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CHEMICAL ABLATION AS SUCCESSFUL ALTERNATIVE FOR TREATMENT OF INCOMPETENT PERFORATORS

ХЕМИСКА АБЛАЦИЈА КАКО УСПЕШНА АЛТЕРНАТИВА ЗА ТРЕТИРАЊЕ НА ИНКОМПЕТЕНТНИ ПЕРФОРАНТНИ ВЕНИ

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Abstract

Introduction. Superficial venous incompetence (SVI) is the most common cause of lower extremity superficial venous reflux and varicose veins; nonetheless, incompetent perforator veins (PVs) are the most common cause of recurrent varicose veins after treatment, often unrecognized. Current minimally invasive treatment options include ultrasound-guided sclerotherapy (USGS), endovascular thermal ablation (EVTA) with either laser or radiofrequency energy sources, subfascial endoscopic perforator surgery (SEPS) and the relatively new chemical ablation procedure using cyanoacrylate adhesive, which we chose as our primary treatment option for this study, using and comparing the results of two different adhesives.

Methods. A retrospective review of a prospectively managed database of chemical ablation as perforator vein treatment performed at a single institution from September 2023 to March 2024 was conducted. The indications for PV treatment were >4 mm in diameter and reflux of >500 milliseconds upon leg compression.

Results. A total of 32 patients and 49 limbs presenting PV insufficiency (coexisting with GSV insufficiency in 19 patients) were divided into 2 groups of 16 patients, each group based on the chosen chemical ablation adhesive - VenaBlock and VenaSeal. The VenaBlock group had PV closure rate of 100% immediately intraoperative, at 3 days, 2 weeks, 3 weeks and 1 month from the procedure for each treater perforator. From the VenaSeal group, 13 patients had immediate and continuous treatment success during the follow-up, while in 3 patients there was intraoperatively registered treatment failure (P=0.0127).

Conclusion. We find the chemical ablation procedure to be safe and effective for PVs, specifically in the case of using rapid polymerization adhesive. Due to its simplicity and short procedural time, we consider this to be the procedure of choice in case of multiple incompetent PVs present, as well as in significant PV tortuosity.

Keywords: superficial venous incompetence, perforating veins, chemical ablation, VenaSeal, VenaBlock

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Апстракт

Вовед. Површната венска инсуфициенција е најчестата причина за површниот венски рефлукс на долните екстремитети и проширените вени, додека некомпетентните перфораторни вени се најчестата причина за рецидивни проширени вени по третманот, коишто често остануваат неидентификувани. Современите минимално инвазивни опции за третман вклучуваат ултразвучно водена склеротерапија (USGS), ендоваскуларна термална аблација (EVTA) со ласерски или радиофреквентни енергетски извори, ендоскопска субфасциална перфораторна лигација (SEPS) и релативно новата процедура на хемиска аблација, којашто ја избравме како примарна опција на третман во оваа студија, како и употребата на две различни лепила (slow polymerizing vs fast polymeryzing) и споредбата на резултатите меѓу нив.

Методи. Во оваа ретроспективо-проспективна студија во нашата институција во периодот од септември 2023 до март 2024 беа третирани 32 пациенти со хемиска аблација, поради инкомпететни перфорантни вени. Индикациите за третманот вклучуваат: перфоратор со дијаметар над 4мм и рефлукс над >500 милисекунди.

Резултати. Вкупно 32 пациенти или 49 екстремитети кои се презентираат со инсуфициенција на перфоратори, беа поделени во 2 групи од по 16 пациенти врз основа на избраниот атхезив- брзоделувачки (Венаблок) или спороделувачки (Венасил). Кај 19 пациенти беше регистрирана коегзистирачка инсуфициенција на ВСМ. Групата Венаблок имаше стапка на затворање од 100% веднаш интраоперативно, по, 3 дена, 2 недели, 1 месец и 2 месеца од процедурата, за секој третиран перфоратор. Од групата Венасил, 13 пациенти беа успешно третирани, додека кај 3 пациента беше констатиран неуспех при првата апликација, поради што се наложи повторна апликација на лепило (P=0.0127)
Заклучок. Ние сметаме дека процедурата на хемиска аблација со цианоакрилат е безбедна и ефикасна за затварање на инсуфициентни перфорантни вени, посебно кога се користи асстхезив со брза полимеризација. Поради едноставноста и брзината на процедурата, сметаме дека ова е процедура на избор во случај на присутни повеќе некомпетентни перфоратори, како и при изразен тортуозитет.

Клучни зборови: површна венска инсуфициенција, перфорантни вени, хемиска аблација, Venoseal процедура, VenaBlock

Introduction

One of the most frequently reported health problems worldwide is the chronic venous insufficiency (CVI) and venous ulceration, resulting in a significant patient morbidity. Aside from the chronic physical disability caused to the patient and its subsequent psychological effect, it also generates a substantial economic impact to the health care administration. Global prevalence rates of CVI are variable but may be as high as 40% among females and 17% among males [1]. This variation in global prevalence is due to the wide variability in reporting, diagnosis and risk factors. Nevertheless, its morbidity and health care economic burden remain universal.

In his landmark publication, as early as 1917, Homan described the pathophysiology of CVI caused by superficial and deep venous incompetence along with the importance of perforator vein incompetence (PVI) in the development of venous ulcerations [2]. The importance of PVI in the manifestation of CVI and ulceration has since been well-acknowledged and widely studied. However, while the role of definitive management for junctional and truncal venous reflux in symptomatic CVI is well-established, the exact indications for management of PVI in isolation remains, in some part, unclear.

The current recommendation by the guidelines of the American Vascular Society is to treat the PV in cases of CEAP score 5 and 6, with treatment of the perforator at the level of previous or active venous ulceration [3]. Several authors also suggest treating incompetent perforator veins in cases of focal pain, focal swelling, associated varicose veins, focal skin irritation and/or discoloration in the area of the incompetent perforator vein [4,5]. Nevertheless, there is growing consensus that perforators which are >4 mm in diameter and show reflux of >500 milliseconds upon leg compression should be categorized as incompetent [6,7], and those are the parameters which we have adopted in our practice.

Minimally invasive treatments have replaced traditional surgical treatments for incompetent perforator veins. Current minimally invasive treatment options include ultrasound-guided sclerotherapy (USGS), endovascular thermal ablation (EVTA) with either laser or radiofrequency energy sources, subfascial endoscopic perforator surgery (SEPS) and the relatively new chemical ablation procedure using cyanoacrylate adhesives. Advantages and disadvantages of each modality and knowledge on these treatments are required to adequately address perforator venous disease.

Cyanoacrylate chemical ablation is a relatively new treatment for treating varicose veins. This procedure introduces a resilient glue into the large veins through a small catheter via the Seldinger technique or through small incision. Upon contact with blood, the adhesive begins to bond with the intima and compression is applied to close the vein. The adhesive is designed to remain permanently in the diseased vein and is encapsulated by chronic fibrosis.

While there are multiple articles reporting results of the VenaSeal procedure for truncal insufficiency, such literature remains deficient regarding the PVs.

Chemical ablation has the advantage of not requiring anesthesia before treatment and has been found to be very effective for closing the large saphenous veins. It delivers immediate and lasting vein closure with its proprietary medical adhesive formula, with a demonstrated 94.6% closure rate used for the GSV at 5 years [8-12].

In September 2023 we were presented with an alternative product: the short-chain obliterating agent named VenaBlock (Invamed Saglic Ilac A.S., Ankara, Turkey), which is characterized by its low viscosity and fast polymerization. Given these attributes, which would theoretically make it an excellent choice of treatment of PVS, we have decided to include it in our PV closure procedure and compare it against Venaseal - slow polymerizing long-chained cyanoacrylate, which has been in the market since 2011.

Materials and methods

A retrospective review of a prospectively managed database of chemical ablation of perforator vein performed at a single institution from September 2023 to March 2024 was conducted. The main inclusion criteria for PV treatment were >4 mm in diameter and reflux of >500 milliseconds upon calf compression. A Duplex scan was performed at 3 days, 2 weeks, 1 month and 2 months after the procedure. Standard statistical methods were used to compare subgroup characteristics.

Results

A total of 32 patients and 49 limbs presenting PV insufficiency coexisting with GSV insufficiency in 19 patients (which we treated concomitantly by RFA of the subfascial GSV and VenaSeal of the distal portion of GSV in the same act), were divided into 2 groups of 16 patients (25 limbs and 24 limbs respectively), each based on the chosen adhesive kit. Each group had 2 further subgroups, solely based on the PV diameter: subgroup A diameter 3.5-5 mm, subgroup B >5 mm.

Table 1. Patient population

Variable	VenaBlock (n=16)	VenaSeal (n=16)
Age	43±14.4	48±11.2
BMI	28.2±9.5	30.4±11.8 kg/m^2
Comorbidities		
Mild hypertension	4(25%)	3(18.75%)
Hashimoto disease	2(12.5)	1(6.25%)
Clinical stage CEAP		
2-4	12(75%)	16(100%)
5	3(18.75%)	
6	1(6.25%)	
Concomitant GSV insufficiency	10 (62.5%)	9(56.25%)
Diameter of the treated PV		
Subgroup A 3.5-5 mm	9(56.25%)	10(62.5%)
Subgroup B >5 mm (5-7 mm)	7(43.75%)	6(37.5%)
Length of the treated PV	1.9±0.56 mm	1.8±0.47 mm

Each of the 16 patients in the VenaSeal group were in CEAP stage 2-4, while 12 patients in the VenoBlock group were in CEAP stage 2-4, 3 in CEAP stage 5 and 1 in CEAP 6. The average age of the VenaSeal group and the VenaBlock group were 43±14.4 and 48±11.2, respectively (P=not significant [NS]). Body mass index was 28.2±9.5 and 30.4±11.8 kg/m^2, respectively (P=not significant [NS].

The VenaBlock group had PV closure rate of 100% immediately intraoperative, at 3 days, 2 weeks, 1 month and 2 months from the procedure for each treated perforator. From the VenaSeal group, 13 patients (81.25%) had immediate, as well as continuous treatment success during the follow-up period, while in 3 patients (18.75%, P=significant [S], P=0.0127) there was intraoperatively registered treatment failure, which we assigned to our hesitation to use adequate amount of this prolonged polymerization glue in this short length and relatively large diameter (6, 6.2 and 7 mm, respectively) perforator vein, due to the high estimated risk of adhesive leakage toward the deep venous system. We subsequently retreated the PV with the VenaBlock adhesive and achieved immediate and durable closure. The Duplex scanning revealed complete obliteration of the treated PVs in both groups (except in the aforementioned cases), with the PVs having dense, well rounded cross-section image in the VenaBlock group and flatter cross-section shape in the VenaSeal group. The single patient presenting active ulcer in the VenaBlock group showed progressive ulcer diameter reduction at each visit and the ulcer was healed by the 3rd week. There was no clinical or instrumental evidence of DVT in any patient. There were no infectious complications and/or hematomas of the puncture site. No extravasation of the glue was registered at duplex scanning. No foreign-body type reaction was observed during the follow-up period.

Discussion

Chemical ablation procedure is a relatively new treatment for treating varicose veins. It is the only FDA-approved procedure that uses an injection of medical adhesive to close varicose veins, and so far, has been reported as highly effective, according to several authors [8-12].

There is no risk of thermal nerve and skin injury, hence the hyperpigmentation is avoided and there is less pain and bruising than in thermal treatment. Tumescent anesthesia is not required. The application itself is very simple and the procedure time is short.

We perform the procedure in outpatient settings, without any anesthesia, under ultrasound guidance, via venepuncture with 21G needle, directly above the incompetent perforator, in its portion closest to the superficial vein. We use 2cc syringe for adhesive delivery, which we flush beforehand by 10% Dextrose solution. Gently, we apply just the necessary amount

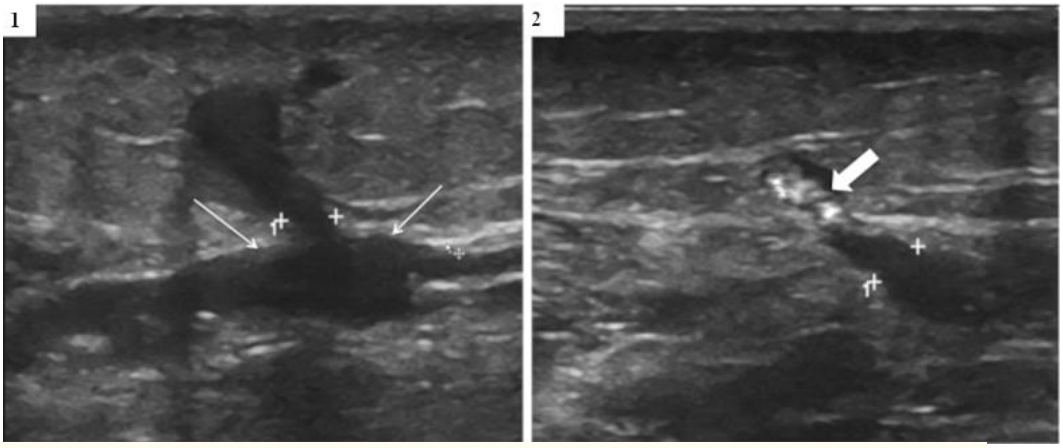

Fig. 1. (1) Ultrasound (US) imaging showing an abnormally dilated perforator vein connecting dilated superficial varicose veins to the deep venous system. Thin arrows show the deep fascia; (2) US image after treatment with VenoSeal, showing thrombosis and fibrosis of the perforator vein up to its connection with the deep system. Thick arrow shows bridging polymerized adhesive

to achieve visual confirmation of occlusion only in the segment above the deep fascia and we apply manual compression to the puncture site. Ultrasound confirmation of unobstructed flow in the contacting deep vein is mandatory (Figure 1).

It is our observation that the miniphlebectomy of the tributaries in the lower leg, following chemical ablation of the incompetent large veins and PVs, seems to have a significantly reduced intraoperative bleeding compared to other procedures, due to the immediate intraoperative occlusion of the lumen.

We apply thigh-level compressive stockings CCL 2, which are advised to be worn during the next 4 weeks. We prescribe a peroral broad-spectrum antibiotic for the first 5 days. The patient is discharged within 2 hours from the procedure.

The problem with this treatment is that the glue never fully dissolves, meaning it will become a permanent fixture in the vein, which can be felt under the skin, specifically in the mobile areas, like the knee joint. Additionally, according to the worldwide literature, about 5% of patients treated with VenaSeal have an allergic reaction to the glue that can cause pain and inflammation-especially problematic considering the glue cannot be removed.

There is also the high financial cost aspect to this procedure, considering the adhesive cannot be purchased separately and we are obligated to order the full kit, even when the application of long catheters and most of the other elements in the kit is redundant in cases of isolated PVs.

In our institution, we have used the fast-polymerizing VenaBlock and the slow polymerizing VenaSeal adhesives, both having similar features of their deployment catheters, with the important difference being the adhesive characteristics due to a difference in the chemical structure (short-chained *vs.* long-chained cyanoacrylate) resulting in different polymerization times and viscosity).

It is important to note that PV application is not included in any of the manufacturers' instruction manuals.

A polymerization time of 24-54 sec for the VenaSeal glue with significantly higher viscosity, with its final form being softer and more flexible, and less likely to be felt by the patient, as opposed to the extremely short polymerization time for the VenaBlock adhesive of 2-5 secs, with its much lower viscosity and high pushability, leading to rapid formation of a firm seal, which we find to be significantly safer to use near the deep veins, but has denser final structure, more likely to be felt under the skin. We find them both equally echo-positive (Figure 1).

In this trial, we have noticed a statistically important difference in treatment success between the 2 adhesives exclusively for the large diameter PVs (>6 mm), which we mainly attribute to our restraint while filling up relatively large and short perforators with the slow-polymerizing glue.

Its high viscosity formula makes it difficult to inject and the slow polymerization leads to a more difficult visual control of the precise occlusion point, which in the case of PVs is paramount.

Based on these differences, we prefer the VenaSeal set when treating the longer segments of the GSV, while for closing perforators we find the Venablock adhesive safer and easier to apply, whose extremely short polymerization time makes it less likely to penetrate and embolize the deep venous system.

Derived from our results, we find this closure procedure, regardless of the adhesive type, to be safe and highly effective for treatment of incompetent PVs.

Conclusion

Minimally invasive treatment of perforating veins will continue to improve. We find the chemical ablation procedure to be safe and effective for PVs, specifically when using a rapid polymerization adhesive. Due to its simplicity and short procedural time, we consider this to be the procedure of choice in case of multiple incompetent PVs present.

Conflict of interest statement. None declared.

References

1. Beebe-Dimmer JL, Pfeifer JR, Engle JS, Schottenfeld D. The Epidemiology of Chronic Venous Insufficiency and Varicose Veins. *Ann Epidemiol* 2005; 15: 175-184.
2. Homan J. The etiology and treatment of varicose ulcer of the leg. *Surg Gynecol Obstet* 1917; 24: 11.
3. O'Donnell TF, Passman MA, Marston WA, *et al*. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery ® and the American Venous Forum. *J Vasc Surg* 2014; 60: 3S-59S.
4. Alden PB, Lips EM, Zimmerman KP, *et al*. Chronic Venous Ulcer: Minimally Invasive Treatment of Superficial Axial and Perforator Vein Reflux Speeds Healing and Reduces Recurrence. *Ann Vasc Surg* 2013; 27: 75-83.
5. Dillavou ED, Harlander-Locke M, Labropoulos N, *et al*. Current state of the treatment of perforating veins. *J Vasc Surg Venous Lymphat Disord* 2016; 4: 131-135.
6. Eidson JL, Bush RL. Diagnosis and Current Management of Incompetent Perforator Veins. *Semin Vasc Surg* 2010; 23: 113-117.
7. Labropoulos N, Tiongson J, Pryor L, *et al*. Definition of venous reflux in lower-extremity veins. *J Vasc Surg* 2003; 38: 793-798.
8. Morrison N, Gibson K, McEnroe S, *et al*. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). *J Vasc Surg* 2015; 61(4): 985-994.
9. Proebstle T, Alm J, Dimitri S, *et al*. Three-year follow-up results of the prospective European Multicenter Cohort Study on Cyanoacrylate Embolization for treatment of refluxing great saphenous veins. *J Vasc Surg Venous Lymphat Disord* 2021; 9(2): 329-334.
10. Gibson K, Ferris B. Cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of post-procedure compression: Initial outcomes of a post-market evaluation of the VenaSeal System (the WAVES Study). *Vascular* 2017; 25(2): 149-156.
11. Almeida JI, Javier JJ, Mackay EG, *et al*. Thirty-sixth month follow-up of first-in-human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. *J Vasc Surg Venous Lymphat Disord* 2017; 5(5): 658-666.
12. Morrison N, Gibson K, Vasquez M, Weiss R, Jones A. Five-year extension study of patients from a randomized clinical trial (VeClose) comparing cyanoacrylate closure versus radiofrequency ablation for the treatment of incompetent great saphenous veins. *J Vasc Surg Venous Lymphat Disord*. November 2020;8(6):978-989.