Long-term vein diameter reduction by perivenous hyaluronan instead of tumescence for endovenous procedures

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• counselor to Venartis® Inc.

• no funds received for travel or presentation
Varices: 90 - 95 Vol-% = blood

1. Obtain empty vein (positioning, aspiration)
2. Destroy endothelium (thermal, chemical)
3. Option: destroy parts of media
4. Prevent re-entry of blood for 4 – 8 weeks

Basics of endovenous therapy

(film bandage)

“Standing magnetic resonance imaging ... showed... stockings with a pressure of 22 mmHg were able to reduce the calibre of deep calf veins, but not of superficial varices. These were compressed only by bandages exerting pressures between 51 and 83 mmHg. To empty a varicose vein after venous ablation much higher pressures are required.”

Dear friends, it´s just bandage-enhanced compression by muscle activation ;)

Compression: Not effective for epifascial veins
Compression strategies depend on diameter & position to skin level


Thermal closure methods are currently replacing surgery in the treatment of saphenous vein insufficiency. However, the majority of cases will experience discomfort or pain along the treated area. Why?

Any thermal/chemical vein ablation is based on “intended local inflammation”, depending on the degree of wall destruction and volume of blood.
Saline-based tumescent vein shaping is not suitable for optimal results, as the target vein is just compressed for 6 – 48 hours.

N. Devereux, A.L. Recke, L. Westermann, A. Recke, B. Kahle: Catheter-directed foam sclerotherapy of great saphenous veins in combination with pre-treatment reduction of the diameter employing the principals of perivenous tumescent local anesthesia.

However, cross-linked hyaluronan (shown for heat-degraded Macrolane, Venartis/Galderma) was effective to prevent any symptoms, residuals or discolorations.

After basic experience with hyaluronan gels (*UIP poster prize 2013, ACP platinum poster award 2015*) we now evaluated a new **monophasic sodium hyaluronate hydrogel of lower viscosity** for saphenous veins to provide initial and long-term vein lumen reductions.

The average 70 kg (154 lb) person has roughly 15 grams of hyaluronan in the body, one-third of which is turned over (degraded and synthesized) every day.
Patients

- 20 patients (13 f, 7 m, 41 – 72 yrs.)
- insufficiency of the GSV including SFJ
- diameter D = 7.8 – 17.6 mm (mean 9.7)
- target segment* length 20 – 35 cm
- *vein diameter constant (+/- 10%) excl. valves
- distance d to skin > 10 mm
### Vein diameter in target segments

<table>
<thead>
<tr>
<th></th>
<th>TA tumescent anesthesia</th>
<th>HM hyaluronan, monophasic</th>
<th>H hyaluronan, native</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>supine:</strong></td>
<td>7.1 – 8.2 mm</td>
<td>7.3 – 8.3 mm</td>
<td>7.2 – 8.2 mm</td>
</tr>
<tr>
<td><strong>vertical:</strong></td>
<td>8.1 – 9.3 mm</td>
<td>8.1 – 9.0 mm</td>
<td>7.9 – 8.9 mm</td>
</tr>
</tbody>
</table>
Methods

Coaxial perivenous injection, cannula 120 mm, 21G

A: novel monophasic hyaluronan gel of low viscosity \( (\eta = 10^3-10^4 \text{ mPa} \cdot \text{S}) \) injected after sclerofoam deployment

B) standard tumescent fluid injected prior to laser but post sclerofoam

C) Some cases \((n = 5)\) native hyaluronan of same viscosity like A in a separate segment

Compression stocking class 2 for 2 weeks.
Clinical follow-up including ultrasound: After 1 d, 2 and 8 weeks.
Methods

Ragg JC et al. Novel Biomatrix Sclerofoam: Equal to or Better Than Thermo-Oclusion?
Journal of Vascular Surgery: Venous and Lymphatic Disorders 2017, 5(1); 147
Methods

Sequence: 1) Laser + TA, 2) sclerofoam, 3) TA or hyaluronan.

PhleboCath®

biomatrix sclerofoam
deployment of hyaluronic acid

cannula
vein lumen, foam (!)
vein wall
Minimal invasive procedure
“no touch“ - injection of hyaluronan

coaxial access, 12 o’clock position

hyaluronan proceeds tip
tumescent anesthesia versus monophasic hyaluronan
Results

Technical success (> 50% lumen reduction): 20/20

Complications: 0/20
<table>
<thead>
<tr>
<th></th>
<th>tumescent fluid</th>
<th>monophasic hyaluronan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lumen reduction</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at day 1</td>
<td>17 – 33% (22.5%)</td>
<td>52 – 75% (63.3%)</td>
</tr>
<tr>
<td>at end of week 2</td>
<td>11 – 27% (18.1%)</td>
<td>51 – 69% (60.2%)</td>
</tr>
<tr>
<td>at end of week 8</td>
<td>23 – 42% (34.5%)</td>
<td>58 – 81% (68.7%)</td>
</tr>
<tr>
<td>example</td>
<td>34.5%</td>
<td>68.7%</td>
</tr>
</tbody>
</table>
Vein diameter in target segments

TA tumescent anesthesia  HM hyaluronan, monophasic  H hyaluronan, native
Vein diameter reduction by saline vs. hyaluronan

10.8 mm vs. 4.8 mm
decrease of effective volume

tumescent fluid
monophasic hyaluronan type HM
## Results at end of week 8

<table>
<thead>
<tr>
<th></th>
<th>Tumescent Fluid</th>
<th>Monophasic Hyaluronan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Segment-related findings/symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>visible hematoma</td>
<td>16/20 (80%)</td>
<td>1/20 (5%)</td>
</tr>
<tr>
<td>painful inflammation</td>
<td>15/20 (75%)</td>
<td>0</td>
</tr>
<tr>
<td>mini-thrombendarpirations</td>
<td>5/20 (25%)</td>
<td>0</td>
</tr>
<tr>
<td>oral analgetics</td>
<td>7/20 (34.5%)</td>
<td>0</td>
</tr>
<tr>
<td>discolorations</td>
<td>8/20 (40%)</td>
<td>0</td>
</tr>
<tr>
<td>Discomfort not related to a particular segment</td>
<td>4/20</td>
<td></td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumescent solution</td>
<td>2.2 – 3.2 ml/cm</td>
<td>2.5 ml/cm</td>
</tr>
<tr>
<td>Native hyaluronan</td>
<td>0.4 – 0.7 ml/cm</td>
<td>0.55 ml/cm</td>
</tr>
<tr>
<td>Monophasic hyaluronan</td>
<td>0.3 – 0.42 ml/cm</td>
<td>0.38 ml/cm</td>
</tr>
</tbody>
</table>

![Saline 2 ml/cm](image1.png)
![precise](image2.png)
Perivenous compression by hyaluronan

Targets: Large veins, deep below skin level

T > 0.5 – 2 x d

T > 0.5 – 2 x d

6.3 mm

pre

vein

3.7 mm

post

vein

0.5 ml HA/cm

skin

vein

hyaluronan

vein compressed
Conclusions

Initial and long-term vein lumen reduction for endovenous methods, providing asymptomatic postprocedural periods, can not be obtained with saline tumescent solutions, but easy and safe with monophasic sodium hyaluronate hydrogel of low viscosity.

At this stage, the method is recommendable for large and straight veins (GSV, SSV) for sclerofoam treatment, but also (with anesthetic added) for all kinds of thermo-occlusion.
Money and honour for your ideas!

www.venartis.org:  1.000 USD Innovation Prize 2018
Apply for travel stipend!

Innovation Session!
Thank you very much for your attention!

Work Group Dr. Ragg     www.venartis.org

“To improve everything in the field of phlebology”