Does Post-sclerotherapy Thrombus Removal Reduce Pigmentation? A Randomized Trial*

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Since the introduction of liquid sclerotherapy in the late 1920s, this important modality for the treatment of varicose veins has undergone a number of important modifications related to technique, post-sclerotherapy compression, and the use of foam sclerotherapy using different types of detergent sclerosing agents. At the same time, the number of sclerosing agents has increased to the point that, at present, there are safe and effective sclerosants available throughout the world. As with any therapeutic method, it has its desirable and undesirable effects. Pigmentation of the injected areas has been reported in nearly 30% of the patients treated with sodium tetradecyl sulfate (Sotradecol [STD]).[1-3] Pigmentation disappears spontaneously between 6 to 24 months in 80% of the patients. However, in some patients, a brownish discoloration persists and is the main reason for patient complaints. Different factors contribute to the production of post-sclerotherapy pigmentation. Migration of melanin pigment to the skin is a definite factor.[4,5] Another factor is the release of erythrocytes into the epidermis secondary to post-sclerotherapy inflammation of the venous endothelium.[6-8]

We have hypothesized that, to a great extent, pigmentation is the result of the hemosiderin degradation originated in the thrombus that forms after the acute chemical inflammatory reaction produced by the sclerosing agent. We also consider that the early removal of the thrombus through small stab incisions may decrease or prevent the incidence of post-sclerotherapy pigmentation. Several authors have reported the use of thrombectomy to prevent pigmentation. However, as far as we know, the observations have been anecdotal and not documented.[9-11]

Materials and Methods

A multicenter, randomized protocol was approved by the internal review board of the two research centers involved. Written consent was obtained from all patients. We enrolled a total of 101 patients with varicosities in the lower extremities, measuring 1 to 3 mm in diameter. Patients were divided into two groups. Group 1 consisted of 50 patients with veins 1 mm or less in diameter (spider veins); group II was composed of 51 patients with veins 3 mm or less in diameter.

Noneligible patients were those with valvular incompetence of the main saphenous veins as determined by duplex ultrasonography in the upright patient; those with very dark skin, which would make the assessment of pigmentation difficult; those with varices greater than 3 mm; and those who were pregnant, anticoagulated, or had severe allergy, generalized systemic disease, lower extremity arterial insufficiency as defined by ankle-brachial index < 0.7, or acute superficial venous thrombosis. Eligible patients were those older than 18 years and less than 65 years of age with varicose veins of the lower extremities.

Selection of Study Area

In each patient, an area of varicosities of the lower extremities that could be easily divided into two similar halves was selected. For future identification, the area was drawn on a special sheet and incorporated in the case report form. The two halves were identified as upper or lower and left or right, depending on their location in the extremity. In addition, tracings of varicosities were made on a transparent sheet to facilitate the exact localization of the selected areas after treatment. Fixed anatomic landmarks such as knee crease, moles, freckles, and other forms of identification were drawn on the transparent sheet to assist in recognition of the treated area. Using a computer-generated randomization schedule, one area was assigned to microthrombectomy and the other served as the control. With a standardized photographic technique, color photographs of the selected areas were obtained before and 16 weeks after the treatment.

Sclerotherapy Technique

A color photograph of the study area was obtained before initiating the sclerotherapy treatment. Varicosities in both sections of the study area were injected with STD at a concentration of 0.25% for telangiectasias and 0.50% for reticular veins. Thirty-gauge hypodermic needles were used for telangiectasias and 27-gauge for veins 3 mm or less. Appropriate sclerosing agent concentrations were prepared by the hospital pharmacy. The investigator was provided with a 1 mL syringe labeled with the STD concentration prescribed for the size of vein to be treated. The air-block technique in an empty vein was used. Entire study area was injected through several veno-punctures using no more than 0.5 mL at each site. The total amount of injected solution was not to exceed 3 mL. Immediately after treatment, the injected area was covered with 10 x10 cm sponges held in place with gauze bandages (Kerlix). The leg was then firmly wrapped from the toes to the knee or to the groin with a 15 cm elastic bandage. In subsequent visits, patients were given calf-length or thigh-length elastic stockings (Jobst 25 to 30 mm Hg). Compression was maintained continuously for 72 hours in telangiectasias and for 1 week in the larger veins.

Thrombectomy Technique

Despite the appropriate compression, in most patients a thrombus formed in the injected vein as a result of the endothelial injury. One to 3 weeks after treatment, microthrombectomy was performed while the thrombus was still soft and not yet organized. After tracing the study area on the transparent sheet, the assigned randomized half-area underwent microthrombectomy and the other half was left as the control. After skin asepsis, quick ministab incisions were made 3 to 5 mm apart along the entire length of the thrombosed vein using a sterile no. 65 Beaver blade or a microsurgical

knife. We avoided the no. 11 blade because incisions with this blade were painful and incision depth is more difficult to control. Incisions were 1 mm long along the thrombosed spider veins and 2 mm long in the case of larger veins. In the larger veins, incisions were made 5 to 10 mm apart. Efforts were made to incise only the anterior aspect of the vein wall and avoid through-and-through incision. Using a two-cotton-tipped swab or the sterile gloved fingers of the operator, the thrombus was gently extruded. This procedure produced minimal discomfort and was well tolerated without the need for local anesthesia. After thrombectomy, the area was cleansed and covered with sterile compression cushions, and elastic bandages were applied as before. Treatment of the selected area was completed in one or two sessions, 1 to 3 weeks apart. Microthrombectomy was performed at the end of the second treatment in patients in whom two microthrombectomy sessions were necessary. Using the technique described, the procedure took 10 to 15 minutes, including dressing the treated area and applying compression bandages.

Photographic Evaluation

Color photographs of the study area were obtained before and 16 weeks after treatment. An adhesive sticker with the patient's code number and the date of injection was visible in each photograph. The photographs were taken by the principal investigator or co-investigators trained in this technique using a Nikon F4 single lens reflex camera and Kodak Gold 100 ASA film. A black background was used for each photograph.

Photographs were evaluated by three blinded, independent vascular surgeons who had been trained in the evaluation process by the principal investigator and the statistician. Each reviewer received an identical set of two 10 x15 cm photographs, one obtained before and one 16 weeks after treatment. Following the parameters described below, they compared the two halves of the study area and completed a scoring sheet. The average of their scores was used to assess the degree of pigmentation and overall clinical and cosmetic results.

Study End Points

The objective of this trial was to compare the effect of thrombectomy versus nonthrombectomy in the development of pigmentation in the same patient. The primary end point was to determine the degree of pigmentation or brownish discoloration on a standardized brown scale, where no pigmentation = 4, tan = 3, light brown = 2, and deep brown = 1. The secondary end point was the assessment of overall clinical improvement by comparing three variables: vein disappearance, pigmentation, and neovascularization. The scores of these three variables were the factors that the reviewers used to evaluate overall clinical improvement. Clinical improvement was assessed on a scale of 0 to 10, where 0 was poor and 10 was excellent. An average of the reviewer's scores was used to assess this end point.

At the termination of the study, the patients were asked to privately fill out a patient satisfaction sheet and express their own degree of satisfaction or dissatisfaction with the treatment. The patients drew a circle around the number that best represented the assessment of the results: 1 = not satisfied, 2 = moderately satisfied, 3 = satisfied, and 4 = very satisfied.

The results were statistically analyzed using two statistical methods. The chi-square test was used to assess different percentages among the three categories (better than, equal than, and worse than) and the second method, the paired t-test, was used to determine differences between the thrombectomized and nonthrombectomized areas. The significance level was set at 5%.

Results

Eighty-five patients completed the study per protocol. Forty-two were in group 1 (veins ? 1 mm) and 43 were in group II (veins ? 3 mm). Immediate local adverse events were pain, inflammation, and swelling. These were mild and were expected after sclerotherapy. There were no systemic adverse events. Delayed adverse events included thrombosis of the injected vein and ecchymosis. No patients had skin necrosis. There were no deaths and no patient withdrew from the study because of adverse events. There were no complications owing to the thrombectomy procedure.

For both vein sizes, in a higher percentage of patients, the microthrombectomized areas were better or the same than the control areas for the variables of pigmentation, vein disappearance, neovascularization, and patient satisfaction.

In group 1, vein telangiectasias, pigmentation, and neovascularization were significantly better in the treated areas ($p = .0084$) than in the control area ($p = .0377$). There were statistically significant differences in the other variables between treated and control areas. In the larger veins in group II, there was no significant difference between thrombectomized and control areas. However, patients consistently reported relief of pain and discomfort after microthrombectomy.

Discussion

Despite its efficacy and safety in the treatment of vascular blemishes, sclerotherapy has side effects that jeopardize its cosmetic results. The most common side effects were pigmentation and localized thrombophlebitis. Less common were neovascularization and skin necrosis secondary to extravasation or to injection into an arteriole. Several observations have been made regarding the incidence and origin of pigmentation. The type of sclerosing agent influences the development of pigmentation. The incidence is 10 to 30% for STD, polidocanol, and hypertonic saline solution. Much has been written about the incidence, rate of disappearance, prevention, and treatment of post-sclerotherapy pigmentation. We found only a few anecdotal reports of the benefit of microthrombectomy in the prevention of pigmentation. There were no prospective randomized studies to document those observations. To our knowledge, our study is the first multicenter, randomized study designed to document the role of post-sclerotherapy thrombus removal in the genesis of pigmentation and the possible benefits of early thrombus removal in the prevention or amelioration of the pigmentation process.

In our study, early removal of the thrombus was able to prevent or decrease pigmentation in veins 1 mm or less in diameter and improve overall clinical and cosmetic results. This supports our hypothesis that, among other factors, the thrombus has an important role as the cause of post-sclerotherapy pigmentation and that its early removal may decrease or prevent its appearance. Removal of the thrombus in larger veins did not result in a significant difference between treated and control areas. A possible explanation is that these veins are deeper and that the deposits of hemosiderin are less visible. However, over the course of the study, it was evident that patients experienced considerable pain relief and that the induration of the phlebitic inflammatory process was shortened after thrombectomy. This has also been our experience in the management of spontaneous varicophlebitis in patients with large varicose veins of the lower extremity.

NOTES

One weakness of this study was the relatively high incidence of dropouts. This was due to the nature of our patient population in a military environment. Unforeseen sudden assignments out of state accounted for most of the 16 patients lost to follow-up. In two patients, thrombi did not develop in the veins, which made it impossible to perform microthrombectomy. A possible explanation for this is that compression after sclerotherapy is more effective in larger veins than in spider veins. Optimal compression over the sclerosed vein ideally would prevent blood from forming a thrombus by opposing the vein walls. However, this was not always achieved. Differences in activity of the fibrinolytic system may also have played a role in the development of thrombi in some patients.

Another potential drawback of the trial is that the photographic evaluation made by the independent reviewers was by its own nature subjective. We tried to minimize this limitation by standardizing the photographic technique and using three judges who were blinded to the identity of the treated areas.

With the advent of the laser, the side effects of sclerotherapy may be improved.[11-14] No long-term studies have evaluated the effects of laser therapy on the development of pigmentation. Efforts have been made to treat persistent pigmentation and neovascularization with laser therapy. In our opinion, however, it is preferable to prevent pigmentation by performing microthrombectomy shortly after the sclerotherapy procedure than to allow its development and then spend additional time treating it. Other methods, such as using different light sources, bleaching agents, and so on, have had moderate success.

Conclusions

In summary, early post-sclerotherapy microthrombectomy is a safe, inexpensive, and efficient method for decreasing or preventing post-sclerotherapy pigmentation. In larger veins, it shortens the inflammatory process and decreases pain.

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