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TREATMENT OF CRANIO-FACIAL VENOUS MALFORMATIONS WITH ETHANOLAMINE OLEATE - A DESCRIPTIVE STUDY OF 41 CASES

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Summary:

Background and Study aims: Cranio-facial Venous Malformations are the most common Venous Malformations. The lesions of Venous Malformations may be discrete or diffuse. Surgery can often be curative for both the discrete and diffuse disease, but larger diffuse lesions and lesion in surgically 'difficult approachable' sites may not be removed completely. Incompletely removed lesions have a higher propensity for recurrence. In this study (case series), we describe the outcome and complications following Ethanolamine Oleate injections for the treatment of Cranio-facial Venous Malformations.

Patients and Methods: In the present prospective case series, 41 patients (irrespective of symptoms) with 42 lesions were followed clinically for about 1 year following treatment. The cases were enrolled between April 2001 and March 2003 in two large referral teaching hospitals in the capital city of Bangladesh (Bangladesh Institute of Child Health and Bangabandhhu Sheikh Mujib Medical University). The amount of Ethanolamine Oleate per treatment session ranged from 0.50 ml to 5 ml and maximum dose was 0.40 ml (20 mg) per kg body weight. All patients were evaluated after 8 weeks of last injection session. All of the treatment sessions were performed as a day case basis except one who needed General Anesthesia having lesions within oral cavity.

Results: Patients age ranged from 3 months to 16 years (mean age 4.3years). Seventeen patients were male and twenty-four female. 42 lesions have under gone 89 sclerotherapy sessions with 19 requiring one, 15 requiring two and 7 lesions requiring more than two sessions. Sclerotherapy with Ethanolamine Oleate provided complete resolution of symptoms in 41 lesions and significant improvement of 1 lesion. All patients experienced pain and swelling to a variable degree for short duration. Skin sloughed out in two patients. No other complications were observed in our study.

Conclusion:
Treatment of Cranio-facial Venous Malformations with injection Ethanolamine Oleate is safe and effective.

Introduction:

Venous Malformations (VMs) are composed of thin-walled channels, with sparse irregular islands of smooth muscle, that are lined by quiescent endothelium[1] They usually occur in pure form, but they can be combined, such as capillary-venous malformations or lymphatic-venous malformations. They most commonly present on cranio-facial area. They are low flow vascular malformations that can cause significant clinical problems and some times difficult to treat. Though they are present at birth but may not evident[2] They never regress but even may expand and grow proportionately with the patient [3,4] Venous Malformations can be present as single or multiple lesions in any location of body. They occur in both sexes equally. They can be cosmetically inconsequential or tragically distorting [2] Venous malformations are mislabeled both in medical parlance and literature as cavernous haemangioma. History and physical examination can do diagnosis of venous malformation [2]

At present various therapeutic options for venous malformation are-

1. Sclerotherapy
2. Surgery
3. Combined surgery and sclerotherapy
4. Embolisation
5. Laser therapy

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Such numerous modes of treatment actually reflect the fact that no single agent is entirely satisfactory for the treatment of venous malformation. Surgery can cure the disease but may not possible in all case such as in case massive Venous Malformations and may not also possible in difficult approachable sites such as oropharynx, mediastinum, esophagus, etc. Surgical treatment is also costly, risky, time consuming and causes psychological embarrassment to the patients and their parents and it may need hospital stay. The laser therapy is costly and also inadequate for all except the thinnest lesions [5]. Embolisation requires technical sophistications [6] and is not feasible in all cases. In such situation sclerotherapy may be quite helpful.

There are numbers of sclerotherapeutic agents for the treatment of venous malformations.

Such as

1. 5% Ethanolamine Oleate [7,8,9]
2. Absolute Ethanol [100% Ethanol] [10,11]
3. Ethibloc [1]
4. 1% and 3% sodium tetradecyle sulfate [6,10]
5. Polidocanol [12]

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

Patients and Methods:

A prospective case study was performed in Bangabandhu Sheikh Mujib Medical University and Bangladesh Institute of Child Health (Dhaka Shishu hospital) of Bangladesh from April 2001 to December 2003. All patients up to 16 years of age with clinical cranio-facial venous malformations were studied. Post-operative patients with recurrent and residual disease of venous malformations were also included. Patients associated with other diseases like RTI, PUO, etc. were excluded from the study temporarily. Patients with history of previous infections on venous malformations were excluded to avoid confusion. A total of 41 patients with 42 lesions were studied.

Patients were diagnosed clinically. Investigations like Doppler ultrasonography done in some cases for documentation and academic purpose.

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

The maximum dose of Ethanolamine oleate was 0.4ml (20mg)/kg body weight.[12]. The dose was adjusted according to the site and size of lesions and weight of patients, which was-0.4-0.6 ml/sq.cm. Injections were pushed directly into the lesion (intravascular) on multiple sites with 23G or hypodermic (26G) needle until slight elevation of lesion. The patients were allowed to go home few hours after injection and observed on 3rd and 7th 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 given after 8 weeks of last session to evaluate the effect of Ethanolamine Oleate and reduction of size of Venous Malformations. When in initial procedure we can't cover the whole lesion in that case, patients were advised to attend after 3 weeks interval for second and subsequent procedures and follow up given after 8 weeks of last session to evaluate the effect of Ethanolamine Oleate. For large diffuse lesions up to 7 procedures were performed.

Results:

A total of 41 patients were studied and included in the study. These 41 patients have venous malformation on 42 sites of cranio-facial area. In this study, 17 patients are male and 24 patients are female. M : F = 1 : 2 . The patients were aged from 3 months to 16 years. Mean age was 4.3 years, SD was 1.01 (Table-I).

Table-I

Age distribution.

Age group	No. of Patients n/N	%
Up to 1 years	9/41	22
2 - 4 years	15/41	37
5 -14 years	11/41	28
15 - 16 years	6/41	13

Out of the 42 lesions, 19 (46%) lesions were present at birth. The rest gave history of appearance after birth at different ages. The lesions were variegated in size and shape- focal, diffuse, serpentine, cystic, etc. Table-II shows the gross distribution of the lesions.

Table-II

Distribution of lesions in various sites of the body.

Sites	No of lesions
Face	29
Oral cavity	2
Tongue	2
Head	5
Neck	4
Total	42

* 1 patient had more then one lesions.

Among the 42 lesions 2 were previously treated initially with steroid and then surgery – at least 6 months back. In all of these cases, steroid was non-responsive and surgery was incomplete.

Another one was treated surgically previously but recurs after 6 months. 11 were treated with oral steroid at least three months back, 4 were treated with intra-lesional steroid also, at least 3 months back and 18 had no history of treatment (Fig-1).

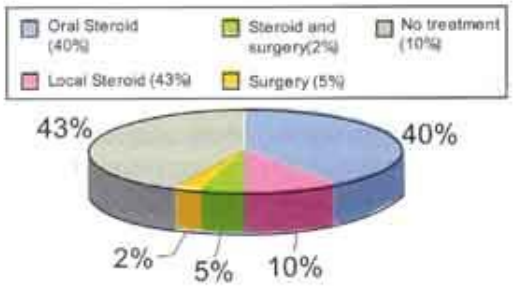

Fig.-1: *Mode of Previous Treatment*

The frequency and amount of injection depends upon the site and size of lesions and the weight of patients.

The amount of injections used varied from 0.5ml to 5 ml per session.

All of the procedures were performed as a day case basis with out anesthesia except one lesion of oral cavity that needed general anesthesia.

19 lesions were regressed after single injection session; rest needed multiple injection sessions, highest being 7 injection sessions.

Response:

All of lesions respond to Inj. Ethanolamine Oleate sclerotherapy. Figure 2 and 3 show the response of Injection Ethanolamine Oleate.

Fig-2: *Before and after 8 weeks of last inj Ethanolamine oleate on tongue.*

Fig -3: *Before and 8 weeks after last inj Ethanolamine oleate on right side of nose.*

The responses of Ethanolamine Oleate were evaluated after 8 weeks of last injection. They were graded in four groups-

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

Among the 76 lesions, 71 had complete cure of disease. Rest 5 lesions (which were diffuse) had significant improvement of disease and palliation of symptoms (Table -III).

Table-III

Response of treatment

Response	n / N	%
Cure	41 / 42	98
Good response	1 / 42	2
Poor response	0	
No response	0	

Skin necrosis occurred in 2 patients. It was full thickness necrosis in a small area in 1 case and in other case it was partial thickness and cured without surgical intervention. No other side effect observed in our study. The site of lesion did not have any bearing in the out come of sclerotherapy. There were no age and sexual variations of responses observed in our study. In four cases, there was firm to hard non-compressible residual fibrosed tissue. All of the patients were followed up at least one year after evaluation of result, i.e. 14 months after last injection. There was no recurrence in our study.

Discussion:

Intra lesional injection of Ethanolamine Oleate into the VMs is an effective mode treatment. There are various sclerosing agents other than Ethanolamine oleate like Ethanol, Ethibloc, Polidocanol etc. Ethanol causes extensive tissue damage if extravaseted, but ethanolamine has no such effect[13]. Ethibloc, Polidocanol, etc are not available in our country. We have chosen to use Ethanolamine oleate because of its availability in our country and its ability to produce vascular block by necrosis of vascular endothelium as well as vessel wall[14]. Ethanolamine oleate is a mild sclerotherapeutic agent. So it will not cause any harmful side effects to other tissues if extravaseted[14]. Though Ethanolammine oleate can cause serious hazards like hemolysis, renal shutdown but in therapeutic doses it highly dilutes in circulation. In circulation, serum albumin and globulin inactivates diluted ethanolamine oleate[15,16] and serious systemic hazards like hemolysis or renal shut down can not occur. There may some hypersensitivity[14] reactions like any other drugs for which we were prepared but we didn't face any such situations. It was used successfully as a sclerotherapeutic agent for the treatment of Venous Malformation in many countries like Korea,[17] UK,[18] USA,[19] Japan,[7,20] Brazil[21]. All of our patients had response to Ethanolamine Oleate, which correlates the result of others [2,4,7,8,15-18]. All patients observed swelling after injections, which also correlates with others[10]. Side effects noted were epithelial sloughs out which healed spontaneously. No other side effects except epithelial sloughed out experienced in our study. There is no variation in rate of complication in our study with others[18]. Thus our result regarding response and complications correlates with the result of others. With the above findings, our study shows that the sclerotherapy with ethanolamine oleate for the treatment of venous malformations is an effective one.

Conclusion:

Sclerotherapy with Ethanolamine Oleate is effective and reasonably safe for the treatment of cranio-facial Venous Malformations, though on some occasions the injection sclerotherapy had to be repeated.

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