Oleate Sclerotherapy in Management of Pediatric Maxillofacial Low Flow Vascular Malformations: A Randomized Clinical Trial: A Randomized Clinical Trial"

Funding: No funding received

Conflicts of Interest:

The authors declare that they have no conflict of interest.

*Glaxo Pharmaceuticals, Research Triangle Park, NC

References

1. National Institutes of Health. Human prescription drug label. National Institutes of Health; 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a9c1d8c5-443e-400e-a42c-16a25fb47231. [Accessed on: Feb 2024]
2. Meirelles-Santos JO, Carvalho AF Jr, Callejas-Neto F, et al. Absolute ethanol and 5% ethanolamine oleate are comparable for sclerotherapy of esophageal varices. GastrointestEndosc. 2000; 51 (5): 573-576. doi:10.1016/s0016-5107(00)70292-6
3. Masaki M, Obara, K, Suzuki S, et al. The destructive effects of sclerosant ethanolamine oleate on mammalian vessel endothelium. *Gastroenterol Jpn*. 1990: 25 (2): 230 - 235. doi:10.1007/bf02776821
4. Johann AC, Aguiar MC, do Carmo MA, Gomez RS, Castro WH, Mesquita RA. Sclerotherapy of benign oral vascular lesion with ethanolamine oleate: an open clinical trial with 30 lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2005; 100 (5): 579 - 584. doi:10.1016/j.tripleo.2004.12.021
5. Alexander MD, McTaggart RA, Choudhri OA, Marcellus ML, Do HM. Percutaneous sclerotherapy with ethanolamine oleate for venous malformations of the head and neck. J Neurointerv Surg. 2014; 6 (9): 695 -698. doi:10.1136/neurintsurg-2013-010924
6. Kato CNAO, Ribeiro MC, do Amaral MBF, Grossmann SMC, de Aguiar MCF, Mesquita RA. Experience with 5% ethanolamine oleate for sclerotherapy of oral vascular anomalies: A cohort of 15 consecutive patients. J Craniomaxillofac Surg. 2019; 47 (1): 106-111. doi:10.1016/j.jcms.2018.11.009
7. Jin CJ, Wang Q, Wang M, Chen Y, Yuan SM. Therapeutic evaluation and analysis of complications of ethanol sclerotherapy for intramuscular vascular malformations: a single-center retrospective study. Front Surg. 2023; 10:1274313. Published 2023 Oct 24. doi:10.3389/fsurg.2023.1274313
8. Krishnakumar Raja, V.B. (2021). Temporomandibular Joint Dislocation. In: Bonanthaya, K., Panneerselvam, E., Manuel, S., Kumar, V.V., Rai, A. (eds) Oral and Maxillofacial Surgery for the Clinician. Springer, Singapore. https://doi.org/10.1007/978-981-15-1346-6_64
9. Said Ahmed W. Efficacy of Ethanolamine Oleate Sclerotherapy in Treatment of Peripheral Giant Cell Granuloma. J Oral Maxillofac Surg. 2016;74 (11): 2200-2206. doi:10.1016/j.joms.2016.04.025

10. De Carvalho MF, Kaline N, Duailibi E. et al. Extensive arteriovenous malformation in the face of a pediatric patient – Case report. Rev Port Estomatol Med Dent Cir Maxilofac. 2014; 55 (4): 250 – 255
11. Fernandes DT, Elias RA, Santos-Silva AR, Vargas PA, Lopes MA. Benign oral vascular lesions treated by sclerotherapy with ethanolamine oleate: A retrospective study of 43 patients. Med Oral Patol Oral Cir Bucal. 2018; 23 (2): e180-e187. Published 2018 Mar 1. doi:10.4317/medoral.22253
12. Kato CN, Ribeiro MC, Abreu MH, et al. What is the preferred concentration of ethanolamine oleate for sclerotherapy of oral vascular anomalies?. Med Oral Patol Oral Cir Bucal. 2020; 25 (4) :e468-e473. Published 2020 Jul 1. doi:10.4317/medoral.23448
13. Ragab M, Arafat S, Mohamed W, Abouelfadl MH, Arafa A, Aboul Hassan M, Eltagy G. Intralesional ethanolamine oleate injection for management of venous malformations: Case series. Indian J Public Health. 2020; 11 (3): 1686 - 1691.
14. Duffy DM. Ethanolamine oleate: a dangerous and outmoded sclerosant. Dermatol Surg. 2011; 37 (3): 402. doi:10.1111/j.1524-4725.2011.01897.x
15. Fujiki M, Ozaki M, Kurachi I, Iwashina Y, Takushima A. Risk Factors for Macroscopic Haemoglobinuria After Sclerotherapy Using Ethanolamine Oleate for Venous Malformations. *Eur J Vasc Endovasc Surg.* 2019; 58 (1): 105-111. doi:10.1016/j.ejvs.2018.12.018
16. Lee JY, Moon SH, Lee SM, et al. A case of noncardiogenic pulmonary edema by ethanolamine oleate. Korean J Intern Med. 1994; 9 (2): 125-127. doi:10.3904/kjim.1994.9.2.125
17. De Maria L, De Sanctis P, Balakrishnan K, Tollefson M, Brinjikji W. Sclerotherapy for Venous Malformations of Head and Neck: Systematic Review and Meta-Analysis. Neurointervention. 2020; 15 (1): 4 - 17. doi:10.5469/neuroint.2019.00213
18. Bordas JM, Feu F, Vilella A, Rodés J. Anaphylactic reaction to ethanolamine oleate injection in sclerotherapy of esophageal varices. Endoscopy. 1989; 21 (1): 50. doi:10.1055/s-2007-1012897
19. Arafat et al.Complications of Ethanol-amine Oleate Intralesional Sclerotherapy Injections of Pediatric Maxillofacial Venous Malformations. Australian Journal of Basic and Applied Sciences, 2021 August; 15(8): 10-18. https://doi.org/10.22587/ajbas.2021.15.8.2