Treatment of Venous Malformations with Ethanolamine Oleate

Bijoy Krishna Das¹ and Shafiqul Hoque,² ¹Department of Paediatric Surgery, Gono-Shasthaya Samaj Vittik Medical College, and ²Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

OBJECTIVE: To describe the outcome and complications following ethanolamine oleate treatment of venous malformations.

METHODS: Seventy-two patients (27 male, 45 female; age range, 3 months to 16 years) with 76 lesions were treated with ethanolamine oleate at 0.50–16 mL per session, with a maximum dose of 0.40 mL/kg. All patients were evaluated 8 weeks after the final injection and were followed-up for about 1 year. All the patients were treated on a day-case basis except for one who required general anaesthesia.

RESULTS: Seventy-six lesions underwent 149 sclerotherapy sessions, with 41 requiring one session, 21 requiring two and 14 requiring more than two. Ethanolamine oleate significantly improved five lesions and completely resolved symptoms in 71. All patients experienced pain and swelling to a variable degree for a short time. Skin sloughing took place in three patients. No other complications were observed.

CONCLUSION: Treatment of venous malformations with ethanolamine oleate is safe and effective.

Key Words: ethanolamine oleate, sclerotherapy, venous malformations

Introduction

Cavernous haemangioma may have discrete or diffuse lesions. Surgery is often curative, but larger diffuse lesions and those in inaccessible sites may not be removed completely and have a higher propensity for recurrence. Venous malformations are low-flow vascular malformations that can cause significant clinical problems and are sometimes difficult to treat. They may be present at birth but may not always be evident.¹ Venous malformations occur equally in both sexes, never regress and may increase in size. They can present as single or multiple lesions in any part of the body: face, oral cavity, tongue, limbs, trunk, pharynx, genitalia, urinary bladder, brain, spinal cord, liver, lungs, skeletal muscles and bones. They can be cosmetically inconsequential or very distorting.¹ Venous malformations are wrongly classified in medical parlance and the literature as cavernous haemangioma. History and physical examination can lead to a diagnosis of venous malformation.¹

At present, therapeutic options for venous malformation are: sclerotherapy, surgery, combined surgery and sclerotherapy, embolization and laser therapy. Such a range of treatment modes reflects the fact that no single approach is entirely satisfactory for the treatment of venous malformation. Surgery can be curative but may not be possible in all cases, in particular in large malformations and for those in inaccessible sites such as the
oropharynx, mediastinum and oesophagus. Surgical
treatment is also costly, risky, time-consuming, causes
psychological distress to the patients and their parents,
and may require a long hospital stay. Laser therapy is
costly and also inadequate for all but the thinnest
lesions. Embolization is technically sophisticated but is
not feasible in all cases.

There is a number of sclerotherapeutic agents for the
treatment of venous malformations, such as 5% ethanol-
amine oleate, absolute ethanol, Ethibloc, 1% and 3%
sodium tetradeacyl sulfate, and polidocanol. Among
these agents, ethanolamine oleate is one of the safest and
most readily available in Bangladesh.

Patients and methods

A prospective case study was performed at Bangabandhu
Sheikh Mujib Medical University and Bangladesh Insti-
tute of Child Health (Dhaka Shishu Hospital) from April
2001 to December 2003. A total of 72 patients with
76 venous malformations (27 male, 45 female; age range,
3 months to 16 years; mean age, 4.9 ± 1.2 years) were
included in the study (Table 1). Postoperative patients
with recurrent and residual venous malformations were
also included. Patients associated with other diseases,
such as respiratory tract infection (RTI) and pyrexia of
unknown origin (PUO) were excluded from the study.
Patients with a history of previous infections or venous
malformations were excluded to avoid confusion. A total
of 72 patients with 76 lesions were studied. Patients were
diagnosed clinically, using investigations like Doppler
ultrasonography and venography in some cases for docu-
mentation and academic purposes. Plain X-ray of relevant
parts was done in a few cases to see the effects of venous
malformations.

Patients were treated with intralesional injection of
ethanolamine oleate not exceeding 0.4 mL/kg on multiple
sites of the lesion until slight elevation of the lesion. Patients were allowed
to go home a few hours after treatment. They were observed
on days 3 and 7 and advised to report any complications.
In the case of small lesions in relation to body weight,
which can be treated in a single session, the effects of
ethanolamine oleate and reduction in venous malformation
size were investigated 8 weeks after the final treatment
session. If the initial procedure could not treat the whole
lesion, patients were advised to attend at 3-week intervals
for subsequent treatments and follow-up was at 8 weeks
after the final session. For large diffuse lesions, up to 12
treatments were performed.

Results

Out of 76 lesions, 42 (55.26%) were present at birth. The
remainder appeared at different times after birth. The
lesions varied in size and shape, and were focal, diffuse,
serpentine or cystic. The most common site of occurrence
was the craniofacial area, with 41 lesions (54%). Venous
malformations were also present in the axilla, trunk,
limbs, genitalia and perineum (Table 2).

Four of the 76 lesions were initially treated with
steroids followed by surgery, at least 6 months previously.
In all of these cases, the lesions were non-responsive to
steroids and surgery was inadequate. Another two lesions
were previously treated surgically but recurred after
6 and 8 months respectively. Thirty-two lesions were
treated with oral steroids at least 3 months beforehand,
four were also treated with intralesional steroids at least
3 months previously, and 34 had no history of treatment
(Figure 1).

The injection dose and frequency of ethanolamine
oleate depended on the site and size of the lesions and the

Table 1. Age distribution of the 72 patients enrolled in the
study

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>17 (24)</td>
</tr>
<tr>
<td>2–4</td>
<td>26 (36)</td>
</tr>
<tr>
<td>5–14</td>
<td>20 (28)</td>
</tr>
<tr>
<td>15–16</td>
<td>9 (13)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Site</th>
<th>Lesions, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>29</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>2</td>
</tr>
<tr>
<td>Tongue</td>
<td>2</td>
</tr>
<tr>
<td>Head</td>
<td>4</td>
</tr>
<tr>
<td>Neck</td>
<td>4</td>
</tr>
<tr>
<td>Axilla</td>
<td>1</td>
</tr>
<tr>
<td>Trunk</td>
<td>16</td>
</tr>
<tr>
<td>Limb</td>
<td>16</td>
</tr>
<tr>
<td>Perineum</td>
<td>2</td>
</tr>
</tbody>
</table>
body weight of the patients. The surface area of the lesions varied from 1 cm² to 192 cm². Mean surface area was 16.76 ± 1.37 cm². The dose varied from 0.5 mL to 16 mL (mean, 6.01 ± 0.69 mL) per session. All of the procedures were performed on a day-case basis without anaesthesia, except for one patient with two lesions in the oral cavity, who was treated under general anaesthesia.

Forty-one lesions regressed after a single injection. The rest needed multiple sessions, the highest number of sessions being 12 (mean, 2.47).

Response
All of the lesions responded to ethanolamine oleate sclerotherapy (Figures 2–6). Responses were evaluated 8 weeks after the final injection session. Responses were graded into four groups: excellent, complete regression; good response, > 50% regression; poor response, < 50% regression; no response. Seventy-one of the 76 lesions were completely cured and the remaining five lesions (which were diffuse) showed a significant improvement (Table 3).

Skin necrosis occurred in four patients: one with full thickness in a small area, and three with partial thickness which were resolved conservatively without surgical intervention. No other side effects were observed. The site of the lesion did not have any bearing on the outcome of sclerotherapy. There were no age and sexual variations in responses. In four cases, there was firm-to-hard, non-compressible residual fibrosis tissue. All of the patients
were followed-up for at least 1 year, i.e. 14 months after the final injection. There was no recurrence.

Discussion

Intralesional injection of ethanolamine oleate into venous malformations is an effective mode of treatment. There are various sclerosing agents other than ethanolamine oleate, such as ethanol, Ethibloc and polidocanol. Ethanol causes extensive tissue damage if it is extravasated 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. Ethanolamine oleate is a mild sclerotherapeutic agent, therefore, it does not cause any harmful side effects to other tissues if extravasated. 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. It may cause some hypersensitivity reactions. Ethanolamine oleate has been used successfully as a sclerotherapeutic agent for venous malformation in many countries, including Korea, the UK, the USA, Japan and Brazil. It is also used for other diseases like renal cyst, hydrocoele, bleeding peptic ulcer, and oesophageal varices.

All of our patients responded to ethanolamine oleate, which correlates with the results of other studies. All patients observed swelling after injections, which also correlated with other studies. Side effects noted included epithelial sloughing, which healed spontaneously. No other side effects were observed in our study and the rate of complications did not differ from that of other studies. The results of the present and previous studies show that sclerotherapy with ethanolamine oleate is effective for the treatment of venous malformations.

In conclusion, sclerotherapy with ethanolamine oleate is effective and reasonably safe for the treatment of venous malformations, although on some occasions, injections had to be repeated. However, the long-term safety and efficacy of ethanolamine oleate should be further evaluated in a larger series of cases over a longer period of follow-up.

References