Foam Therapy for the Superficial Venous Pathology - 2016

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Ariel D. Soffer, M.D, F.A.C.C
• Fellow of the American College of Cardiology since 1998 with cardiovascular fellowship training at Cedars-Sinai, Beverly Hills, UCLA.

• Professor at Florida International University School of Medicine. Published the first article on the importance of venous insufficiency in the cardiovascular practice, Endovascular Today, 2007 & 2011.

• Founder of Soffer Vein & Vascular with 8 offices in South Florida.

• Founder of AppwoRx™ - Patented clinical photography applications used heavily in the venous space.
RELEVANT DISCLOSURES

- PRINCIPAL INVESTIGATOR FOR BTG’S VARISOLVE TRIAL
Medically Significant Venous Incompetence

Most patients seek treatment to relieve symptoms rather than cosmetic concerns.
What is the need?

- Microfoam Chemical Ablation Therapy is a comprehensive tumescentless treatment for:
  - GSV, Accessory Saphenous Veins and Visible Varicosities
  - Tortuous veins (above and below the knee)

- Minimally invasive, safe and effective treatment for incompetence of GSV system

- Clinically meaningful improvement in symptoms and appearance ABOVE AND BELOW THE KNEE

- Designed to
  - Reduce number of treatment modalities
  - Reduce number of treatment sessions
  - Improve patient experience (no tumescent anesthesia)
  - Reduce the risk to anatomical structures associated with endothermal ablation
PEM (Polidocinol Endovenous Microfoam) Attributes

- FDA approved as first line treatment for GSV Incompetence
  - Not adjunctive or subsequent to surgical ligation or thermal ablation
  - Unlike thermal ablation, does not require tumescent anesthesia
- PEM fills an unmet need related to limitations in currently available treatment options
  - Comprehensive treatment above & below the knee
- For medically significant disease; NOT just cosmetic
- Endovascular procedure performed under ultrasound guidance by specially trained physicians and staff
- Two pivotal, blinded, multicenter, randomized controlled studies proved safety and efficacy with statistical significance

Before

After
Microfoam Chemical Ablation Therapy with PEM

Catheter based endovascular procedure performed under ultrasound guidance
- Physician performed 18 step procedure
- Procedure requires at least 2 professionals

FDA agreed upon physician training Risk Management Plan (RMP)
- Physician prerequisite of ≥ 100 vein procedures within past two years & attestation of experience
- Must complete four online training modules with documented proficiency (exam)
- Must successfully complete training program to gain access to product
Polidocanol injectable foam- 1% Properties

- FDA approved
- Manufactured drug/device under
- Low density, sterile, cohesive microfoam has a mechanism of action which
  o Displaces blood from vein to be treated
  o Chemically ablates endothelial layer

- Proprietary soluble gas mixture
  o Low Nitrogen Content <0.8%
  o 65% O₂ / 35% CO₂
  o 1:7 Liquid to gas ratio by volume

- Small consistent bubble size
  o Median bubble size <100 μm
  o No bubble >500 μm

Physician compounded foam (PCF)
- Reported cases of patients with pulmonary embolism and neurologic events (including stroke) following treatment with PCF made with ambient air
- PCF is highly variable in concentration, gas composition, bubble size, stability, sterility, and drug used
Biomimetic Model

Degradation Rate or Dwell Time
– Establish a foam plug
– Observe the decay
– Linear with time
– Represents stability
– Speed of degradation inversely proportional to the contact time expressed as dwell time
– Slower degradation rate (DR) or longer dwell time, results in longer endothelial contact time
Biomimetic model

(a) PEM has the longest dwell time compared to any PCFs, including foams made using room air (RA)
(b) The same result was obtained at different liquid to gas ratios (1:4 and 1:7 liquid:gas)
• 100% CO2 foams were least stable in all tests performed
and different O2:CO2 mixtures had intermediate performance
Product Description

- Polidocanol injectable foam- 1% is a drug/device combination that generates injectable foam for intravenous injection using ultrasound guidance

- Available injectable foam delivers a 1% polidocanol solution. Each mL of injectable foam contains 1.3 mg of polidocanol

- One canister of PEM yields 45 mL of usable foam for injection when following instructions for use
  - Use up to 5 mL per injection and no more than 15 mL per session

- Once activated, the canister of must be used within seven (7) days

- Manufactured in accordance with FDA Current Good Manufacturing Practices (cGMPs)

- Local anesthetic may be administered prior to cannula insertion, but neither tumescent anesthesia nor patient sedation is required
Administration Pack

Patient ancillary components:
- Three 10 mL silicone-free syringes
- A 20-inch manometer tube
- Two compression pads
Safety Information

- The use of PEM is contraindicated in patients with known allergy to polidocanol and those with acute thromboembolic disease.

- Severe allergic reactions have been reported following administration of liquid polidocanol, including anaphylactic reactions, some of them fatal. Observe patients for at least 10 minutes following injection and be prepared to treat anaphylaxis appropriately.

- Intra-arterial injection or extravasation of polidocanol can cause severe necrosis, ischemia or gangrene. Patients with underlying arterial disease may be at increased risk for tissue ischemia. If intra-arterial injection of polidocanol occurs, consult a vascular surgeon immediately.

- PEM can cause venous thrombosis. Follow administration instructions closely and monitor for signs of venous thrombosis after treatment. Patients with reduced mobility, history of deep vein thrombosis or pulmonary embolism, or recent (within 3 months) major surgery, prolonged hospitalization, or pregnancy are at increased risk for developing thrombosis.

- The most common adverse events observed were pain/discomfort in extremity, retained coagulum, injection site hematoma or pain, common femoral vein thrombus extension, superficial thrombophlebitis, and deep vein thrombosis.

- Physicians administering PEM must be experienced with venous procedures, possess a detailed working knowledge of the use of the duplex ultrasound in venous disease and be trained in the administration of Varithena®.
Summary

- Foams are not the same, impossible to compare clinical results unless characteristics are known and reproducible
- Air foams have good performance but have associated risks, with persistent bubbles in the circulation –
- Small bubbles and narrow bubble distribution, with slow drainage and separation times, improves foam performance by enhancing stability
Combination Therapy - Laser Side

- Facts
  - Endothermal Ablation (both Laser and RF) had reproducibly shown greater than 95% of the time, long term closure of the intended GSV in the recent literature.
  - Perforators are the most common cause of either failure of primary ablation or recalcitrant symptoms.
  - Tumescence, although minimally uncomfortable, remains one of the most uncomfortable portion of the modern endovenous thermal ablative procedure.
Combination Therapy: Foam Side

• Facts

• Historical foam data as well as recently presented data suggests that a limitation of sclerosant/gas treatment to truncal vessels might exhibit a long term re-opening rate that is somewhat greater than thermal ablation.

• Historical foam data suggested that deep vein thrombosis might have been seen at a somewhat higher rate. Current data suggests that with adequate junctional compression (along with other reasons) this DVT concern is less of an issue.

• No tumescence is typically used in foam treatment to truncal, branch or perforator vessels. However, foam seems to travel to many of these intended targets with relative frequency and ease of administration.
Combination Therapy: Hypothesis

- By combining the two techniques we may maximize the intended benefits while minimizing the unwanted side effects.
Adequate, safe closure of the truncal Great and Small Saphenous Vein as well as insufficient tributaries.

Additionally, as the proximal thermal procedure is done first it might yield the reduction in DVT’s due to immediate spasm of the truncal vessel and less likelihood of significant foam reaching the deep system.

Reduce the amount of tumescence delivered, thus reducing overall procedural and post procedural pain.

Reach and disrupt more residual pathologic venous vessels, thus more efficiently and completely treating patients venous insufficiency.
Soffer Vein Institute Experience

- Retrospective review of 2176 patients seen between 2012-2013 (24 months)
- Chart review (via our EMR, E-ClinicalwoRx)
- NOT meant to be a proper scientific review presentation or publication. Only meant to give further support to our hypothesis that might inspire further properly designed research.
Soffer Vein Institute Experience

- Pre-op - Out of 2176 patients
  - 78% were female, 22% male
  - Average age was 45.7 years old
  - Average size of the GSV was 5.5 cm with over 3 seconds of reflux
  - Average size of the SSV was 4.1 cm with over 3 seconds of reflux
  - Average objective score (VCSS, CEAP, CIVIQ) was improved by greater than 33%
Soffer Vein Institute Experience

- Procedural experience
  - Average thermal burn length: 10.7 cm
  - Average thermal energy: 667 J
  - Delivered 73% with 1470nm and 27% with 940nm
  - Tumescence delivered generally under 50 cc of NS/1% lidocaine with Bicarb using power injector
  - Average of 6 cc of 1% polidocinol with 2:1 dilution of CO2 after laser ablations
Soffer Vein Institute Experience

• Post procedural results (at 1 month).
  - 98% occlusion rate of Greater Saphenous above the knee
  - 95% occlusion rate of Greater Saphenous below the knee
  - 99% occlusion rate of Lesser saphenous
  - Pain Score was improved by greater than 33%
When compared to either Thermal Ablation alone or Ultrasound Guided Foam Sclerotherapy alone;

- Closure rate was significantly higher than foam alone, and slightly higher than thermal ablation alone.
- Discomfort (Pain Score) was reduced when measured at 1 week. At the 1 month interval Pain Score was not materially different.
- In all cases of foam usage a small but consistent percentage of patients required a Retained Coagulum Release (RCR) procedure. This routinely improved the Pain Score in these patients immediately.
Patients experienced a significantly higher level of overall satisfaction of procedure at the 3 and 6 month interval with the combination procedure.
Based on our non-scientific, retrospective review of one clinic’s informal data, we have concluded that our hypothesis of combination therapy with thermal ablation and foam is supported and we would hope to proceed with a formal, multi-center, prospective analysis in the future.
The issue of *Retained Coagulum*

- TREATMENT METHODOLOGY FOR SCLEROSED VEINS- OUR SINGLE-CENTER TECHNIQUE AND OBSERVATIONS
  - Global Vascular Digest, June, 2016
  - Ariel Soffer, MD, FACC, Swapna Upparlapalli, MD, Cecelia Pernas, ARNP, Maryanne Martinez, PA-C
Coagulum Identification
Coagulum Release
Summary

- Foam is here to stay and often a necessary part of complete venous treatment.
- Both commercially available and physician compounded capacity exists.
- Useful as stand alone procedure or in combination with thermal ablation.
- Retained Coagulum in experienced hands is easily identified and treated with high overall patient satisfaction rates.
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