Sclerotherapy for Leg Telangiectasia—A Blinded Comparative Trial of Polidocanol and Hypertonic Saline

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BACKGROUND. **Hypertonic saline (HS) and polidocanol (POL) have been in use around the world for sclerotherapy of telangiectasia for many years. However, despite numerous articles in the literature extolling the virtues of their individual use, few studies scientifically compare their relative efficacies.**

OBJECTIVE. **To compare, in a statistically significant number of female patients, the relative efficacy of hypertonic saline and polidocanol as sclerosants of leg telangiectasia and reticular feeding veins, using each patient as her own control.**

METHODS. **Eighty-one women with roughly matching leg telangiecasia were treated with sclerotherapy. One leg was injected with 20% saline/2% lignocaine, the other with 1% polidocanol, with the patients blinded as to the sclerosant used for each leg. Assessment of percent reduction of vessels, and the complications of matting and hemosiderin staining was conducted at 2 months by 3 methods: the patient's satisfaction, the treating physician's evaluation, and blinded assessment of before and after photographs.**

RESULTS. **There was no statistically significant difference between HS and *POL* treated legs when assessed clinically or photographically. However, *POL* caused more staining and matting, and despite patients finding HS more painful at injection, patient satisfaction at follow-up was higher with the HS treated leg.**

CONCLUSION. **20% HS and 1% *POL* have equal efficacy in sclerosing leg telangiectasia and reticular feeding veins. *POL* causes more adverse sequelae, although these may be related to the solution concentration.**

SCLEROTHERAPY HAS become the gold standard treatment for leg telangiectasia over the last 3 or so decades, and has been popularized worldwide. Numerous sclerosants have been trialled, and various have achieved popularity in different regions. Polidocanol (*POL*) (Hydroxypolyethoxydodecane) was first used as a local anaesthetic in France in the 1950s. However, after initial trials using it for this purpose demonstrated a vascular sclerosant effect that was undesirable when the drug was injected into tissue, it has become popular as a sclerosant for small to medium-sized vessels, and more recently for varicose veins. The detergent mechanism of sclerosis on the endothelium are documented, and its efficacy well known in the world of phlebology.[1–5] However, there are very few reports in the literature comparing *POL* to other sclerosants for the treatment of leg telangiectasia.[6,7]

Hypertonic saline (HS) has been used for over 50 years for the treatment of varicose veins, although several reports of extravasation necrosis sent it into disrepute until the mid 1970s. At this time, the advent of very fine disposable needles made intravascular injection of sclerosant solutions easier, and HS enjoyed a resurgence in popularity, significantly aided by its lack of any allergic events.[8–10] It works by osmotic action, causing denaturing of vessel walls, and relies on the concentration gradient between the intravascular space and the endothelial cells for its efficacy. It is therefore ineffective if allowed to be diluted by a volume of blood; it must displace blood from the vessel lumen as it contacts the endothelium if it is to be maximally effective.

Although there are numerous reports citing the indications for use, common side effects, efficacy, and complications of these sclerosants, controlled comparative studies of statistical significance are surprisingly lacking. This study was therefore designed to compare 2 sclerosants commonly used for telangiectasia and reticular veins, under controlled conditions using a variety of assessment methods.

Materials and Methods

Subjects

Patients with primary idiopathic telangiectasia on the legs were eligible to participate in the trial if they demonstrated symmetrical areas of vessels on both legs and identifiable reticular feeding veins. Telangiectasia around the ankles or clusters of microvessels arising secondary to surgical scars were excluded because they are rarely symmetrical, and in the authors' experience results of treatment are unpredictable in these instances. Other exclusion criteria included previous sclerotherapy (although patients who had undergone previous venous surgery were included), clinical or duplex doppler evidence of major saphenous or large perforator incompetence, history of ischaemic heart disease, vasculitis of

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any aetiology, diabetes mellitus, current pregnancy or the regular use of anticoagulants. Eighty-one informed, consenting women participated. Participants ranged in age from 21 to 76 years with an average of 44.3.

Procedure

The study was a randomized, controlled, blinded trial. Morphologically similar telangiectasia and reticular feeding veins were identified in matching locations of the legs of each patient. The posterolateral thigh and the anteromedial knee constituted discrete regions. Hence, for example, the lateral thigh of one leg was compared to the equivalent area of the other leg, but not with a different region.

For each patient, one leg was randomly assigned *POL* and the other HS as the sclerosant. Patients were unaware of the choice of sclerosant for each leg until after the 2-month assessment. However, the treating physician was aware at the time of treatment.

Sclerosants were used in the concentrations commonly used for telangiectasia and reticular veins. HS 20% was derived by combing 2 ml of 30% saline with 1 ml of 2% lignocaine hydrochloride to constitute 3 ml of sclerosant. *POL* 1% was derived by diluting *POL* 3% with normal saline. While *POL* 1% has been reported to be a slightly stronger sclerosant than HS 20%, weaker concentrations have been found to increase the risk of recanalisation, although this has only been observed in the rabbit ear vein model.[4] A concentration of 1% *POL* was used in this trial on the recommendation of executive members of the Australian and New Zealand Society of Phlebology.

All treatments were undertaken with the patient in the supine position. Becton-Dickinson needles #30 gauge and 3 ml disposable syringes were used. Sufficient solution to completely blanch a reticular feeding system and all of its visible branches and telangiectasia was infused. This quantity was not specifically recorded. The reticular feeding vessels were injected first, followed by telangiectasia. These were approached in a "downstream" direction, such that the flow of sclerosant into the vein followed the normal blood flow in that vessel. One treatment only was performed per leg.

Immediately after injection a small cotton wool ball was placed over each puncture site and secured with 2.5 cm Micropore tape. Patients were advised to leave these tapes in place for half an hour. Compression was not employed, and no specific restrictions were placed on patients regarding activities or exercise following the treatment.

Treatment sites were photographed immediately prior to treatment and again 2 months after both legs had been treated, using the same camera, lighting conditions and focal distance. All patients were photographed in the standing position.

Assessment

Assessment at the 2-month follow-up was performed by 3 methods.

Patient Satisfaction

Each patient was asked how satisfied she was with the treatment of each leg, on a scale of 0 (not satisfied at all) to 10 (completely satisfied). This assessment was performed with patients unaware of the sclerosant used for each leg.

Clinical Assessment

The treating physician rated improvement on a scale of 0 (no improvement) to 10 (complete disappearance of all vessels) based on the estimated percentage clearance of vessels in the treated sites at 2 months compare to pretreatment photographs. These ratings were not blinded because the treating physician was aware of the choice of sclerosant for each leg. HS and POL have different viscosities, perceptible by the clinician during injection, and are therefore impossible to perform blinded. This nonblinded method of assessment was included because it is often difficult to see minor details such as telangiectatic matting, and to discern residual patent vessels from haemosiderin staining on posttreatment photographs. Assessment based on photographs alone therefore would tend to overestimate the improvement in vessel clearance and underestimate adverse effects.

Blinded Photographic Assessment

A nontreating physician, blinded to sclerosants used for each leg, rated improvement based on before and after photographs using the same 0 to 10 scale method.

Side effects of treatment were also assessed. Patients rated pain of injection for each leg from 0 (not painful at all) to 10 (extremely painful). Immediate reactions, either local or systemic, were noted and injections ceased if such reactions occurred. Patients were counseled to return before the 2-month follow-up should there be ongoing pain, edema, superficial thrombosis, or ulceration. These events were noted.

At the 2-month follow-up, treatment sties were examined by the treating physician for telangiectatic matting and haemosiderin staining. There side effects were scored as 0 = not present, 1 = mild, 2 = moderate, or 3 = severe.

Results

Five patients returned prior to the 2-month follow-up because of uncomfortable thromboses. These were aspirated under local anesthetic. Four of these were in HS treated legs, 1 in the POL limb. There were no ulcers with either sclerosant and no instances of systemic allergy, although one patient reported signifi-

cant swelling and itching in the *POL*-treated leg, for several days after treatment.

The results for all legs treated regardless of sclerosant were analysed. The mean patient satisfaction score was 7.11 (SD = 1.74), the mean clinical assessment score was 7.26 (SD = 1.47) and mean the photographic assessment was 7.41 (SD > = 1.5). As expected, the photo rated score was higher than the clinical assessment score although this difference did not reach statistical significance ($p = 0.2$).

The results of comparisons between the two sclerosants for each method of assessment are given in Table 1. There was no significant difference between scores for legs treated with HS and *POL* when clinical or photo assessments were analysed. However, patients reported significantly greater satisfaction with sites treated with HS.

The mean pain score for all legs treated was 3.31 (SD = 1.60), and scores followed a normal distribution. When pain scores for each sclerosant were compared, injections with HS were rated significantly more painful than *POL* (Table 2). Scores for telangiectatic matting and haemosiderin staining were both skewed to the right signifying that the majority of sites showed only minor degrees of these treatment sequelae. *Twenty-nine legs (36%)* treated with *POL* and *25 (31%)* treated with S showed *some evidence of matting* at the 2-month follow-up (Figures 1A, B, C, and D). Staining was a more common complication (Figures 2A, B, C, and D), with *59 (73%)* of the *POL* treated legs and *44 (55%)* of the HS treated legs *demonstrating this side effect*. Both of these adverse effects, rated only by clinical assessment, were significantly higher with *POL* than HS (Table 2).

To examine in more detail reasons for finding enhanced patient satisfaction when HS was used as the sclerosant, despite both a lack of objective evidence of better clearing of vessels and greater pain of injection using HS, the relationship between patient satisfaction and side effects was analysed using Pearson correlations. For this analysis, each site was considered a separate observation, giving a total of 162 observations (injected legs) in total. A significant negative correlation was found between the degree of matting and patient satisfaction ($r = -0.29$, $p < 0.01$).

Table 1. Comparison of Results between Legs Treated with Polidocanol and Hypertonic Saline

Method of assessment score range 0–10	*Polidocanol (mean ± S.D.)*	*Hypertonic Saline (mean ± S.D.)*	*POL Value*
Patient satisfaction[a]	7.20 ± 0.19	7.23 ± 0.14	0.4
Clinical assessment[b]	7.26 ± 0.21	7.56 ± 0.14	0.5
Photographic assessment[b]	6.93 ± 0.20	7.30 ± 0.19	0.04

[a] paired t-test.
[b] Wilcoxon signed-ranks test.

Table 2. Comparison of Pain of Injection and Side Effects between Legs Treated with Polidocanol and Hypertonic Saline (n = 81 for each sclerosant)

Side effect	*Score using Polidocanol (mean ± S.D.)*	*Score Using Hypertonic Saline (mean ± S.D.)*	*POL Value*
Pain of injection[a] (score range 0–10)	2.79 ± 0.15	3.84 ± 0.18	0.00001
Telangiectatic matting[b] (score range 0–3)	0.54 ± 0.84	0.33 ± 0.52	0.04
Hemosiderin staining[b] (score range 0–3)	1.15 ± 0.91	0.77 ± 0.83	0.003

[a] paired t-test.
[b] Wilcoxon signed-ranks test.

Similarly a significant negative correlation was found between degree of staining and patient satisfaction ($r = -0.21$, $p < 0.01$). This supports the hypothesis that the presence of these minor and transient sequalae affect patients' satisfaction with the outcome of sclerotherapy.

Discussion

Although these 2 sclerosants at the concentrations used in this trial are not identical in potency, they were injected at concentrations commonly used in clinical practice. Consideration was initially given to injecting different-sized veins with differing sclerosant strengths, but it was felt that this would create too many variables. We nonetheless felt that some meaningful conclusions could be drawn. Clearly, the most scientifically valid method of assessment was the blinded photographic score. With this method, as with nonblinded clinical assessments, there was no difference in the degree of vessel clearance between the 2 sclerosants. However, it is interesting to note that although the patients found HS more painful than *POL* at the time of treatment, when they returned for their 2-month follow-up a greater number favored the results of the HS to the *POL* treated leg. The difference between mean pain scores (2.79 for *POL*, 3.84 for HS) was clearly not sufficiently memorable for patients to base their opinion of outcome on this factor. In addition, the dilution of 30% hypertonic saline with lignocaine undoubtedly significantly reduces the level of pain experienced during treatment. Had hypertonic saline alone been used, the difference between pain scores for each sclerosant would likely have been far greater.

The clinical assessors ignored matting and staining when evaluating percent vessel clearance. Likewise, matting and staining do not usually show up as clearly on photographs as they do in vivo, and the photo-

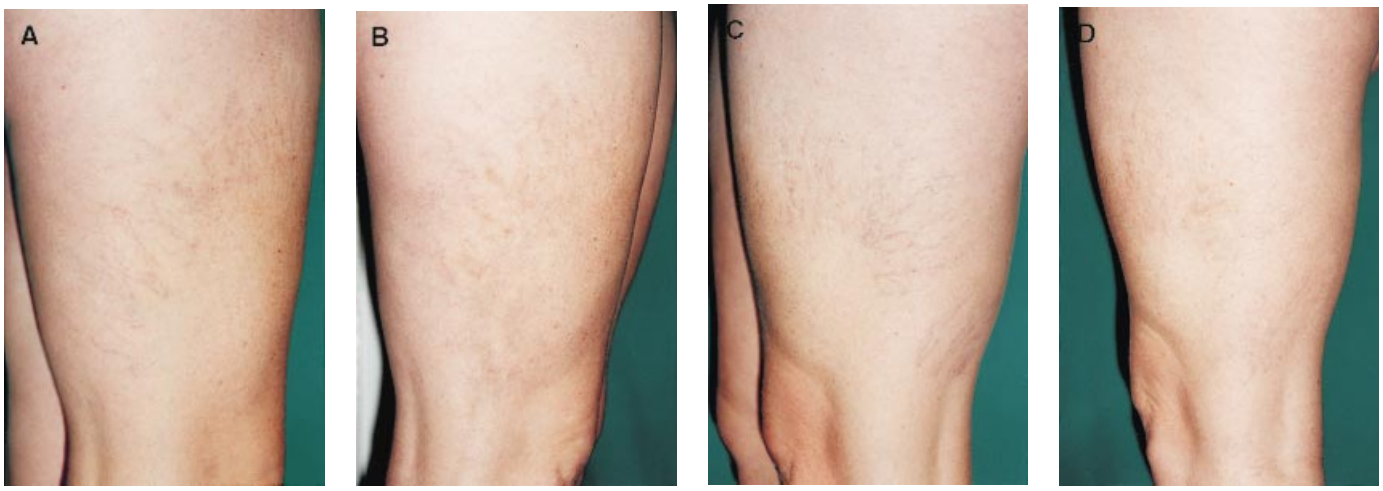

Figure 1. A 37-year-old woman with typical lateral thigh telangiectasia and reticular veins, before and 2 months after sclerotherapy. A and B show the right leg treated with polidocanol, with moderate matting (score = 2) and mild staining (score = 1). C and D show the left leg treated with saline, with mild matting (score = 1) and mild staining (score = 1). The patient's satisfaction with the right leg was score = 8, and the left was score = 9. The photo assessment was similar, but clinical assessment rated the scores lower, at 7 and 8 respectively.

graphic assessments were based more strictly on vessel clearance than overall appearance of the leg. A patient's satisfaction level was dependent on all factors—vessel clearance, matting, and staining. Our correlations clearly suggest that patients favored the outcome of treatment with HS over *POL* more because of the greater amount of staining and matting that because of any real difference in vessel clearance.

The greater incidence of matting and staining using *POL* compared to HS may be due to the fact that *POL* at 1% concentration may be too "strong" for telangiectasia, although undoubtedly such a concentration or higher is necessary to treat reticular feeding veins, many of which were 3 to 4 mm in diameter or occasionally larger. Sclerosant solutions that are too concentrated for the size of the vessels being treated are known to cause *damage to the media and adventitia* as well as the intima of ectatic vessels, allowing extravasation of red cells into the perivascular tissue, resulting in haemosiderin staining, and possibly some perivascular inflammation, which may predispose to new vessel formation (matting).[11] On the other hand, it has also been suggested that 20% HS is stronger than is ideal for microvessels,[12] but less effective for treating vessels over 4 mm in diameter,[7] many of which were included in this trial. Regardless, we

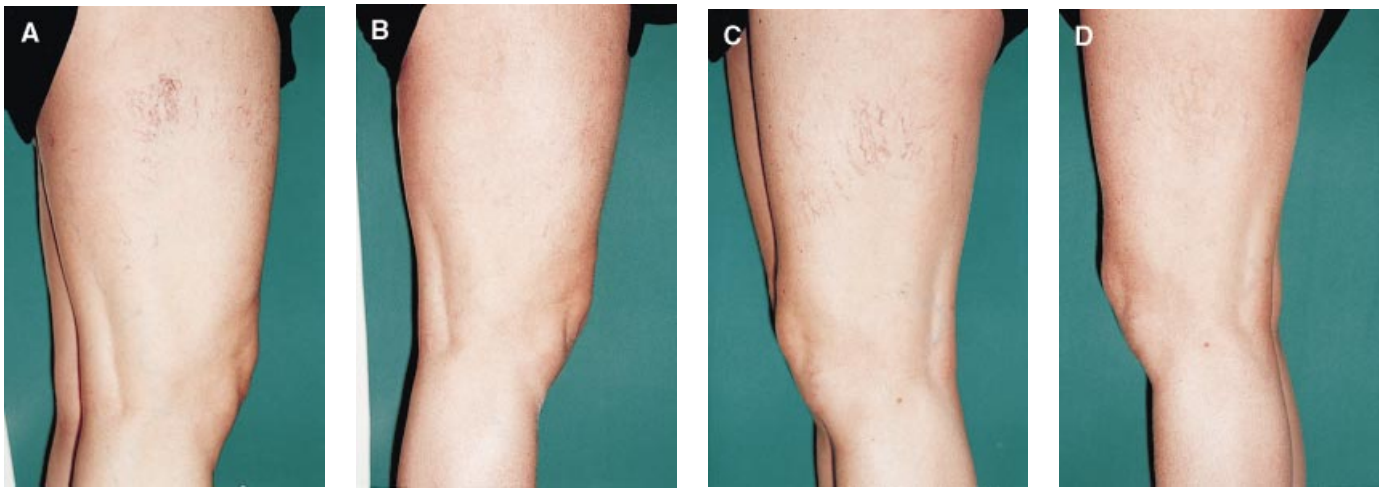

Figure 2. A 44-year-old woman with telangiectasia and prominent reticular veins, before and 2 months after treatment. A and B show the right leg treated with hypertonic saline with no staining (score = 0) and mild matting (score = 1). C and D show the left leg, treated with polidocanol, and mild staining (score = 1) and mild matting (score = 1). Clearance of veins is equivalent (photo score = 8) for both legs.

found that reticular feeding veins responded to HS with efficacy equal to *POL* when reviewed at 2 months.

We acknowledge that had all patients used post-sclerotherapy 30–40 mm compression stockings for 1 to 3 weeks,[13] there would have been a lower overall incidence of staining. However, this study was designed to test the comparative efficacy of the 2 sclerosants by using each patient as her own control while trying to minimize treatment variables. As not all patients had both legs injected during a single treatment session, it was anticipated that some patients might remove the stocking from 1 or both legs prematurely, should the long Australian summer deliver its typical bouts of very hot weather. Therefore, consistency of posttreatment management could only be assured if no compression was used.

Although this trial was not designed for further follow-up at 6 or 12 months, 10 patients have been reassessed after more than 6 months since treatment. Again, no difference between legs with regard recurrence or new vessel formation has been noted, although these observations are clearly anecdotal and of no statistical significance.

Conclusions

Hypertonic saline at 20% and polidocanol at 1% concentrations result in equal clearance of telangiectasia and reticular veins of the lower limbs of women. Despite finding HS more painful at the time of injection, patients preferred the outcome of the HS treated leg, most likely because the transient common side effects of haemosiderin staining and telangiectatic matting are more common with POL at the concentrations used in this study.

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Commentary

The authors are to be commended for putting together a well-performed follow-up study of 81 women with leg telangiectasia treated with 2 sclerotherapy solutions. Unfortunately, the 20% hypertonic saline solution cannot be equated with 1% Polidocanol. Therefore, a strict comparison of these two agents is beyond the scope of this paper. A more accurate comparison would have been 20% hypertonic saline compared to 0.5% Polidocanol. If one were to have compared these solutions, it is likely that Polidocanol would not have caused any more "staining or telangiectasia." Thus, the conclusions reached by the authors are fundamentally flawed.

However, one can glean important information from this study. The most important concept is that if one uses a sclerosing solution well in excess of the minimal sclerosing concentration necessary to produce endofibrosis of telangiectases, one will get an increase in complications. Certainly, the literature, as well as those who use Polidocanol, do not see the degree of complications using the more appropriate minimal sclerosing concentration of Polidocanol as the authors demonstrated through the use of a concentration twice that normally used.

Other important pieces of information were that the authors described treatment of the feeding reticular system and all of its visible branches including telangiectases.

Finally, the authors demonstrated that the use of graduated compression stockings in patients with telangiectasia was not absolutely necessary in this patient population. The corollary was that 5 patients developed uncomfortable thromboses, which needed to be aspirated under local anesthesia. This complication is extremely rare, in my experience, when using a 30 mm to 40 mm graduated compression stocking after treatment. The

incidence of telangiectatic matting of 36% with Polidocanol and 31% with hypertonic saline is also much higher than seen in practices utilizing post-sclerotherapy compression. Finally, the development of pigmentation in 73% of Polidocanol and 55% of hypertonic saline is far in excess of that reported in literature, especially in studies utilizing graduated compression stockings after sclerotherapy. Thus, the authors also demonstrate the importance of utilizing post-sclerotherapy graduated compression even though this was not the purpose of their study.

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