Journal University of Kerbala , Vol. 15 No.1 Scientific . 2017

Ethanolamine oleate as a secleroting agent in the treatment of low flow facial and oral vascular lesions

العلاج التصلبي لآفات الوجه والفم الوعائية باستعمال مادة أوليات الأيثانول الأميني

Ali Abduljabbar Mohammad*
Mohammad Abdul-Ameer Al-Tayyar**
Yasir Lafta Hassoun***
*Oral and maxillofacial surgeon , head of the department of oral and maxillofacial surgery, Al-Sader Medical City/Najaf/Iraq F.I.B.F.M B.D.S
**Consultant radiologist head of the department of radiology , AL-Sader Medical City /Najaf /Iraq F.I.B.M.S
***Consultant otolaryngologist , assistant professor in otolaryngology , department of surgery / otolaryngology , college of Medicine ,University of Kufa /Iraq FIBMS-ENT , DLO

Abstract:
Background : Vascular lesions of the head and neck are wide range of different pathologies including haemangiomas and vascular malformations. The diagnosis is usually clinical . The vascular elements and blood flow are better diagnosed by angiography . Vascular lesions require treatment when they are symptomatic or causing patient discomfort. A number of therapeutic ways and procedures were proposed for the management of vascular lesions including systemic and intralesional steroids , intralesional sclerosing agents , interferon , laser therapy, embolization , cryotherapy as well as radiation. Ethanolamine oleate is an organic chemical compound as a primary amine and a primary alcohol can cause a dose related inflammatory reaction when introduced inside the tissues leading to fibrosis and reduction of the size affecting lesions.
Aim: To evaluate the efficacy of ethanolamine oleate 5% in the treatment of oral and facial vascular malformations.
Patients and methods: This is a prospective cross-sectional study included 24 patients with vascular lesions ranging between 1 and 65 years of age in Al-Sader Medical City , Najaf , Iraq during the period from 2012 to 2015 . Ethanolamine oleate 5% solution was used to treat these lesions . The age and gender of patients, site and size of the lesion , the dose of the agent used , the immediate tissue reactions , the general constitutional symptoms and the outcome were all studied.
Results: Among 200 patients visited the maxillofacial department in the Al-Sader Medical City, 24 patients appear to have an oral or facial vascular lesion. All the 24 patients were included in this study. The amount of the agent used in the treatment was calculated , 0.3 -2.5 mL according to the size of the lesion. Sever pain , swelling and ulceration were constant in all treated patients. Lesions of one cm to 2.5 cm size showed good response after the first session , but larger lesions required a second or even a third session.
Discussion: Vascular lesions of the oral cavity and face are treated in many different ways .High flow lesions require presurgical embolozation followed by aggressive ablative therapy. Slow flow vascular malformations can be managed in numerous ways including sclerotherapy. The size and site of the lesion determines the dose and the number of injections of athanolamine oleate as a sclerosing agent. Sever pain , immediate swelling and airway embarrassment when the lesion is oral , ulceration and corresponding bleeding are important clinical aspects but if they are weighted against the dramatic reduction in size and appearance , the results are fruitful both for the patient and the doctor.
Key words : Ethanolamine oleate sclerotherapy , oral & facial vascular malformations

الخلاصة

تضم الآفات الوعائية الدموية للوجه والفم مجموعة من الأورام الدموية والتشوهات الخلقية الدموية. يتم تشخيص هذه الآفات اعتمادا على الملاحظات السريرية عادة أما الفحوصات الشعاعية والصوتية فتتم العودة اليها لتحديد امتدادات هذه الأورام والتشوهات وتعيين الأوعية الدموية المغذية لها . يلجأ إلى معالجة هذه الآفات عندما تكون هناك أعراض مرضية أو قلق أو عدم ارتياح المصاب من وجودها وتتبع طرق كثيرة جدا لمعالجة هذه الحالات منها على سبيل المثال لا الحصر تناول أو الحقن ألموضعي بالعقاقير مثل الكورتزونات او الأنترفرون او العقاقير المصلبة او الجراحة الليزرية أو العلاج عن طريق التجميد ووسائل أخرى.

استعملت مادة اوليات الأيثانول الأميني في هذه الدراسة عن طريق الحقن المباشر لإحداث حالة من الالتهاب النسيجي الحاد الذي ينتهي بتليف الورم أو التشوه مما يؤدي الى انكماش الموضع أو اختفاءه نهائيا.

طريقة البحث: تم إجراء هذه الدراسة على 24 مريض مصابين بآفات وعائية من تشوهات أو أورام في مدينة الصدر الطبية تتراوح أعمارهم من سنة واحدة إلى 65 سنة ، جميع هؤلاء المرضى تمت معالجتهم بالحقن المباشر بمادة أوليات الأيثانول الأميني بتركيز 5% ومن ثم معاينة النتائج والتفاعلات الموضعية والعامة لهذا النوع من العلاج.

النتائج:من بين 200 مريض زار استشارية الوجه والفكين في مدينة الصدر الطبية للفترة من 2012 الى 2015 ، كان 24 مريضا يعانون من آفات الأوعية الدموية في الفم أو الوجه. وشملت هذه الدراسة جميع المرضى الأربعة والعشرين . استعملت مادة أوليات الأيثانول الأميني بمقدار 0,3 الى 2,5 مل وحسب حجم الآفة ولوحظت علامات وأعراض في جميع المرضى على شكل الم شديد وتورم وتقرح موضعي الا انها انتهت بسرعة مخلفة بعدها اختفاء تام أو انكماش واضح في حجم الآفة بعد جلسة علاجية واحدة او جلستين وفي أحيان قليلة ثلاثة جلسات.

المناقشة:يتم التعامل مع الآفات الوعائية في تجويف الفم والوجه بطرق مختلفة. الآفات ذات التدفق الدموي العالي تتطلب استعمال طرق التخثر للأوعية المغذية ومن ثم استعمال العلاج التصلبي أما الآفات ذات التدفق البطيء فتتم معالجتها بالعديد من الطرق بما في ذلك التصليب. يحدد حجم وموقع الآفة الجرعة وعدد الجلسات باستعمال اوليات الأيثانول الاميني كعامل مصلب. يحدد حجم الافة وموقعها التشريحي كمية المادة المستعملة في كل جلسة لما لهذين العاملين من اهمية في احداث التفاعلات النسيجية والالتهابية ، لوحظ بانه الالم الشديد والتورم والتقرح هي من العلامات السريرية الهامة ولكن إذا قورنت هذه التفاعلات مقابل الانخفاض الهائل في حجم ومظهرهذه الافات فان هذه النتائج تعد مثمرة للمريض والطبيب على حد سواء.

Introduction:

Vascular lesions of the head and neck are wide range of different pathologies including hemangioma and vascular malformations. The diagnosis is usually clinical. The vascular elements and blood flow are better diagnosed and evaluated by angiography. Vascular lesions of head and neck encompass a wide range of different pathologies. These are classified as hemangiomas and vascular malformation. Mulliken and Glowacki first described this classification in 1982 on the bases of clinical behavior and endothelial cell characteristics. Laboratory techniques are not necessary to assign a lesion to either hemangioma or vascular malformation. Diagnosis can usually be made by an accurate history and physical examination. [1,2,3]

There are two major categories of vascular anomalies: tumors and malformations. Vascular tumors are endothelial neoplasms characterized by increased cellular proliferation. Hemangioma is the most common and is almost exclusive to infants. Other tumors are hemangioendotheliomas, tufted angioma, and other rare vascular neoplasm, including angiosarcoma. [4]

Vascular malformation, on the other hand, is the result of abnormal development of vascular elements during embryogenesis and fetal life. These may be single vessel forms (capillary, arterial, lymphatic, or venous) or a combination. Malformations with an arterial component are fast-flow, while the remainders are slow. [1,4,5]

Hemangiomas usually present at birth but mostly diagnosed by the age of one year, they rapidly grow until the age of 6–8 months then slows and involutes by the age of 5–9 years. They are neoplastic growths with increased endothelial cell turnover with rare osseous involvement . Female:male ratio is about 5:1 .They are usually associated with low blood flow. Treatment is frequently not needed.

Vascular malformations are also present at birth but usually manifest at the second decade , growth is slow with increase in size in response to infection, trauma, or hormonal fluctuation; they do not involute due to flow dynamics through the lesion and recruitment of collateral supply. Osseous involvement occurs in 35% with female:male ratio of 2:1 , they may be of low flow

(capillary, venous, lymphatic) or high flow when they are (arterial or arteriovenous). Treatment is often required for these lesions. [6]

Vascular malformations or even hemangiomas require therapeutic intervention if they start to cause clinical symptoms or personal discomfort. [1,2,3,7]

A number of therapeutic ways and procedures were proposed for the management of vascular lesions including systemic and intralesional steroids, intralesional sclerosing agent, interferon, laser therapy, embolization, cryotherapy as well as radiation. Ethanolamine oleate is an organic chemical compound as a primary amine and a primary alcohol can cause a dose related inflammatory reaction when introduced inside the tissue leading to fibrosis and reduction of the size affecting lesions.[8, 9]

The treatment employed in the present cases was sclerotherapy which is ethanolamine oleate. In some patients the treatment was combination of sclerotherapy and embolizations. Ethanolamine, also called 2-aminoethanol or monoethanolamine (often abbreviated as ETA or MEA), is an organic chemical compound that is both primary amine and primary alcohol. Injection of ethanolamine causes an acute, dose-related inflammatory reaction of the intimal endothelium of the vein. This leads to scarring and possible occlusion of the vein. [10]

Emblo-therapy, is one of the more commonly used adjunctive procedures in treatment of vascular tumors. Many emblo-therapy agents are used, some of them are absorbable like autologous blood clot, gel-foam , and oxycel. Others are non-absorbable like acrylic spheres, sialastic sphere, and stainless steel coils. [11]

Aim of the study:

To evaluate the efficacy of Ethanolamine Oleate 5% w/v in the treatment of oral and facial vascular malformations and hemangioma.

Patients and Methods

This prospective cross-sectional study involved 24 patients with vascular lesions both males and females, the age range from 1 year to 65 years. The study was conducted in Al-Sader Teaching Hospital /Najaf/Iraq during the period between 2012 to 2015. History taking and clinical examination was performed for all the patients to start the primary diagnosis. Consultation for the plastic surgeon, dermatologist, physician and sometimes paediatrician was asked before initiating the treatment. Some patients were sent for ultrasonography , Doppler study , CT scan or MRI to evaluate the extent of the lesion. CT angiography was requested in some cases to identify the feeding vessels or to allocate the anatomical relation of the large vessels. An informed consent is applied to the patients or their relatives including description of the drug used , its side effects, the need for more than one session sometimes and possible consequences. Strict precautions regarding massive bleeding or airway threats were taken.

The site of the lesion , the size , the age of the patients, the gender, the dose of the drug used , the immediate tissue reactions, the general constitutional symptoms and outcomes of the treatment modality, all were charted for statiscal analysis.

According to lesion size the amount of the agent was injected , about 1cc ethanolamine oleate 5% for each 1.5 cm of lesion size, figure (1) , but if the lesion size is 5 cm or more 2-3 cc ethanolamine oleate was used figure (2) , patients were followed up three to five days to evaluate the local action of the agent .Patients with vascular malformations managed by sclerosing agent ethanolamine oleate 5% w/v by using 23G needle , preceded by aspiration of blood from the lesion to insure exact insertion of the sclerosing agent into the lesion ,after injecting the agent manual squeezing or compression around the lesion for 15-20 minutes to reduce diffusion of the scleroting agent. Figure (1)

Figure (1) The amount of the sclerosing agent in relation to the size of the lesion

Some lesions were sutured all around because effective squeezing or compression of the lesion is impossible like the posterior part of the tongue and the palate. In some patients , combination of embolizing coils and embolizing spheric particles through catheterization followed by injection of the scleroting agent and compression of the lesion after 5-7 days . Others , the injection was under doppler ultrasonography.The patients were observed on the third and fifth day to report any complication. Small lesions needed single session, follow up was considered after 4-5 weeks to evaluate the effect of the ethanolamine oleate and reduction in the size of vascular lesion. In cases with large lesion, single session was inadequate, patients were advised to attend after 2 weeks for second session and subsequent procedure. Patients were followed for 6-8 weeks after the last session to evaluate the effect of the agent. Further, patients were followed up to 4-6 months to register any recurrence or complications . Photographs were taken during injection and during follow up to document the effects and results.

Results:

Two hundred twenty patients (145 males and 75 females) were seen during the period of this study in the maxillofacial department at Al-Sader medical city complaining of different issues, cystic lesions of maxilla and mandible, benign tumors (ameloblastoma, ossifying fibroma, etc.), salivary gland tumors benign and malignant, RTA, mandibular fractures, maxillary fractures, zygomatic fractures and panfacial fractures and 24 patients (15 females from one year to thirty year and 9 males from twenty year to sixty five years) complaining vascular malformation and hemangioma, as congenital malformation or due to trauma observed by the patient or incidentally detected during dental treatment. The size of the lesions ranges from 2.5-7 cm measured grossly or by ultrasonography and CTA scan. The distribution of the lesions was at the buccal mucosa of the cheek, buccal sulcus, lower and upper lip, the tongue, palate, uvula, and retromandibular raphe area .Table -1- and table -2-

Table 1 : Site and gender distribution of the lesion.

Lesion site	Number of patients	female	male	percentage
Buccal mucosa of the cheek	3	2	1	12.5%
Buccal sulcus	3	2	1	12.5%
Lower lip	5	3	2	20.8%
Upper lip	6	4	2	25.6%
Uvula	2	2	0	8.3%
Retromandibular raphe	2	2	0	8.3%
Tongue	3	-	3	12.5%

Table 2 .Age, size of the lesion , the amount of injected agent and the signs and symptoms after injection

Age	No. of patients	Size of the lesion	Amount of injected agent	Sign and symptoms
1-5 years	5	0.9 X 1.4 cm - 2.6 X 5cm	1ml - 2.5ml	Swelling ,ulcer, severe pain
12-25 years	5	0.74 X 1.9cm - 3.8cm	0.5ml - 2.5ml	Swelling, cutaneous and mucosal blistering(ulcer) , sever pain
30-40 years	8	0.8 X 1.1cm - 0.5 X 1cm	0.3ml - 0.5ml	Swelling ,ulcer, severe pain
50-65 years	6	0.2 X 0.7cm - 0.7 X 1.3cm	0.5ml - 2ml	Swelling, ulcer, severe pain

Evaluation of the effectiveness of the agent depends on the color change of the lesion and the reduction in size. There was magic response when the lesion size is 1 cm or less without deep tissue involvement shown by Doppler ultrasonography with complete physical disappearence. After two weeks of injection of ethanolamine oleate, Doppler ultrasonography shows successful seclerosing of blood vessels. Figure (2)

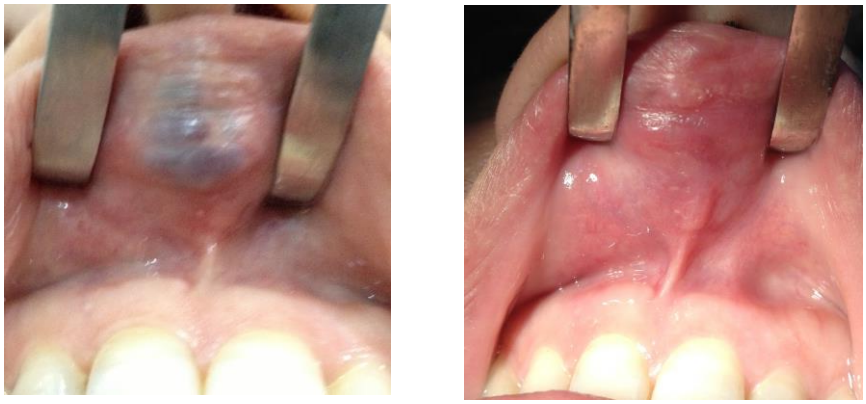

Figure (2) ,The pre and postoperative appearance of small lesions

Regarding large deep lesions, 2.5cm – 5cm the size was reduced into a half or less in comparison with the original. The reduction in dimensions of the lesion was confirmed by Doppler ultrasonography with sclerosis of blood vessels.

Scattered non-secleroted blood vessels needed another session of injection of the agent under guide of Doppler ultrasonography to prevent any recurrence. Three cases needed three sessions to reduce the size of the lesion to less than half of the original size during two months interval. Two cases where the lesion was scattered along the lateral aspect of the tongue and the floor of the mouth and the sulcus, three sessions of injection were scheduled to overcome complications like oedema and airway obstruction after the injection. Figure (3) and figure (4)

Figure (3) one of the relatively large lesions pre and after two sessions of sclerotherapy

Figure (4) Large lesion that required three sessions

One complication was facial nerve palsy where the lesion is situated near the parotid gland and there was diffusion of some material outside the blood vessels during injection. Fortunately, the palsy was temporary and recovered after three months.

Discussion

Various treatment methods have been reported in the treatment of vascular lesions. High flow lesions require pre-surgical embolization followed by aggressive ablative therapy. Low flow vascular malformations can be managed in numerous ways, sclerotherapy, laser therapy, cryotherapy or surgery . [6]

The value of identification of the site of the lesion especially in the lateral surface of the tongue , posterior surface of the tongue ,floor of the mouth and soft palate is to avoid airway obstruction caused by swelling of the site of the lesion shortly after the treatment. Severe pain should be controlled by giving pain killers .The necrotic tissue may become a focus of infection indicating the need to an antibiotic. The size of the lesion is important in the treatment schedule, single dose is adequate for small lesions where in large lesions and multifocal lesions multiple sessions are needed .Ethanolamine oleate destroys the endothelial cells of the vessels within one minute after injection into vessels of the rats and dogs. An accumulation of fibrin and platelets on the surface of the damaged vessels was observed electron microscopically . Mural thrombus was formed in few hours and the thrombus occluded the blood stream in the vein. [12]

Ethanolamine oleate works by causing localized inflammatory reaction , obliteration thrombosis of hemangiomatous space, subsequent fibrosis of the endothelial spaces, then regression of the lesion. [13]

The ethanolamine oleate is very irritating to tissues , minor extravasation may lead to serious complications and that may explain the temporary facial palsy in one of our patients. All vascular malformations in this study were in the buccal or oral cavities without any scattered lesions elsewhere in the body , Kenya Koayashi et al in 2013 found other lesions of vascular malformation somewhere in the body 14-65%. [14]

Evaluation of the procedure of sclerotherapy on our 24 patients with oral cavity vascular malformations was done by photography and Doppler ultrasound , Kaji et al in 2009 evaluated the procedure of sclerotherapy on 112 patient with head and neck vascular malformations, they used the pre and postoperative photography and MRI. [15]

In our study, ethanolamine oleate was used on 24 patients, almost all the complications registered were minor with no need for postoperative airway emergency or interference during the observation period, most of the minor minor complications disappeared gradually within 5-7 days. Costa RJ et al in 2011 used 5% ethanolamine oleate on 53 patients with 15 days interval, they registered no complications. [16]

The dose of the agent was calculated according to the size of the lesion, 0.2 cm -1.5 cm,,0.3 ml- 1 ml agent was given , 2.5 cm- 5 cm,, 2 ml – 2.5 ml agent was given. Seventeen of the patients required one session to cure the lesion ,two patients required two sessions, three patients required

three sessions and two patients required three sessions because the lesion was scattered throughout the oral cavity and lateral aspect of the tongue when multiple sessions was followed to avoid oedema and subsequent airway obstruction. Bijoy Kirshna et al in 2008 used ethanolamine oleate for the treatment of 72 patients with venous malformations with maximum dose of 0.40 ml/kg body weight, half of the number of his patients required only one session, one third needed two sessions and only 14 cases required more than two session. [17]

Conclusion;

Low flow vascular lesions of the face and the oral cavity , particularly the small lesions can be successfully treated by ethanolamine oleate on outpatient bases with minimal morbidity and low complication rates . Large lesions or lesions with deep tissue involvement requires more than one session and associated with more ulceration and subsequent scarring .

References;

1. Robbins Basic Pathology international edition ,8th. Edition 2007.
2. Mulliken MD and Glowaacki JG. Hemangioma and vascular lesion malformations in infant and children ; A classification based on endothelial characteristcs.Plastic and Reconstructive Surgery 1982 ;69:412-420.
3. LeezaPradhan ,Quazi Billur Rahman,Effectiveness of sclerotherapy with Ethanolamine Oleate in benign oral and perioral vascular lesions [BSMMUIJ 2011;4(2):110-115]
4. Jennifer J Marler, MD, John B.Mulliken.MD. clinc in plastic surgery 32(2005) 99-116
5. Fonseca,Macinani,Turvey, oral and maxillofacial surgery ,second edition, volume II. 2009.
6. Hemant Bajpal and Sarika Bajpal,comparative analysis of intralesional sclerotherapy with sodium tetradecyl sulfate Versus Bleomycin in management of low flow craniofacial soft tissue vascular lesion .J.Maxillofacial oral surgery 2012 Mar,11(1):13-20
7. Paul Rogero Ferret Bonan et al,Effectiveness of low flow vascular lesions sclerosis with monoethanolamine, Med Oral Pat 01 oral Cir Bucal.2007 Nov 1,12(7)
8. FarisFoco and AmilaBrekic , vascular anomalies of maxillofacial region :diagnosis and management. J basic clinpharma 2015 ;6:40-43.
9. ShettyDC,et al. case series on vascular malformation and their review . contempclin dent 2010;1:259-62
10. SitraG,et al .A new venture with sclerotherapy in oral vascular lesion. J Basic ClinPharma 2015;6:40-3
11. Akira Kitagawa et al .ethanolamine oleate sclerotherapy combined with transarterial embolization using n-butyl cyanoacrylate for extra cranial arteriovenous malformations. Cardiovascular and interventional Radiology.April2014,vol 37,issue 2, pp 371-380
12. Atsushi Dan Jo et al. intralesional sclerotherapy with ethanolamine oleate for subcutaneous venous malformations in oral and maxillofacial region . J. of the Japanese stomatology society vol.61(2012)No.3 p.243-250
13. Jia Wei Zheng, et al. guideline for treatment of head and neck venous malformations. Int. j. clin. exp . med. 2013; 6(5):377-389.
14. Kenya Koayashi, et al .auris , nusus , larynx 2013 feb 40(1) 89-92.
15. Kaji N et al ,experience of sclerotherapy and embolosclerotherapy using ethanolamine oleate for vascular malformations of the head and neck.Scand J plastic reconstrsurg hand surg,2009, 43(3):126-36.
16. Costa JR ,et al .sclerotherapy for vascular malformations in oral and maxillofacial region :treatment and follow-up of 66 lesions. J.oralmaxillofacsurg ,2011jun ;69(6);e 88-99
17. Bijoy Krishna Das and shafiqulHoque. Treatment of venous malformations with ethanolamine oleate. 20th congress of AAPS