Catheter-Directed Sclerotherapy for Saphenous Vein Incompetence

An update on the recent progress and current areas of clinical study and development using this therapeutic option.

BY JOSÉ I. ALMEIDA, MD, FACS, RVT, AND JEFFREY K. RAINES, PHD, RVT

Sclerotherapy refers to the introduction of a drug into the lumen of a vein with the intended consequence of endoluminal venous fibrosis and subsequent vein closure. Clinically, vein closure is desired to mitigate the effects of venous hypertension caused by retrograde venous flow. The mechanism of action of sclerosing solutions is directed toward the complete destruction of endothelial cells lining the venous lumen, exposure of subendothelial collagen fibers, and formation of a fibrous cord. Endothelial damage must be as complete as possible, because otherwise, thrombus will form and layer endoluminally. Some thrombus is expected because of platelet deposition and initiation of the intrinsic coagulation pathway once collagen is exposed; however, excessive thrombosis is detrimental because it can lead to recanalization of the vessel and excessive intravenous and perivenous inflammation.

CURRENT USES OF SCLEROTHERAPY

Sclerosing solutions are categorized as either detergent, chemical, or osmotic. In the US, although many are used, only one drug is approved by the FDA. Sodium tetradecyl sulfate ([STS; Sotradecol] Bioniche Pharma USA, Inc., Lake Forest, IL), a detergent, received FDA clearance for venous sclerotherapy in 2004, and subsequently, there has been interest in maximizing its effectiveness, particularly on the great saphenous vein (GSV). Historical data suggest that chemical ablation of

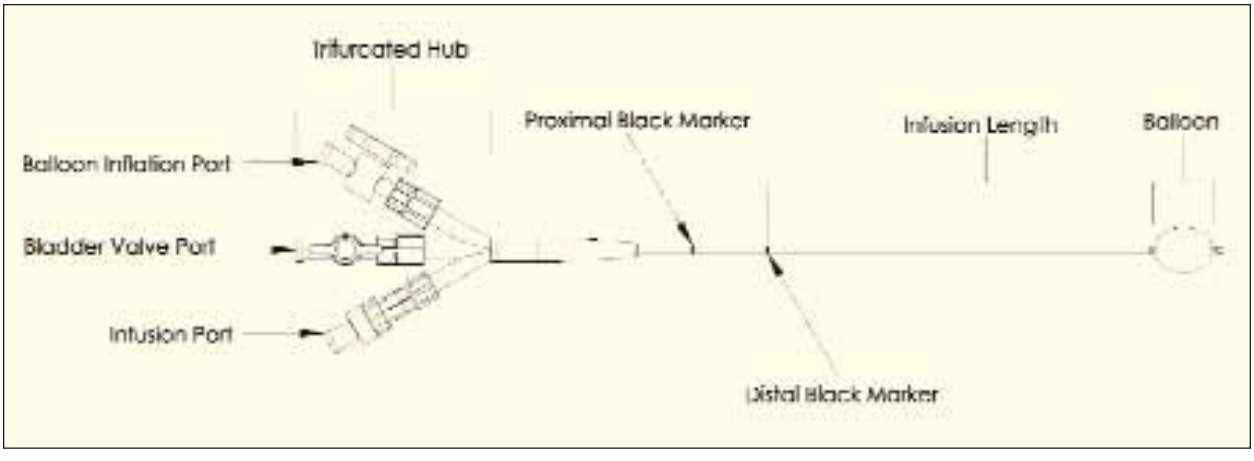

Figure 1. An endovenous catheter with distal balloon occlusion at the saphenofemoral junction.

the GSV using liquid sclerosant delivered percutaneously via syringe and needle will fail in more than half of the cases at 1 year. Methods to optimize the effectiveness of saphenous chemical ablation are under investigation.

> "Foam is believed by many investigators to be more potent than liquid STS of an equal concentration."

The sclerotherapy community is currently focused on two methods for enhancing STS: one method changes the biologic behavior of the drug, and the other alters the drug delivery system. Schneider and Fischer[1] showed that endothelial damage is concentration-dependent and occurs immediately after injection, with resulting rapid thrombus formation leading to vascular sclerosis. However, STS availability is limited to a concentration of 3%. Although we cannot use higher concentrations of STS to increase its effectiveness, we can alter its biologic behavior. Because STS is a detergent, it can be mixed with air to produce a soapy substance known as foam. Foam has tensioactive properties and can displace blood, thereby rendering it less vulnerable to dilution, and hence, it can more effectively and evenly destroy venous endothelial cells. Foam is believed by many investigators to be more potent than liquid STS of an equal concentration. Importantly, 3% STS foam has not yielded 100% GSV closure when injected with a standard needle and syringe; therefore, catheters that can enhance the interaction of the drug to the vein wall are under investigation.

OUR EXPERIENCE

At Miami Vein Center, we have worked with two catheter systems, each quite different in design, that enhance drug interaction with venous endothelium. At the 2006 American Venous Forum, we presented results of 75 saphenous veins treated with an endovenous catheter (Figure 1) with an occlusive balloon at the saphenofemoral junction (VeinRx Inc., Miami, FL). The idea was to isolate a column of 3% STS foamed sclerosant at the desired target site with a controlled dwell time of 4 minutes. The amount of drug delivered by the catheter was calculated based on vein volume of the target saphenous vein.[2] At 6-month follow-up, the primary closure rate was 87%, and the primary assisted closure rate was 96%. Three limbs (4%) were treated for asymptomatic deep venous thrombosis. Interestingly, in our series, thrombus formed only at sites of decreased flow in duplicated femoral veins. In all three cases of DVT, the foam was forced into the femoral vein, via a thigh perforator from the GSV, because the balloon blocked the outflow to the common femoral vein.[3] Also of interest in this trial was the difference that drug quality played in the role of effective ablation. A pharmaceutical-grade drug was profoundly more effective than a drug prepared by a compounding pharmacy.[4] In the compounded STS group, 45.7% of veins demonstrated segments of incomplete ablation at some time during follow-up. In the pharmaceutical-grade STS group, SIAs were observed in only 12.5% of veins. This difference was statistically significant (P=.02).

Although foam sclerotherapy is used universally and has become standard of care, foamed sclerosants can embolize to the arterial side via patent foramen ovale. Only one permanent adverse event from paradoxical embolization of foam has been published,[5] however, several transient neurological events have been reported anecdotally, and therefore, foam remains controversial.

The second catheter device (Figure 2), presented at the 2008 American Venous Forum, attempts to maxi-

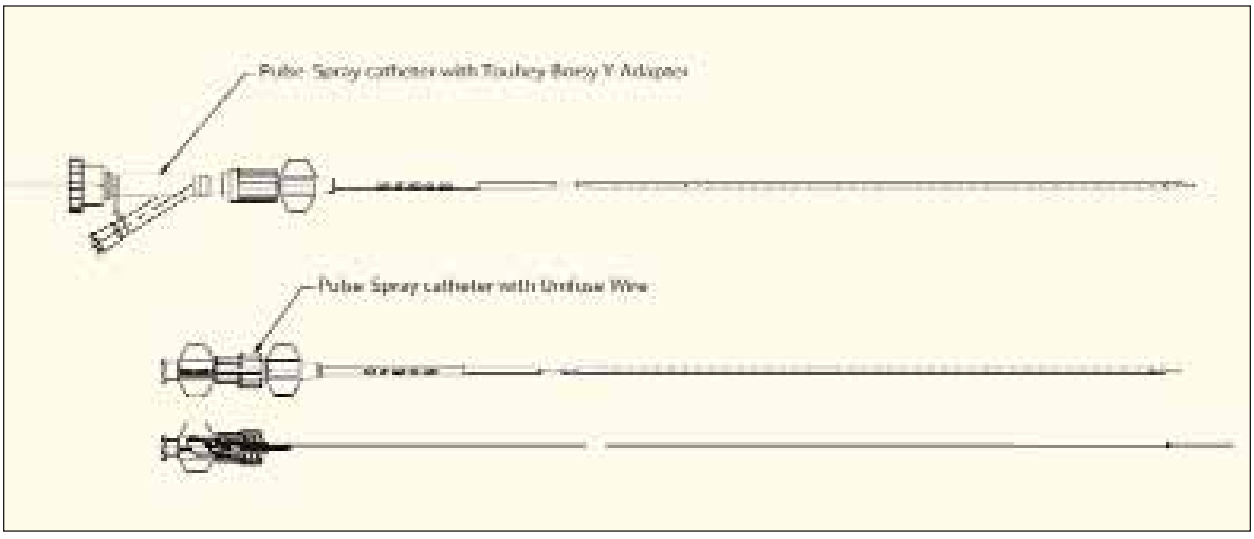

Figure 2. Diagram of a pulse-spray sclerotherapy catheter.

mize effectiveness of 3% liquid STS sclerosant by delivery under pressure, in a pulsed fashion (AngioDynamics, Inc., Queensbury, NY), to the GSV endoluminally. In a pilot study of 10 limbs followed for 1 year, we reported 80% primary occlusion.[6] Sixty percent of treated veins demonstrated SIAs at some point during the 1-year follow-up. All treated GSVs were limited to a size of <10 mm in diameter. This catheter does not occlude the saphenofemoral junction, and one thrombus extension into the common femoral vein was observed postprocedure. The thrombus extension resolved spontaneously without anticoagulation.

> "Although we commonly see segments of incomplete ablation in follow-up after CDS, these areas are easily closed with needle injection of additional sclerosant. . ."

PROS AND CONS OF CDS

Catheter-directed sclerotherapy (CDS) is attractive because it requires no power source. Lasers and radiofrequency generators cost about $25,000, in addition to the disposables required per case. CDS requires no delivery of time-consuming and often uncomfortable perivenous anesthesia to the extremity. CDS also offers more control of the treatment than sclerotherapy with a syringe and needle (ie, drug interaction with the vein wall is enhanced). Although we commonly see segments of incomplete ablation in follow-up after CDS, these areas are easily closed with needle injection of additional sclerosant to the affected area (assisted closure). On balance, sclerotherapy still has a cosmetic connotation and is not reimbursed by many third-party payers. Additionally, primary occlusion rates are lower than with thermal ablation of the GSV, and thrombus identified in the deep system has been seen more frequently in our experience with CDS than when compared to thermal ablation. CDS efficacy is also limited by vein size, and, importantly, the aforementioned catheters are not yet commercially available. ■

José I. Almeida, MD, FACS, RVT, is Founder, Miami Vein Center, and Voluntary Assistant Professor of Surgery at the University of Miami Miller School of Medicine in Miami, Florida. He has disclosed that he receives grant/research funding from VeinRx and AngioDynamics. Dr. Almeida may be reached at jalmeida@miamiveincenter.com.

Jeffrey K. Raines, PhD, RVT, is Director of Research, Miami Vein Center, and Professor Emeritus of Surgery at the University of Miami Miller School of Medicine in Miami, Florida. He has disclosed that he receives grant/research funding from VeinRx and AngioDynamics. Dr. Raines may be reached at drjraines@yahoo.com.

1. Schneider W, Fischer H. Fixierung and bindegewebige organization artefizieller thrombin bei der varizenuerodung. Dtsch Med Wochenschr. 1964;89:2410.
2. Raines JK, Garcia de Quevedo W, Jahrmarkt S, et al. Abbreviated method of determining vein volume in balloon-controlled vein ablation. Phlebology. 2007;22:40–44.
3. Almeida JI, Raines JK. Comparison of thermal and chemical saphenous endoablation. Poster presented at: American Venous Forum 18th Annual Meeting; February 2006; Miami.
4. Almeida JI, Raines JK. FDA approved Sotradecol versus compounded STS for venous sclerotherapy. Dermatol Surg. 2007;33:1037-1044.
5. Forlee MV, Grouden M, Moore DJ, et al. Stroke after varicose vein foam injection sclerotherapy. J Vasc Surg. 2006;43:162-164.
6. Almeida JI, Raines JK. Pulse spray sclerotherapy: a pilot study. Poster presented at: American Venous Forum 20th Annual Meeting; February 2008; Charleston, South Carolina.