Effects of Mesoglycan Treatment in the Prevention of Venous Thrombosis after Superficial Vein Surgery

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Abstract

Aim: To demonstrate the effectiveness of a two months treatment with Mesoglycan after superficial vein surgery in the prevention of superficial vein thrombosis (SVT) and deep vein thrombosis (DVT).

Methods: From January 2014 to April 2015, all patients underwent superficial vein surgery were enrolled and analyzed. Clinical examination through CEAP class identification, Venous Clinical Severity Score (VCSS), and color Duplex ultrasound scanning (CDUS) were performed before treatment, two days post-operatively and at the 2 month follow-up time. Prophylaxis with heparin was given for 1 week after treatment. Mesoglycan 50 mg tablet BID was continued for 2 months. Primary endpoint was Mesoglycan side effect rate. Secondary endpoints were postoperative DVT and/or SVT, endovenous heat induced thrombosis (EHIT) after laser treatment and recanalization/recurrence rate.

Results: 381 venous interventions in 334 consecutive patients were performed. After exclusion of 18 patients, 363 veins were treated in 361 enrolled patients. Female were 242 (76.6%), mean age was 52 years and mean BMI was 25.2 kg/m2. Sixty patients had a history of venous thrombosis (18.9%); 17 had thrombophilia (5.3%). CEAP classification was C2 130 (36.1%), C3 138 (38.2%), C4 77 (21.3%), C5 7 (1.9%) and C6 9 (2.5%) patients. Surgical techniques performed were endovenous laser ablation, sclerotherapy, crossectomy, perforator ligation and/or phlebectomies. All patients enrolled complete the Mesoglycan 2-months therapy. Mesoglycan side effects were referred in 4 patients (1.2%).

At the 2 days FU, CDUS evidenced pathological conditions in 3 cases (0.8%): 1 contralateral SVT, 1 EHIT of the great saphenous vein, and 1 ipsilateral SVT associated to a perforator vein thrombosis. No deep venous thrombosis were documented at the 2 months FU.

Conclusion: Mesoglycan 50 mg tablet BID is a safe and well tolerated therapy after superficial venous ablation procedures with very low thrombotic complications rate at the 2 month postoperative follow-up time.

Keywords: Mesoglycan; Venous thromboembolism; Vein surgery; Endovenous laser ablation

Introduction

Venous thrombosis and thromboembolism are still not so rare as complication after superficial vein surgery, even if correctly performed (5.3-16% of patients) [1-10]. Postoperative superficial vein thrombosis (SVT) and deep vein thrombosis (DVT) can affect all venous treatments. Furthermore, thermal techniques as Endovenous Laser Ablation (EVLA) and Endovenous Radiofrequency Ablation (EVRA) are related to Endovenous Heat Induced Thrombosis (EHIT), in which the thrombus is extended from the superficial venous system into the deep venous system close to the site of the recent ablation. The incidence of this complication is referred to be 0.2-8% [9,11,12].

Mesoglycan is a pharmacological treatment approved for Chronic Venous Disease (CVD). It is a sulphated polysaccharide compound designed for the treatment of vascular disease with an associated thrombotic risk. Mesoglycan is extracted from porcine intestinal mucosa and it is composed of heparan sulphate (47.5%), dermatan sulphate (35.5%), electropheretically slow-moving heparin (8.5%) and chondroitin sulphate (8.5%).

Heparan and dermatan sulphate are thrombin inhibitors acting through complementary antithrombin III and heparin cofactor II pathways [13,14]. Mesoglycan has been documented to inhibit neutrophil adhesion and activation, to decrease capillary permeability, to enhance systemic fibrinolysis, and to prevent venous thrombus formation [15]. In medical literature, no data are available about the utility of postoperative Mesoglycan treatment in the prevention of venous thrombosis and thromboembolism after intervention on superficial venous system for CVD.
The aim of this study was to demonstrate the safe and effectiveness of a 2 months therapy with Mesoglycan after superficial venous interventions.

Methods

Patients with Clinical, Etiologic, Anatomic, and Pathophysiologic (CEAP) C class 2 or higher, treated for CVD, from January 2014 to April 2015, were examined.

Accurate clinical examination, Venous Clinical Severity Score (VCSS), and color Duplex ultrasound (CDUS) scan analysis of the lower extremity veins were performed prior to treatment, at 2-day and at 2-month follow-up time.

Vein incompetence was assessed with reflux in response to manual calf compression or Valsalva maneuver with the patient standing, and reflux was defined as evidence of reverse flow >500 ms in a vein segment. Patients were thoroughly informed about surgical procedure, operation risks, recurrence. All patients signed a written informed consent form before the procedure.

In case of EVLA, the target vein was cannulated percutaneously just below the knee under ultrasound guidance. A 5F introducer sheath was positioned and a J guide wire was inserted into the treated vein. The correct position of the fiber tip was confirmed by ultrasound imaging. The laser wavelength was 1470 nm diode. Laser energy was always delivered with a pull-back rate of about 60 J/cm under ultrasound guidance to make the procedure safe and assist the vein obliteration. The immediate occlusion of the treated vein was confirmed by ultrasound imaging.

Crossectomy was performed with a small incision at the groin under ultrasound guidance. Ultrasound Guided Foam Sclerotherapy (UGFS) was obtained with the use of Lauromacrogol (Atossisclerol) at the percentage of 0.5%, 1%, 3% according to the diameter of the treated vessels. Patients were asked about postoperative complications, Mesoglycan compliance and adverse effects.

CDUS was performed to detect SVT/DVT, recanalization rate after EVLA and UGFS, hematoma, residual varicose disease and reflux at the treated areas. Thrombosis was detected by the non-compressibility of the vein and filling defects on color mode.

Preoperative, intraoperative and postoperative data were collected prospectively by using a custom made database.

Results

During study period, 381 venous interventions in 334 consecutive patients were performed. Eighteen treatments in 18 patients were excluded from the study: 4 patients because of a co-diagnosis of angiomylipoma, and 14 because of an incomplete 2-month follow-up.

After this exclusion, 316 patients were enrolled, 242 females (76.6%) and 74 males (23.4%). Mean age was 52 years (range 16-86), mean BMI was 25.2 kg/m² (range 17.6-38.4). Seventy-two patients (22.7%) were positive for cardiovascular disease. Sixty patients (18.9%) had a positive history of venous thrombosis: 50 SVT (42 ipsilateral, 6 contralateral, and 2 bilateral); 10 DVT (8 ipsilateral and 2 contralateral in 2 cases complicated by pulmonary embolism). Seventeen patients had diagnosis of thrombophilia (3.5%).

Clinical preoperative evaluation also included stratification of CVD according to the CEAP classification and VCSS Score. Before surgery, the mean VCSS was 5.9 (range 2-14); CEAP classification result is reported in Table 1.

<table>
<thead>
<tr>
<th>CEAP clinical classification</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>C2</td>
<td>130 (36.1%)</td>
</tr>
<tr>
<td>C3</td>
<td>138 (38.2%)</td>
</tr>
<tr>
<td>C4</td>
<td>77 (21.3%)</td>
</tr>
<tr>
<td>C5</td>
<td>7 (1.9%)</td>
</tr>
<tr>
<td>C6</td>
<td>9 (2.5%)</td>
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Table 1: CEAP clinical class.

In summary, 233 great saphenous veins (GSV, 64.2%), 19 anterior accessory saphenous veins (AASV, 5.2%), 39 small saphenous veins (SSV, 10.8%), 3 Giamonini’s veins (GV, 0.8%), 10 perforators veins (PV, 2.8%), 27 tributaries (7.4%), and 32 recurrences varicose veins (RVv, 8.8%) were treated. Surgical techniques chosen are reported in Table 2.

<table>
<thead>
<tr>
<th>Surgical technique</th>
<th>N (%)</th>
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<tr>
<td>EVLA</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>EVLA+phlebectomies</td>
<td>231 (63.9%)</td>
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</table>
No complications or other adverse reactions occurred intraoperatively. Immediate occlusion of the treated veins after EVLA and UGFS were confirmed in all limbs by intraoperative CDUS. The mean time for patient discharge from the hospital was 3 hours (range 3-5 hours).

After 2 days, ecchymosis were documented in 52 operations (14.4%). Hematoma occurred in 6 cases (1.6%) but no one required any invasive treatment for its drainage. No bleeding, skin burns or paresthesia were occurred. LMWH therapy was well tolerated by the entire population. No recanalization was documented.

Venous thrombosis occurred in 3 cases (0.8%): 1 contralateral SVT, 1 EHIT, and 1 ipsilateral SVT associated to a perforator vein thrombosis. Detailed characteristic of patients affected by postoperative thrombosis are reported in Table 3.

### Table 3: Details regarding patients with postoperative thrombosis.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>BMI</th>
<th>CEAP “C”</th>
<th>VCSS</th>
<th>Intervention</th>
<th>Complication</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>45</td>
<td>38.4</td>
<td>3s</td>
<td>7</td>
<td>EVLA</td>
<td>Contralateral SVT</td>
<td>LMWH+painkillers</td>
<td>Resolved at 30 days</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>45</td>
<td>39.4</td>
<td>3s</td>
<td>9</td>
<td>EVLA+phlebectomies</td>
<td>EHIT type II</td>
<td>LMWH</td>
<td>Resolved at 30 days</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>65</td>
<td>26.1</td>
<td>4s</td>
<td>11</td>
<td>Perforator ligation</td>
<td>Perforator thrombosis</td>
<td>LMWH</td>
<td>Resolved at 30 days</td>
</tr>
</tbody>
</table>

Abbreviations: EVLA: Endovenous Laser Ablation; SVT: Superficial Vein Thrombosis; EHIT: Endovenous Heat Induced Thrombosis; LMWH: Low Molecular Weight Heparin.

SVT and DVT remain possible complications in the postoperative period after superficial vein interventions, even if it is correctly performed. Currently, international guidelines recommend a LMWH thromboprophylaxis only with patients with an increased risk of venous thrombosis: patients with thrombophilia, with a history of SVT.
or DVT, and in obese patients [10,17,18]. Based on our experience, we recommend the use of a post-operative thromboprophylaxis with LMWH in all cases.

SVT, DVT and pulmonary embolism are rare but occasionally serious complication [4,8,10,19]. The risk is higher with endovascular treatment, due to EHIT. Even if the EHIT mechanism is not fully understood, factors which may increase its developing include elderly population, undiagnosed hypercoagulable states, severity of CVD [9,11,12] and in treated veins with a diameter of >8 mm [20,21]. For these patients a preventive dose of LMWH before or at the beginning of surgery was suggested but there are only few data about the effectiveness of this procedure [12]. Our case of EHIT was degree 2 according to Kabnick classification [22]. According to the literature, in our patients, EHIT happened in an obese patient with a mean diameter of the GSV of 12 mm and severe CVD (CEAP class C4).

In our experience, all the surgical procedures (EVLA, EVRA, UGFS, and even crossectomy) are performed under CDUS guidance: this allows a complete examination that helps in the control of intra-operative and post-operative complications. We had a low rate of postoperative ipsilateral SVT, 0.6%; this can be related to the fact that during surgery our policy is to remove all the superficial varicose veins in association to the treatment of the saphenous reflux. Before surgery, all the varicose veins that are present on the treated limb are precisely evidenced with the use of CDUS and laser trans-illuminator, and then are completely removed by phlebectomies; this may justify the correct pathway that leads to reduction of the rate of superficial vein thrombosis on residual varicose veins.

Mesoglycan is reported to have several favorable actions on the fibrinolytic system, on micro rheological and macro rheological parameters [13,14]. Due to these properties, the use of Mesoglycan is approved for the treatment of chronic venous ulcers resulting in faster and more frequent healing [23], in the secondary prevention of long term sequelae after DVT [24], and in patients with CVD [25]. It has been demonstrated that Mesoglycan is effective for the prevention of postoperative venous thromboembolism in patients with cancer [26], but there are no data about its use in the prevention of SVT and DVT. In our patients, all the SVT and DVT were diagnosed at the 2 days control, during LMWH therapy and before starting Mesoglycan therapy. At the 2 month follow-up control, after 2 month of Mesoglycan therapy, no new case of vein thrombosis was detected.

Our study was limited by the lack of a control group. However, it showed a very low thrombotic rate (0.8%) compared to the other cases presented in literature: furthermore, all cases resolved in short period.

**Conclusion**

We present a wide range of venous treatments with a low postoperative complication rate. Mesoglycan 50 mg BID for two months seem to be a valid option during the postoperative period, due to low adverse effect rate, low incidence of thrombotic complications and safe profile.

**Conflict of Interest**

None. Publication costs was covered by IFI – Italian Phlebological Institute.


