0.5% Polidocanol for Treatment of Varicose Veins

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**Background:** The use of sclerosants approved by the US Food and Drug Administration for treatment of varicose veins, including sodium morrhuate, ethanolamine oleate, and sodium tetradecyl sulphate, has resulted in complications that include allergic reactions and occasional deaths. Polidocanol, which has not been approved by the Food and Drug Administration, has been well studied and well described in the literature as a safer, more effective sclerosant for varicose veins at 3.0% concentration.

**Objective:** The purpose of this study was to examine the efficacy of 0.5% polidocanol as a sclerosant for varicose veins.

**Methods:** A test dose of polidocanol is injected 1 week before the start of treatment to test for allergic response. Sclerotherapy sessions last 10 minutes, and an average of 10 to 20 mL of 0.5% polidocanol is injected through use of 30-gauge half-inch tuberculin syringes. The treated varicosities are compressed with Coban wrap and compression hosiery for 48 hours after treatment and with compression hosiery alone for another 2 weeks.

**Results:** Having performed approximately 1600 sclerotherapy sessions using 0.5% polidocanol over the last 6 years, I have observed that an average of 3 sclerotherapy sessions are required to attain an 80% to 85% improvement in varicose veins. The number of sessions required for successful treatment ranged from 1 to 15. Results have been long lasting. Localized thrombus formation and hyperpigmentation occurred in some degree in every treated patient but generally did not require treatment for resolution. No ulcerations, pulmonary emboli, or anaphylactic reactions were observed. Superficial chemical thrombophlebitis occurred in 3 patients.

**Conclusions:** Polidocanol is a painless, nonscarring, effective treatment for a condition that previously has been treated surgically. The minimal sclerosant concentration for the treatment of varicose veins is 0.5%.

In the United States, sclerotherapy is often performed with polidocanol or hypertonic saline (HS), both of which have been well studied and well described in the literature but neither of which has been approved by the US Food and Drug Administration (FDA) for use as a sclerosant. FDA-approved sclerosants such as sodium morrhuate, ethanolamine oleate, and sodium tetradecyl sulphate (STS) were approved before 1950; as such, they were not evaluated and scrutinized for safety and efficacy by today’s standards and guidelines. Complications including allergic reactions and occasional deaths.
have been reported in patients treated with these approved sclerosants.2-4

The FDA has approved 23.4% HS for use as an abortifacient, and as such it is commercially available in the United States. Although it is not associated with hypersensitivity reactions, HS is not generally considered to be an ideal sclerosing agent because it causes pain and muscle cramping on injection and effectively treats only a small area around the injection point. To decrease the level of pain and the incidence of ulceration associated with HS treatment, it is frequently mixed with lidocaine, diluted with saline, or both. HS and the FDA-approved sclerosants are associated with a high incidence of necrotic ulceration resulting from extravasation, as well as with postsclerosis hyperpigmentation.5-7

Polidocanol

Polidocanol was developed in the early 1950s for use as a local anesthetic, but it was soon noted that intravascular and even intradermal instillation of the agent produced sclerosis of small-diameter blood vessels; for this reason, it was no longer used as a local anesthetic. The agent’s anesthetic properties prevent it from causing pain on injection, so patient comfort is maintained during the sclerotherapy session. The available literature has shown that polidocanol has a high therapeutic index and is associated with an extremely low incidence of allergic reactions, tissue necrosis after intradermal injection, and postsclerosis hyperpigmentation.8-10

A 2-year Australian study compared the effectiveness and complication rate of sclerotherapy with polidocanol, HS, and STS.11 Ninety-eight investigators performed sclerotherapy with polidocanol on a total of 16,804 limbs; 6,474 of these limbs were classified as having varicose veins and 10,328 were classified as having spider veins and venules. Sclerotherapy was performed with 0.5% or 1% polidocanol for telangiectasias or spider veins, and 3% polidocanol was used for treatment of varicose veins. On the basis of their experience with other sclerosing agents, 84% of the investigators found polidocanol to be more effective than HS, and 85% of the investigators found polidocanol to be more effective than STS. Ninety percent of the investigators noted that polidocanol had less frequent side effects than STS, and 80% found the side effects to be less severe. Seventy-four percent of the investigators found that polidocanol had less frequent and less severe side effects than HS.

The active ingredient in polidocanol is a long-chain fatty alcohol topical anesthetic called hydroxypropelyethoxydodecane, which is also used in topical anesthetic ointments and lotions for mucous membranes. Polidocanol acts as a detergent when injected into a vein, disrupting the endothelial cell layer of the blood vessel. The vessel then collapses on itself and forms a fibrotic cord, which is dissolved by macrophages over the course of 4 to 6 weeks. Occasionally, especially in larger vessels, a thrombotic nodule will form, requiring evacuation.3

HS works by osmotic action, denaturing the vessel walls. Because this process relies on the concentration gradient between the intravascular space and the endothelial cells,
it is ineffective if a volume of blood such as that found in a varicose vein dilutes the HS solution. To be maximally effective, HS must either be injected into an empty vein or displace blood from the vessel lumen as it contacts the endothelium.5

History of Sclerotherapy

Hippocrates practiced surgical treatment of varicose veins and reported traumatizing them with “a slender instrument of iron” that caused thrombosis.4,9,12 The use of intravascular sclerotherapy for treatment of varicose veins, which coincided with the invention of the hypodermic needle, was first performed in 1840 by Monteggio and D'Etiolles with a solution of absolute alcohol.13 In 1851, Charles-Gabriel Pravaz treated varicose veins by injecting a solution of ferric chloride.13 Clinical results were good, but complications included mortality from sepsis and embolism, so the procedure was soon abandoned.4,9,13,14

In the last 150 years, a number of different sclerosants, including grape sugar, cod liver oil extract, bichloride of mercury, quinine, and urethane, have been used for sclerotherapy of varicose veins. In the United States, surgical ligation and stripping gained popularity because of a lack of formal sclerotherapy training, an absence of standardized sclerosing agents, and the occasional reports of severe side effects (pulmonary embolus, anaphylaxis, and mortality) resulting from sclerotherapy. However, surgery is not always successful, and recurrence of the varicosities frequently necessitates multiple procedures. For the last 45 years, sclerotherapy has been the treatment of choice for spider and varicose veins in Europe. In the United States, interest in sclerotherapy is growing because of improvement in the efficacy of the technique as well as the fact that the treatment is nonscarring and painless and can be performed in an ambulatory setting at considerably reduced cost.

Etiology and Symptomatology

Varicose veins are one of the most common disorders of the peripheral vascular system, occurring in at least 10% of the US population. They are approximately 3 times more common in women than men. The term varicose is derived from the Greek word for “grapelike.” Most family doctors view varicose veins as a cosmetic nuisance and do not recommend treatment. In fact, more than one half of patients with varicose veins experience leg pain, heaviness, and leg fatigue that worsens as the day progresses, forcing the patient to elevate the legs for relief in the afternoon.15 Patients may or may not realize that these symptoms are caused by varicose veins. The symptoms arise from telangiectasias just as commonly as they do from varicose veins, and they typically affect women most on the first day of the menstrual cycle. One half of patients with telangiectasias have such symptoms, and 85% of these are relieved with treatment.15 Ultimately, however,
cosmetic concerns may be the most common reason that patients seek evaluation and treatment for varicosities.\textsuperscript{15,16} The main etiologic influences in the development of varicose veins are heredity, female sex hormones, gravitational hydrostatic force, and hydrodynamic muscular compartment force.\textsuperscript{15} More than 90\% of patients with varicose veins report a familial history of telangiectasia and/or varicose veins. The inherited defect may be an alteration in vein wall collagen and/or elastin. The effect of elevated progesterone levels as a result of pregnancy, birth control pills, or hormone replacement therapy on the development of varicose veins is profound. Progesterone inhibits smooth muscle contraction in vessel walls, allowing dilatation of subcutaneous veins so that they expand against the dense subdermal somatic nerve network and cause characteristic symptoms.\textsuperscript{17} Furthermore, progesterone-induced venous dilation may cause sudden rupture of a competent valve. Age, obesity, and nutrition may play a role in the development of varicosities, but their influences are less clearly understood.

Minimal Sclerosant Concentration

Minimal sclerosant concentration is the lowest concentration of a given sclerosant that will provide effective sclerosis. Any side effects of sclerotherapy are related to endothelial disruption, which may be a function of both sclerosant concentration and physician technique. Polidocanol has been shown to produce excellent obliteration of varicose veins at a concentration of 3\%, but careful review of the phlebology literature failed to reveal any papers demonstrating effective varicose vein sclerotherapy at lower concentrations. This article will show that effective sclerotherapy of varicose veins can be achieved at a concentration of 0.5\%, minimizing side effects while maximizing results.\textsuperscript{18,19}

The Sclerotherapy Technique

Polidocanol may be obtained as Sclerovein 3\% (V.S. Ltd., Birmingham, England), Aetoxisclerol 0.5\% (Laboratoires Pharmaceutiques Dexo, S.A., Nanterre, France), or Aethoxysklerol 1\% or 3\% (Kreussler and Company, GmbH, Wiesbaden-Birbrich, Germany). In my practice, I use Sclerovein 3\% and dilute it to a concentration of 0.5\% by adding 130 mL of normal saline to 30 mL of 3\% Sclerovein. One-mL non–Luer-lock tuberculin syringes are then filled with the 0.5\% polidocanol solution and stored at room temperature.\textsuperscript{20} Some of these syringes are capped with a 30-gauge half-inch needle. During the initial consultation, photographs of the patient’s legs are taken. An intravascular 0.5-mL test dose of polidocanol is administered during the initial consultation to ensure that the patient is not allergic to the solution. A small spider vein is usually chosen as the test dose injection site. An allergic reaction is recognized by the presence of a severe, intense blood blister or the persistence of a patch of redness or discoloration in the area surrounding the injection site.

The patient waits for 1 week before starting treatment to test for allergenic response. This also gives the patient an opportunity to read the consent paperwork, which clearly

![Figure 3. A, Pretreatment view of a 45-year-old woman with a longstanding isolated varicosity of the right ankle. B, Posttreatment view demonstrates results of a single sclerotherapy session.](https://academic.oup.com/asj/article-abstract/20/1/19/181917)
states that polidocanol is not an FDA-approved treatment for varicose veins; a thoroughly informed consent is thus obtained before the treatment. The patient is informed that sclerotherapy is not a cure for the condition and that multiple treatment sessions are usually necessary to achieve an 80% to 85% success rate. The patient is also informed that new varicose veins can develop after treatment and that complications such as hyperpigmentation, localized thrombosis, superficial thrombophlebitis, ulceration, and tissue necrosis can occur. The need for posttreatment compression hosiery and the use of cotton ball/Coban wrap (3M, St. Paul, MN) is discussed.

A tourniquet is unnecessary, as are routine pretreatment Doppler studies. If a patient has a history of deep-vein thrombosis or if physical examination reveals clinical signs of advanced venous disease, pretreatment Doppler examination is considered. Each sclerotherapy session lasts 10 minutes, which is an arbitrarily chosen length of time but one that allows adequate sclerotherapy treatment without risking a side effect or an overdose. I generally adhere to this time frame regardless of the severity of the patient’s varicose veins. However, 20-minute sessions may be performed upon patient request in cases in which the patient is required to travel extensively for treatment. A 10- to 20-minute break is taken between the first and second 10 minutes of a double session.

The patient stands during the procedure. Excellent lighting and 4.3x loupe magnification are important to ensure proper injection technique. Five to 7 isopropyl alcohol–saturated cotton balls are applied to the skin just before the start of the procedure. As different areas are treated, additional alcohol is applied. Alcohol changes the refractive index of the skin and enhances visualization of the abnormal varicosities and spider veins.

The 30-gauge half-inch needle is bent to a 45° angle, and with the bevel up, it is inserted into the vein. Blood is withdrawn into the tuberculin syringe to ensure that an intravascular insertion has been obtained and intradermal extravasation will not occur. When it is confirmed that the needle is in an intravascular location, the injection is performed. The entire milliliter is usually injected into the varicose vein, while smaller-diameter vessels are treated with smaller quantities. On average, 10 to 20 mL is used during one 10-minute varicose vein sclerotherapy session, but I have used up to 30 mL in 1 treatment session without complication. An occasional patient will have a syncopal episode during treatment that is stress-related rather than a true side effect of polidocanol. If this occurs, the procedure is completed with the patient in a reclining position.

Once the session is completed, the treated varicose veins may appear swollen or inflamed. In my experience, this is an indication that endothelial disruption is occurring and is an excellent sign that a good response will be obtained. The treated varicosities are compressed with dry cotton balls, which are secured with 6-in Coban wrap, avoiding the need for tape and sparing the skin. Compression hosiery (20 to 30 mm/Hg) is placed on the lower extremities immediately after the Coban wrap is applied. The wrap and hosiery are worn for 48 hours. After this time, the Coban wrap is removed and the hosiery is worn (during active hours only) for another 2 weeks. This compression is needed to seal the irritated vascular lumina and decrease the incidence of recanalization, hyperpigmentation, and thrombus formation.21-23

Light exercise is permitted beginning immediately after the procedure. The patient is asked to avoid hot baths (to prevent vasodilation) and high-impact aerobics for 48 hours. A second sclerotherapy treatment session can be performed as soon as 1 week later, but patients usually wait 2 to 4 weeks before another session is performed.

I view these treatment sessions as purely cosmetic in nature, and fees are paid at the end of each session. I do not submit a bill to the patient’s insurance company for payment inasmuch as reimbursement has historically been poor and is in most cases denied. Varicose veins do cause pain and fatigue in sufferers, and as such, treatment should be considered medically necessary. However, I have been unable to convince insurance companies in my area that this is the case.

Results

I have performed 500 to 600 sclerotherapy treatment sessions per year for the past 6 years. Approximately 50% of these sessions are performed for the treatment of varicose veins. The average varicose vein patient requires 3 treatment sessions for an 80% to 85% improvement to be achieved. An occasional patient will achieve success after 1 treatment session; others may require 10 to 15 sessions. The number of sessions required depends on the diameter of the varicosities at the start of the treatment and the degree of reflux into the central leg veins. The smaller and more localized the varicosities are, the fewer treatment sessions are needed to achieve a successful outcome. Each patient in this study was treated with 0.5%
polidocanol. After the first 2 treatment sessions, most patients reported a distinct reduction in the severity of leg pain and fatigue. The results have been long lasting and there have been few complications (Figures 1-3).

Complications

Localized thrombus formation and hyperpigmentation are the most common side effects associated with polidocanol treatment, occurring to some degree in every treated patient. Endothelial damage activates factor 8, initiating the extrinsic coagulation pathway, platelet adherence, and, eventually, the intrinsic pathway of coagulation. This leads to thrombus formation as well as non-specific perivascular infiltration, organization, and fibrosis. Hyperpigmentation results from leakage of blood into the surrounding soft tissue and is a byproduct of hemosiderin deposition. The larger the varicosities are, the more likely it is that the side effects will occur.24,25

Occasionally, localized thrombi become painful and require stab-wound transcutaneous evacuation with manual compression of the vein. This is done with local anesthetic infiltration of the skin under sterile conditions. The stab wounds do not require suture approximation. Covered with triple antibiotic ointment and bandages, they close within 48 hours.

Hyperpigmentation is treated with application of Hiruval 35 (Vimax Pharma, Inc., London, Ontario, Canada) applied twice daily for 4 months. Even without treatment, hyperpigmentation usually fades in time. I have not seen ulcerations, pulmonary emboli, or anaphylactic reactions resulting from polidocanol treatment for varicose veins. Superficial chemical thrombophlebitis was rare, occurring in 3 patients. This condition responds well to leg elevation, reduced physical activity, warm saline soaks, and oral antibiotics.26,27

Varicosities cannot recur once the vein has thrombosed and formed a fibrotic cord. New varicose veins may form, however, because this treatment does not cure the particular condition that caused the original varicose veins to develop. Varicose veins appearing after polidocanol treatment are usually smaller and less extensive than the original cluster. It is recommended that maintenance sclerotherapy treatment sessions be performed every 4 to 6 months to control the condition.

Conclusions

My experience has shown that 0.5% polidocanol is the minimal sclerosant concentration for the effective treatment of varicose veins. Polidocanol injection is a painless, non-scarring, effective treatment for a condition that previously has been treated surgically. Before-and-after photographs are provided to illustrate the effectiveness of this technique.

References


