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Treatment of Low-flow Vascular Malformations by Ultrasound-guided Sclerotherapy with Polidocanol Foam: 24 Cases and Literature Review

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Abstract *Objectives:* Treatment by sclerotherapy has been suggested as a first-line treatment of low-flow vascular malformations. This study reports our experience in treating low-flow vascular malformations by ultrasound-guided sclerosis with polidocanol foam at the Vascular Medicine Department in Grenoble, France.
Design: Retrospective single-centre consecutive series.
Materials and methods: Between January 2006 and December 2009, we analysed the complete records of patients with symptomatic low-flow vascular malformations of venous, lymphatic or complex type (Klippel–Trenaunay syndrome, KTS) treated by ultrasound-guided sclerosis. The therapeutic indication was always validated by the Consultative Committee for vascular malformations of the University Hospital of Grenoble. All vascular malformations were classified according to the Hamburg Classification. The sclerosing agent was polidocanol used as foam.
Results: A total of 24 patients between 7 and 78 years were treated (19 venous malformations, three KTSs and two venous-lymphatic malformations). The concentrations of polidocanol used ranged from 0.25% to 3%. The average number of sessions was 2.3 (1–16). After a median follow-up at 5 months after the last session, 23 out of 24 patients reported a decrease in pain; in nine cases (37.5%), over 50% reduction in size was observed, and in 14 cases (58.3%), a reduction of less than 50% of the original size was obtained. Two minor side effects were reported.

Abbreviations: VMs, Venous Malformations; KTS, Klippel–Trenaunay syndrome; LM, Lymphatic Malformation; NA, Not applicable.

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Conclusions: Treatment by ultrasound-guided sclerosis using polidocanol foam seems to be well tolerated and can improve the symptoms of low-flow malformations without the risks of more aggressive sclerosing agents, such as ethanol.

The treatment of vascular malformations is unsystematic with too little therapeutic evidence. As a result, it is commonly accepted that the therapeutic strategy should be established by a multidisciplinary medical—surgical—radiological team. In recent years, ultrasound-guided sclerosis with foam has been proposed as an alternative treatment for low-flow malformations, especially when surgery cannot achieve a complete resection or seems too damaging. Among the available sclerosant products, polidocanol has less sclerosant power than ethanol but is better tolerated. The superiority of the foam form over the liquid form in the treatment of superficial venous insufficiency and venous malformations has been demonstrated recently for several sclerosants.[1,2]

Objectives of the Study

The main objective of this retrospective single-centre study was to report the therapeutic efficacy and tolerance of polidocanol foam in the treatment of symptomatic low-flow vascular malformations, performed at the Centre for Vascular Medicine at Grenoble University Hospital.

Materials and Methods

Patients

This retrospective study concerned all patients presenting low-flow malformation according to the criteria of the Hamburg classification.[3] Patients presented one or more symptomatic vascular malformations, uniquely or predominantly venous including those combined with lymphatic malformations or complex cases such as Klippel—Trenaunay syndrome (KTS), treated by foam ultrasound-guided sclerosis at the Grenoble Department of Vascular Medicine from January 2006 to December 2009. The indication for ultrasound-guided sclerosis and the therapeutic strategy were validated by the Committee for Vascular Malformations of Grenoble University Hospital, which includes vascular physicians, dermatologists, vascular surgeons, maxillofacial surgeons and vascular radiologists and meets quarterly. A strategy of combined treatment (sclerotherapy and surgery) could be proposed, with the sclerotherapy being performed first. A history of previous treatment (embolisation, sclerotherapy or surgery) was not an exclusion criterion. There was no age limit for inclusion. The indication for ultrasound-guided sclerosis was rejected in cases of asymptomatic lesions, the presence of associated arterial malformations, poor treatment compliance and the existence of a contraindication to ultrasound-guided sclerosis (such as a history of thrombo-embolic disease or known permeable foramen ovale). The pre-therapeutic evaluation was primarily clinical to clarify the symptoms (pain, neurological signs and trophic disorder) and the type and size of the malformation(s). Photographs were taken. Duplex ultrasonography was routinely performed, often supplemented with an angio-magnetic resonance imaging (MRI) or computed tomography (CT) angiography. Clear information about the ultrasound-guided sclerosis treatment was given to the patient both orally and in writing (IRB number 5891).

Procedure

The treatment was performed in an outpatient operating room. The patient's written consent, or that of the parents of a juvenile patient, was obtained. At the beginning of each treatment session, a pretreatment echo-Doppler was carried out to verify the type, depth and accessibility of the malformation and to choose the most suitable injection method (direct puncture, in most cases, or by catheterisation). Depending on the topography of the malformation and the patient's age, local anaesthesia with Emla® ointment (lidocaine + prilocaine) or light general anaesthesia by nitrous oxide (Kalinox®, particularly for children) was performed.

The sclerosing agent used was polidocanol at concentrations ranging from 0.25% to 3%, according to the size and depth of the lesion and the response to previous treatment. Foam was produced by Tessari's method, the sclerosing liquid being diluted with air at a ratio of 1 volume of liquid sclerosant to 4 volumes of air. Colour Doppler ultrasonography was performed with a TurboM SonoSite® system with a high-resolution probe of 7.5 MHz and a superficial probe of 12 MHz. The patient was supine or prone, according to the topography of the lesion. First, a syringe or a short catheter (20 G 22 G butterfly 1.1 × 48 mm or 0.9 × 22 mm) was inserted under ultrasound-guided control. The next stage was performed under ultrasound-guided control with sterile gel and gloves. The volume of foam injected was estimated by the amount necessary to obtain a venous spasm, but never exceeded 10 ml. Compression by superposing an Elastomousse® band and Elastoplast® tape was applied immediately after treatment and maintained for 3 days (24/24 h) when the topography permitted (trunk or limbs). After this, when the malformation was on a limb, an elastic compression stocking (20—36 mmHg) was worn during the day for 15 days. A prescription was given for Hirucrème® and a paracetamol-based (1 g) analgesic in case of pain, with instructions to rest and to avoid any sports activity for 10 days. The patient was kept under surveillance for 2—3 h after the invasive procedure.

Evaluation of Treatment and Follow-up

A clinical and ultrasound examination was performed on day 8. In cases of repeated procedures, an interval of at least 4—6 weeks between sessions was observed. The decision to continue the treatment or not was made with

the patient on the basis of the clinical efficacy. At the end of the treatment, patients were followed up in a non-standardised manner, usually 1—3 months after the last session. When a consultation was not possible, telephone contact was made with the patient. Complications were classified as minor (pain, marked swelling, haematoma, cutaneous necrosis and superficial thrombosis) or major (allergic reaction, renal failure, deep vein thrombosis, pulmonary embolism, thoracic pain and stroke).

Results

The clinical characteristics of the 24 patients treated are summarised in Table 1. The dose injected per session ranged from 0.25 to 10 ml and the concentrations from 0.25% to 3%, depending on the size of the malformation, its depth, the possible occurrence of a venous spasm and response to previous treatment. The number of sessions also varied, depending on clinical and ultrasound responses, and ranged from 1 to 16 (Table 2). The median follow-up of patients was 5 months after the last treatment session. The criteria for evaluating the effectiveness of treatment were both clinical (reduction in size of the vascular malformation and reduction of symptoms) and by ultrasound (% reduction in volume of the malformation) (Table 3). No serious adverse effects were reported, including any thrombo-embolic events, with or without symptoms. Two minor complications were reported concerning pigmentations in a KTS patient and in an infiltrated extra-truncular vascular malformation.

Discussion

Ultrasound-guided sclerosis with polidocanol as a foam is considered less effective than alcohol or Ethibloc but has many advantages due to it being well tolerated. This technique can be performed as an outpatient procedure, while more powerful sclerosing agents such as alcohol cannot. Indeed, the procedure requires no anaesthesia. In some cases, particularly in children, local anaesthesia or light general anaesthesia with, for example Kalinox®, is performed. Post-intervention surveillance only lasts a few hours, and is not conditioned by the same requirements as when general anaesthesia has been used. Furthermore, additional treatments such as antibiotics or anti-inflammatory medication, frequently used when sclerosis is with alcohol, are rarely needed, although analgesics are often necessary. Few studies on this topic are available in the literature and those that are often are only reports of a small series of case studies. Table 4 summarises the main publications on ultrasound-guided sclerosis with polidocanol foam of venous malformations and KTS, and illustrates, as in our study, the few side effects of this technique.

Polidocanol is not as potent as ethanol, but, unfortunately, few studies have directly compared the effectiveness of the various available sclerosing agents. In our team, we use polidocanol rather than sodium tetradecyl sulphate, which seems to have similar sclerosing power according to our experience in chronic venous insufficiency. However, there are no studies on this subject either for venous insufficiency or for low-flow malformations. The lack of blinded randomised studies is probably because of the heterogeneity of malformations, and the different treatment strategies used for different types of malformation. This is the case in the prospective randomised study of Yamaki et al.,[2] where polidocanol was used for superficial lesions and ethanolamime oleate for deeper lesions, in liquid versus foam forms. The superficial, or not, aspect of the lesion conditioned the choice of sclerosant, preventing blinding. Nevertheless, they showed improved efficiency of

Table 1 Clinical presentation of low-flow venous malformations.

	Venous malformation			Combined malformations		Total $n = 24$ (%)
	Extra-truncular $n = 18$ (%)		Complex $n = 1$ (%)	KTS $n = 3$ (%)	LM $n = 2$(%)	
	Infiltrating $n = 12$ (%)	Limited $n = 6$ (%)				
Baseline characteristics						
Men, *n* (%)	1 (8.3)	4 (66.6)	1 (100)	3 (100)	2 (100)	11 (46)
Mean age in years (range)	34.66 (7—78)	30.8 (12—47)	40	34 (26—36)	28 (19—37)	33.6 (7—78)
Distribution of the lesions						
Head and neck	6	2	0	0	1	9
Trunk	1	0	0	0	0	1
Limbs	5	3	1	3	1	13
Multiple	0	1	0	0	0	1
Size						
below 10 cm	2	5	0	NA	1	8
above 10 cm	10	1	1	NA	1	13
Previous treatment						
Medical	2	1	0	2	0	5
Surgical	5	2	0	0	1	8
Endovascular	2	0	0	1	0	3

Table 2 Details of the percutaneous sclerotherapy procedures in patients with low-flow malformations.

	Venous malformation			Combined malformations		Total ($n = 24$)
	Infiltrating (%)	Limited (%)	Complex (%)	KTS	LM	
Number of sclerotherapy sessions with polidocanol:						
1	2 (16.7)	1 (16.7)	1 (100)	3 (100)	1 (50)	8 (33.3)
2	5 (41.7)	4 (66.6)	0 (0)	0 (0)	1 (50)	10 (41.7)
more than 2	5 (41.7)	1 (16.7)	0 (0)	0 (0)	0 (0)	6 (25)
Mean dose of polidocanol injected (ml/session)	2.7	2	6	10	4.7	5.5
Mean total dose of polidocanol injected (ml/patient)	16.4	4.4	6	31.7	4.7	13.5

the foam form for both products. The heterogeneity of vascular malformations in both nature and topography makes it difficult to assess the therapeutic efficacy of these techniques, as does the use of different classification systems for malformations.

Due to the small number of malformations treated at our centre, we chose to include KTSs that strongly resemble venous malformations but, strictly speaking, are syndromic forms and not exclusively venous malformations. In our clinical practice, the decision as to the treatment strategy to use is based primarily on the symptomatic character of the malformation and is made with goals fixed in consultation with the patient. The therapeutic decision is based on subjective criteria that are sometimes difficult to evaluate. Thus, an improvement in symptoms may lead to discontinuation of therapy sessions, even when the clinical appearance or ultrasound shows no regression in size of the malformation. Our study is nonetheless informative on the choice of concentrations and quantities of sclerosant injected and shows a better therapeutic effect with high concentrations, without increased complications. This notion is not necessarily found in studies of polidocanol foam in chronic venous insufficiency.[4] One issue that has been raised is the maximum quantity of sclerosing agent that can be used at the highest concentration of 3%. In the treatment of venous insufficiency, the consensus report of Tegernsee recommended maximum doses of 6—8 ml for ultrasound-guided sclerosis of the great saphenous vein treated with foam and 3 ml for a small saphenous vein with concentrations usually of 0.5—1%.[5] The treated vascular malformations vary in volume, and this is often difficult to estimate, but is well above the volume of the large or small saphenous veins. Some authors use a maximum dose of 10 ml with 3% foam,[6] while others use up to 1 ml kg^{-1} at 1%.[2] Our attitude was conservative and injections never exceeded 10 ml per session. The methodological limitations of our retrospective study did not allow us to assess the prognostic factors, but the results are consistent with efficacy for well-circumscribed vascular malformations of less than 10 cm in diameter due to a better length of contact between the sclerosant and the vascular walls, as already described by some authors.[6] The lower efficiency in large malformations could be explained by a shorter contact time between the sclerosing agent and the vascular walls. For truncular venous malformations, the faster diffusion of the sclerosing agent into the bloodstream seems to make the treatment less effective.

While it is difficult to establish a clear strategic procedure, the technique is nevertheless refined as the operators gain experience. Initially, the concentrations used were low. There were probably few side effects, but a loss of efficacy. The strategy was therefore modified to use higher

Table 3 Clinical and ultrasound evaluation of sclerotherapy with polidocanol foam.

	Venous malformation			Combined malformation (%)		Total (%)
	Infiltrating (%)	Limited (%)	Complex (%)	KTS	LM	
Mean duration of follow-up (months)	17	6.5	1	19.5	2	9.5
Ultrasound result						
Sclerose greater than 50%	5 (41.7)	3 (50)	0 (0)	1 (33.3)	0 (0)	9 (37.5)
Sclerose smaller than 50%	7 (58.3)	3 (50)	1 (100)	2 (66.6)	1 (50)	14 (58.3)
Stable	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (4.2)
Worsened	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Recanalized	2 (16.7)	0 (0)	1 (100)	1 (33.3)	0 (0)	4 (16.7)
Effect on pain						
Decrease	12 (100)	4 (100)	1 (100)	3 (100)	1 (50)	21 (95.5)
Stable	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (4.5)
Recurrence	3 (25)	1 (25)	0 (0)	1 (33.3)	0 (0)	5 (22.7)
Effect on others symptoms						
Decrease	2 (100)	1 (100)	NA	1 (50)	1 (100)	5 (83.3)
Stable	0 (0)	0 (0)	NA	1 (50)	0 (0)	1 (16.7)

Table 4 Review of the literature on treatments by sclerotherapy with polidocanol foam.

Authors	Number of cases	Type of MV	Site	Treatment	Results	Complications
Yamaki et al[7]	1	VM	Face	Polidocanol 1% 5 cc foam	Reduction in size	0
Cabrera et al[8]	50	19 VM limited 16 VM infiltrated 15 KTS		Polidocanol foam 0.25—4% 6 ml max 1 to 46 sessions (12)	Reduction in size 92% Reduction in pain in 14 cases. Disappearance of pain in 25 cases.	4 pigmentations 3 skin necrosis
Pascarella et al[9]	11	8 KTS 3 VM	Limb	Polidocanol foam 1—3% 1-cc 3.6 sessions	10 cosmetic improvement	1 wound
Bergan et al[10]	12	9 KTS 3 VM	Limb	Polidocanol foam 1—3%	11 Reduction in size, pain and cosmetic improvement	1 wound
Nitecki et al[11]	7	KTS		Polidocanol 2—4% Sessions 9—21 (14.5)	Reduction in symptoms	2 regressive pigmentations 1 superficial thrombosis
Bergan et al[12]	14	8 KTS 12 Extra trunk 2 combined extra trunk and trunk	3 wounds	Polidocanol foam 1—2% 3.6 sessions (1—10)		1 cutaneous ulcer
Mimura et al[6]	31	VM	Face, trunk and members	Polidocanol foam 3% 5 ml	Reduction in pain	Hypotension Bradycardia Avulsion of nail Follow-up of 46 months
Uehara et al[13]	7	VM	Head and neck, trunk and foot	Polidocanol foam 3% Sessions (2—13)	Reduction in symptoms	Œdema and/or pain in 55%

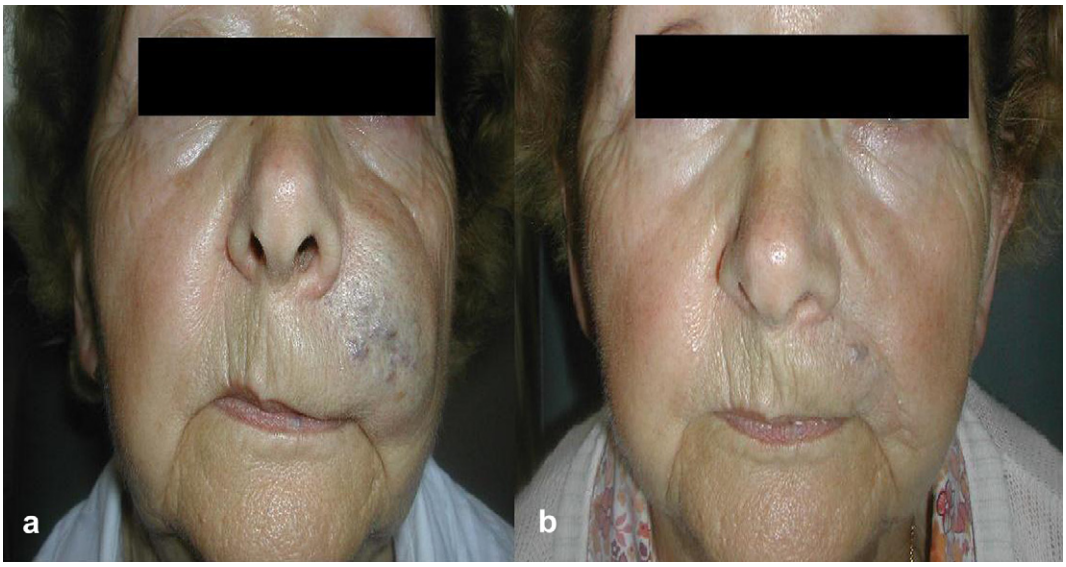

Figure 1 Facial Venous Malformation before (a) and after (b) combined treatment by sclerotherapy with polidocanol foam and surgery.

concentrations from the start of the procedure (2% progressing rapidly to 3%), except when the lesions had a significant cutaneous component.

The volume injected must be adjusted to the volume of each malformation, with the goal of obtaining the longest possible contact time between the agent and the vascular walls, with, for example, the help of ultrasound-guided manual compression. A randomised study would be difficult or impossible to implement in view of the strategic choices necessary to obtain an optimal result, as, in some cases, combined treatment by foam ultrasound-guided sclerosis and, then, surgery is needed (Fig. 1).

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Conflict of Interest

None.

Ethical Approval

None.

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