

SCLEROSING AGENTS

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The purpose of sclerotherapy is to produce endothelial damage that results in permanent endofibrosis and clinical obliteration of the vessel. The ideal sclerosant would have a highly specific mechanism of action, would be free of adverse effects when used for this purpose, and would not produce allergic reactions. Although many agents have been used in treating varicose veins and telangiectasias, thus far none have completely satisfied the criteria for the ideal sclerosant.

The sclerotherapist should have a sound knowledge of the mechanism of action and the adverse effects of all available solutions in order to select the sclerosant that will optimize results in each patient. The following agents are available for use in Australia and New Zealand.

Osmotic Agents

Osmotic agents exert their effects by dehydrating endothelial cells through osmosis, which results in endothelial destruction. They are hypertonic solutions, and their effect is dependent on the existence of an osmotic gradient. Because osmotic agents are rapidly diluted in the bloodstream, they lose their potency within a short distance of injection and are less effective in the treatment of veins larger than 3 to 4mm in diameter.

Hypertonic saline solution. Hypertonic saline is the most commonly used osmotic agent. The advantages of hypertonic saline are its low cost, ready availability, lack of allergenicity of unadulterated solutions, and rapid clinical effect. It also has been reported to cause less telangiectatic matting compared with polidocanol. The significant adverse effects of hypertonic saline relate to its non-specific action of destroying cells within its osmotic gradient. Therefore extravascular injection is liable to cause cutaneous ulceration, which can also occur with intravascular injection via diffusion through a damaged endothelium. Diffusion of hypertonic saline through the vein wall also results in irritation of adventitial nerves, causing postinjection pain and transient muscle cramping. Therefore injection technique, concentration, and volume are particularly important when this agent is being used.

Attempts have been made to reduce postinjection pain from hypertonic saline by the addition of local anesthetics such as lignocaine. However, this practice appears to be counterproductive because the local anesthetics are acidic (and therefore contribute to transient pain on injection) and have known allergenicity, the very properties that proponents of hypertonic saline wish to avoid. The addition of heparin to hypertonic saline in an attempt to prevent thrombosis in larger vessels and to reduce the incidence of thrombophlebitis and postsclerotherapy pigmentation has been found to be of no therapeutic benefit in treating telangiectasias. Concentrations of hypertonic saline used to treat telangiectasias range from 11.7% to 23.4%, the latter being the standard concentration available for use as an abortifacient. The incidence of postinjection pain,

muscle cramping, cutaneous ulceration, and postsclerotherapy pigmentation is proportional to the concentration of solution used.

Detergent Solutions

Detergent solutions include sodium morrhuate, ethanolamine oleate, STS, and polidocanol. These agents act specifically on venous endothelium. They induce sclerosis by damaging the endothelium via interference with cell membrane lipids. They exert their effect along the vessel until either diluted or inactivated by serum surfactants. Only STS and polidocanol are widely used for the treatment of telangiectasias. Table 1 gives the approximate equivalent concentrations of STS and polidocanol required for the treatment of lower limb veins. Because of their different mechanisms of action, it is difficult to compare concentrations of detergent solutions with hypertonic saline. However, in the dorsal rabbit ear vein, polidocanol 1% is equivalent in potency to hypertonic saline 23.4%. Other factors apart from vein diameter need to be considered in selecting the concentration of solution. Patients younger than 25 years of age generally require weaker solutions to achieve effective sclerosis. Also, care should be taken with elderly patients and cigarette smokers because they may have coexisting diminished cutaneous perfusion which increases the risk of post-sclerotherapy cutaneous necrosis. The area to be treated also influences the choice of concentration. Slightly lower concentrations are required on the medial distal thigh and around the ankle; slightly higher concentrations are needed for treating the lateral and posterior thighs and calves.

Sodium tetradecyl sulphate. STS is a versatile sclerosant that can be effectively used for the treatment of a wide range of varicose veins and telangiectasias. The essential concept in using STS successfully is to use the appropriate concentration for the given vein diameter. This will result in minimisation of adverse effects. Although STS has a predictable and constant effect within the same caliber and type of vein at the same level or area of the leg, there can be variation in sensitivity among patients. For example, when treating reticular veins and telangiectasias I have observed that cigarette smokers appear more sensitive to solution concentration, possibly as a result of chronic endothelial damage and increased endothelial permeability caused by carbon monoxide and nicotine.¹⁰ The main disadvantage of STS is the pain it causes for several minutes after injection, particularly when reticular and small varicose veins are being treated. However this disadvantage is outweighed by the relatively large total volumes that can be safely injected in a treatment session, especially with the diluted solutions

STS is commonly used in concentrations of 0.50% to 3% to sclerose lower limb varicose veins. Concentrations of 0.25% to 0.50% are used to treat reticular veins, and concentrations of 0.10% to 0.20% are used for microinjection of telangiectasias. Recently the lower concentrations 0.2%, 0.5% and 1% have become available for use in Australia and New Zealand and are marketed under the brand-name "Fibrovein" (Australasian Medical and Scientific Limited). Other concentrations are achieved by diluting the available strengths of 0.2% 0.5%, 1% and 3% with normal saline. Injection of STS results in immediate vessel spasm, which aids hemostasis after needle withdrawal and can be used as a guide to the effectiveness of a particular injection.

The most common serious adverse effect with STS is anaphylaxis which has an incidence of 1 in 700 when using the 3% solution. Typically, the reaction occurs from 10–30 minutes from commencement of the injections and is manifested by facial flushing, generalised urticaria followed by the patient feeling unwell (a feeling often described as impending disaster), dizziness (hypotension) compensatory tachycardia, shortness of breath and wheeze and finally gastrointestinal symptoms of nausea, vomiting and abdominal pain. Patients with this reaction will generally respond well to immediate injection of adrenaline 0.5mL of 1:1000 aqueous solution subcutaneously or intramuscularly, followed by promethazine HCl 25mg or 50mg intramuscularly. Therefore it is advisable that any physician using STS should be well aware of the early signs of anaphylactoid reaction and have the appropriate emergency equipment immediately at hand, as prompt treatment prevents the patient's condition becoming critical.

Systemic reactions to STS, including allergy and anaphylaxis, are extremely rare in the treatment of reticular veins and telangiectasias probably due to the lower concentrations used.

STS can cause a burning sensation pain for several minutes after injection, especially when reticular veins are being treated. The pain usually is relieved by applying pressure to the injection sites by using cotton balls held firmly in place with paper tape. Alternatively, an ice pack placed over the treated area for several minutes will reduce the pain significantly. The 0.10% to 0.20% solutions used for microinjection cause minor discomfort and pain is minimal when treating large varicose veins with the appropriate concentration..

Cutaneous ulceration has been commonly reported when STS is used for the treatment of telangiectasias. These high rates of cutaneous ulceration always have occurred when excessive concentrations were used for microinjection. Reiner showed that cutaneous necrosis after intradermal injection of STS in rabbits was concentration-dependent, with 0.313% solution producing no necrosis and 1.25% solution producing necrosis. In the microinjection of telangiectasias, STS rarely causes cutaneous necrosis when diluted to 0.1% - 0.15%.

Polidocanol. Polidocanol is used in concentrations of 0.25% to 3% to sclerose lower limb varicose veins and telangiectasias. Concentrations of 1% to 3% are used to treat reticular and varicose veins, and concentrations of 0.25% to 0.75% are used for microinjection of telangiectasias. Polidocanol is available in standard concentrations of 0.5%, 1%, 2%, and 3%. Other concentrations are achieved by diluting with normal saline. Experimental evidence in the dorsal rabbit ear vein indicates that polidocanol is a weaker agent than STS in producing effective endosclerosis of telangiectasias.

Compared with STS, polidocanol causes less vessel spasm and more erythema, resulting in increased bleeding after needle withdrawal. Like STS, polidocanol has a predictable effect within the same caliber of vein and area of the leg, but variation in effect between patients occurs. Systemic reactions to polidocanol when used in the treatment of

telangiectasias have been reported and occur at a frequency of 0.2 - 0.3%. However, it is essential that the manufacturer's maximum dose is not exceeded as bradycardia and hypotension will occur due to the intrinsic negative inotropic effect of polidocanol. This may limit the extent of treatment possible in one session when compared with STS.

Because of its inherent local anesthetic properties, polidocanol causes less pain after intravascular injection compared with STS however it tends to be slightly more painful at the moment of injection, especially if there is any extravasation. Cutaneous ulceration is uncommon when concentrations of 0.25% to 1% are used, but it does occur with solutions over 1%.

A problem that can occur when using polidocanol is inadvertent sclerosis of normal veins far from the site of injection owing to spread of the solution further from the site of injection than anticipated due to its high solubility.

Sclerosant Foam

In the treatment of major varicose veins and incompetent axial trunks, the effectiveness of both STS and POL can be enhanced by converting the standard solution into a foam using a simple 3 way tap and pumping a mixture of sclerosant and air between 2 syringes. By using this method larger veins can be more effectively treated with smaller volumes of sclerosant. This also appears to reduce the incidence of local thrombophlebitis and may reduce the incidence of anaphylaxis with STS.

Alcohol

Alcohol has been used for over 100 years in treating varicose veins. It's quickly diluted and inexpensive. Alcohol is the most potent sclerosant available. It's typically used as either a 95% or a 100% solution and the mode of action is by chemically injuring the vascular endothelium and denaturing blood protein, which results in an intense thrombosis. Alcohol is typically used in the venous type of malformation. It has also been reported to successfully treat extremity and renal arteriovenous malformations and this has led to investigations of its use in the treatment of AVMs, AV fistulas and lymphatic malformations in the head and neck region as well.