DOI: http://dx.doi.org/10.48305/arya.v18i1.2374 Published by Vesnu Publications

Does second generation n-butyl cyanoacrylate embolization really smooth in greater saphenous vein closure?

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Original Article

Abstract

BACKGROUND: Cyanoacrylate (CA) has been used as an embolizing agent in the treatment of greater saphenous vein (GSV) insufficiency in recent years and the results regarding the use of this method have started to be published. To the best of our knowledge, the publications in literature do not mention about a significant negative effect of endovenous CA (EVCA) embolization. We aimed to evaluate the effects and undesirable events of this relatively new treatment method and compare them with literature, using the follow-up data of our patients.

METHODS: Patients who had GSV insufficiency for at least 3 months and were treated with EVCA embolization because of this disease were included in the study. Patients were excluded if they had deep vein thrombosis (DVT), excessive tortuous GSV, and peripheral neuropathy. Hospital archive records were reviewed and undesirable events like DVT, thrombophlebitis, and pain related to this treatment procedure were recorded.

RESULTS: EVCA embolization procedure was performed in a total of 54 patients with an average age of 49.36 ± 13.06 years for the purpose of treating GSV insufficiency. One patient was observed to develop n-butyl CA (NBCA) extension of approximately 5 mm from saphenofemoral junction (SFJ) to the main femoral vein and painful thrombophlebitic reaction was observed in 6 extremities at the first control examination.

CONCLUSION: In our opinion, while EVCA embolization is a treatment option with similar success rates to endovenous thermal ablation (EVTA), it should be kept in mind that there may be a possibility of developing thrombophlebitis and NBCA extension or thrombus extension to the deep veins.

Keywords: Cyanoacrylate; Embolization; Thrombophlebitis

Date of submission: 28 Jan. 2021, ***Date of acceptance:*** 24 Apr. 2021

Introduction

Even though endovenous thermal ablation (EVTA) methods are safe and effective methods in the treatment of greater saphenous vein (GSV) insufficiency and have replaced high ligation and stripping, there are some limitations such as requiring perivenous tumescent anesthesia and side effects such as postoperative pain, burning, and sensory nerve damage.[1] Cyanoacrylate (CA), a well-known chemical substance, has recently been used as an embolizing agent in the treatment of GSV insufficiency, and the results regarding the use of this method, which is based on granulomatous body reaction and fibrotic degradation due to accompanying vein wall inflammation, have started to be published.[2] In addition to the advantages of CA, which has a similar success rate with EVTA methods in the treatment of GSV insufficiency, such as not requiring tumescent anesthesia, eliminating the need for compression stockings, and

How to cite this article: Yilmaz S, Kiziltan F, Zengin S, Kalender M, Cam I. **Does second generation n-butyl cyanoacrylate embolization really smooth in greater saphenous vein closure?** ARYA Atheroscler 2022; 18: 2374.

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absence of treatment-related sensory nerve damage,[1,3] the adverse events related to the procedure are also mild and limited.[1] To the best of our knowledge, the publications in literature do not mention about a significant negative effect of endovenous catheter ablation (EVCA) embolization.

In this study, we aimed to evaluate the effects and adverse events related to this relatively new treatment method and compare it with literature, using the follow-up data of our patients who underwent GSV insufficiency treatment with CA.

Materials and Methods

This retrospective study was undertaken in a tertiary hospital between 2016 and 2017 and the study group was made up of 54 patients undergoing EVCA embolization procedure for GSV insufficiency. Inclusion criteria in the study were being older than 18 years and suffering from GSV insufficiency for at least 3 months. The study was approved by the ethics committee of the institution and the study was conducted in accordance with the Declaration of Helsinki guidelines. GSV insufficiency due to incompetent saphenofemoral junction (SFJ) was detected by color Doppler ultrasound [ultrasonogram (USG)] examination upon the admission of patients to the outpatient clinic. All patients were routinely examined with color Doppler USG for the presence of deep vein thrombosis (DVT) and GSV assessment (for tortuosity, diameter, and pathological reflux) before the treatment procedure. Patients were excluded if they had DVT, excessive tortuous GSV, peripheral neuropathy, and GSV with a diameter of < 5.5 mm [because of Turkish Social Security Institution (SSI) payment criteria]. Patients with known malignancy, those who received any type of surgery or intervention for treatment of GSV insufficiency in the past, or those having a previous history of extremity arterial thromboembolism (ATE) were also excluded. Hospital archive records were reviewed and baseline characteristics, success rate, and undesirable events or complications like n-butyl CA (NBCA) extension, DVT, thrombophlebitis, pain, allergic reaction, and paresthesia related to this treatment procedure were recorded.

The treatment for all patients included endovenous embolization of GSV using a specific NBCA (Venablock, Invamed, Ankara, Turkey) and its catheter in the thigh region with the guidance of USG. EVCA embolization involved a disposable 2 ampoule (2.5 ml total) NBCA and its operation catheter. All operations were performed by the same vascular surgery team under local anesthesia or spinal anesthesia (in patients undergoing simultaneous stab phlebectomy) without applying tumescent anesthesia. In the operational procedure which was based on continuous injection of NBCA in the injector attached to the back of the catheter system into the GSV segment to be treated, full compression was done using SFJ probe by the first administration of NBCA to the GSV point, which was 5 cm away from SFJ, while the NBCA-applied GSV was fully compressed simultaneously with the systematically withdrawn application catheter. 2 minutes after the completion of EVCA embolization, the remaining enlarged varicose veins were treated with phlebectomy in the same session. None of the patients was treated in the same session due to small saphenous vein (SSV) insufficiency. When the procedure was completed, before the patients were taken from the operating room, all patients were checked with USG and it was found that the operated GSV segment was occluded and there was no thrombosis in the main femoral vein of the same side. The patients' operated leg was bandaged with an elastic bandage after the procedure and they were followed up at the cardiovascular surgery service. The patients who were treated under local anesthesia were mobilized at the service 1 hour after the procedure and patients who underwent spinal anesthesia were mobilized 5 hours after the procedure. All patients were given oral analgesic (paracetamol) treatment on the day of the procedure and the patients were discharged from the hospital on the day of operation or on the first postoperative day. The patients were not recommended compression stockings during their recovery, and they were advised to come to the outpatient clinic for follow-up on the postoperative 10th day and 1st month.

Statistical analysis: Descriptive data were expressed as the number of patients due to the fact that the total sample contained less than 100 individuals. No other statistical analyses were performed in this descriptive study.

Results

EVCA embolization procedure was performed on 55 extremities in total for 54 patients with an average age of 49.36 ± 13.06 years (18 to 79 years) for the purpose of treating GSV insufficiency. Simultaneous varicose vein excision procedures were also performed for 45 of the patients (83.3%) due to existing varicose veins. None of the patients received the EVCA embolization procedure in the

same session for both lower extremities for the treatment of GSV insufficiency, and EVCA embolization procedure was performed on 2 lower limbs of 1 patient in different sessions. The baseline characteristics are provided in table 1.

Table 1. The baseline characteristics of patients (n = 54)

Variables	
Age (year)	49.36 ± 13.06
Gender (men)	26 (48.1)
CEAP 2	1 (1.8)
CEAP 3	45 (83.3)
CEAP 4	5 (9.2)
CEAP 5	4 (7.4)
GSV diameter (mm)	81.61 ± 20.33
Obesity	3 (5.5)
Patients undergoing phlebectomy	45 (83.3)

Data are reported as mean ± standard deviation (SD) or number (percent)
CEAP: Clinical, ethiological, pathological, anatomical elements; GSV: Great saphenous vein

With EVCA embolization procedure, the intraoperative complete closure rate of GSV occurred in 54 extremities (98.2%); partial venous flow was observed in the GSV segment on 1 extremity treated during the procedure. No complications, including DVT, was observed, nor did the patients develop any allergic reaction against the embolizing agent used during the procedure.

The patients were discharged from the hospital on the same day of the procedure or on the first postoperative day. One patient (1.8%) was observed to develop NBCA extension of approximately 5 mm from SFJ to the main femoral vein on the 5th postoperative day. This patient underwent low-molecular-weight heparin (LMWH) treatment for 3 weeks, and complete resolution was achieved. DVT and pulmonary embolism (PE) were not observed during the control examinations of the patients. Undesirable events that were observed in control examinations during the postoperative period are shown in table 2.

Table 2. Undesirable events (in the postoperative period)

	n (%)
NBCA extension	1 (1.8)
Thrombophlebitis	6 (11.0)
Pain	3 (5.5)

NBCA: N-butyl cyanoacrylate

Painful thrombophlebitic reaction was observed in 6 extremities (10.9%) at the first control examination. Local stiffness and subcutaneous fibrotic band were sensed with local hyperemia in the painful lower extremities of these patients, and oral non-steroidal anti-inflammatory [diclofenac sodium 100 mg 1 x 1, per oral (PO)], antibiotic (cefuroxime axetil 500 mg 2 x 1, PO) and anti-aggregating (acetylsalicylic acid 100 mg 1 x 1, PO) treatments were started for these patients for 10 days due to the current complaints with the approval of the vascular surgeon. Localized pain without any signs of thrombophlebitic reaction was detected in the lower extremities of another 3 patients (5.5%) at the first control examination. No venous thromboembolism (VTE), paresthesia, and procedure-related serious morbidity or mortality was detected during the control examinations.

Discussion

EVTA methods, which have recently replaced the classical surgery methods in the treatment of venous insufficiency and whose effectiveness and safety have been proven, are accepted as the gold standard in the treatment of this disease.[1] Various thermal ablation methods are among the frequently-used methods in the treatment of GSV insufficiency with high venous occlusion and similar success rates,[3-5] and we have also successfully applied endovenous laser ablation (EVLA) and endovenous readiofrequency (EVRF) treatments for a long time in our current practice.

Need for tumescent anesthesia and side effects such as paresthesia, pain, and burning on the skin are reported to be significant disadvantages of EVTA methods, which cause less undesirable effects in the treatment of GSV insufficiency compared to classical surgery.[1-5] For this reason, EVCA embolization method which is a non-tumescent endovenous embolization method[6,7] was started to be performed in order to avoid these undesirable effects of EVTA methods. It is a relatively new method and is reported to have similar success rates to EVTA methods in literature.[1,3,8] In a publication in the literature, EVCA embolization procedure performed with NBCA was reported to have 99% closure rate in the treatment of GSV insufficiency in a 3-month period.[8]

Another advantage of this method, which has many positive aspects such as returning to everyday activities in the early period and absence of side effects such as hypoesthesia, is that patients do not need to use compression stockings during the postoperative period.[3] In our study, the rate of developing paresthesia was detected to be 0% in our patient group following the EVCA method, which was performed

without need for any tumescent application.

This treatment method is expressed to have promising results in recent studies,[3,6,7] and in some multicenter studies, the success rate of this method at the time of the procedure is stated to be 98.6%,[1,3] and there are even studies expressing the success rate as 100%.[3,7,8] In our study, the complete closure rate of GSV during the procedure is 98.2% which is in conformity with the literature.

NBCA is reported to solidify quickly during the endovenous procedures and form a rapid polymerization reaction, and this reaction causes an inflammatory effect on the vein wall resulting in an ablative reaction, and the closure is ensured due to the compression performed on the vein during injection through the polymerization formed.[1,3,6-8] The catheter systems of EVCA embolization used for the treatment of GSV insufficiency are similar to the systems used for EVTA, and after the first generation NBCAs used for EVCA embolization, which had high viscosity, were polymerizing rapidly, and had a flexible structure when polymerized, the second generation NBCAs developed in Turkey had the chance to be used in clinical practice at our clinic for a long time.[1,9]

In the first system used for endovenous NBCA-embolization, a high viscosity agent was administered in a pressure-push manner with the help of a gun-mediated catheter system.[9] In the second system developed and actively used in our country, low viscosity NBCA is administered/injected continuously, and using this device and method, consecutive case series involving significant number of patients were published by various medical centers in Turkey.[9-12] In our study, we used the second generation NBCA and its administration system called Venablock, which has a specific catheter system with a red light tip, and is known to be widely used in our country and other countries, in the form of continuous injection.

In the publications in literature, rapid closure and minimum procedure durations are reported to reduce the risk for developing VTE, and it is also expressed that SFJ is rapidly closing thanks to quick polymerizing NBCA, and adequate and correct compression applied on SFJ reduces the risk of embolizing agent leak into the main femoral vein.[3] Although DVT development is not mentioned in the most of the publications related to EVCA, it is reported that NBCA extension may occur towards the femoral vein.[1]

In a previous study, where NBCA was used for the treatment of GSV insufficiency embolization, it was stated that thrombus extension was observed in 21% of the treated extremities, which was stated to pose a risk of PE.[1,6] Although this condition was clinically insignificant and known to be resorbed spontaneously without specific treatment, thrombus extension to the deep veins is one of the points that can be perceived as a risk of the procedure.[1] In a study that reported NBCA extension to the deep veins at a rate of 1.4% in EVCA embolization procedure, the factors causing the development of NBCA extension to the deep veins were considered to be the viscosity of the agent used, the administration method of the embolizing agent, and the distance of the first administration point of the embolizing agent in GSV to SFJ (a distance of 5 cm from SFJ is reported to be safe for the first positioning).[1,3] In case of NBCA extension to the deep veins developing after EVCA embolization, LMWH treatment for 2 weeks is reported to improve the extension without any clinical sequel.[1] None of the patients in our study was observed to develop DVT and NBCA extension to the femoral vein during the procedure. However, in early follow-up, 1 patient (1.8%) developed NBCA extension to the main femoral vein, and we think that one of the reasons may be related to the distance of the first application point of NBCA in GSV to the SFJ. We also think that another reason is the possibility of NBCA progression during the post-procedure period. This patient was followed up for about 3 weeks with LMWH treatment and the NBCA extension was improved without any clinical sequel in the patient without developing any PE attack.

It has been reported that there are no significant side effects associated with EVCA embolization, and minor side effects are mostly phlebitic reactions.[7] In addition, in some studies conducted using the first generation NBCA, the rates of developing phlebitis after EVCA embolization procedure were reported as 10%, 11.4%, and 20%,[1,8,10] and in one study regarding the EVCA embolization procedure performed with the second generation NBCA, the rate of phlebitis was stated to be 4.5%.[13] However, in another publication, this rate was found to be 1.4%.[9] It is reported that there are differences between the first used NBCA agent and the second generation NBCA (Venablock) agent in terms of fluidity and polymerization properties.[3,13] In a study where a second generation NBCA agent was administered by continuous injection into the diseased GSV lumen, the authors state that the viscosity of the NBCA agent they used was lower compared to the previously-used agent

and polymerized rapidly (5 seconds),[13] and therefore, they attract the attention to the importance of continuous injection method.[9,13] Another important point is the compression to be done on the vein just after the NBCA injection, and our main purpose here is to stick the opposite endothelia of the vein together without creating a thrombus within the lumen secondary to the reaction. It is expressed that the most important points in the treatment of GSV insufficiency with the EVCA embolization method using NBCA are the viscosity of the agent used and whether the method of administration is in the form of continuous injection,[9] and these may lead to significant differences in the development of phlebitis.[10,12,13] It is explained that the phlebitis formed after EVCA embolization using an NBCA agent is caused by a thrombus-like formation developed secondary to the reaction between the embolizing agent and the blood in the relevant vein segment, and the compression applied on time onto the correct point with sufficient severity is necessary and adequate to stick the opposite endothelium of the vein without enabling its formation of thrombus in the lumen.[9]

We simultaneously applied compression on the GSV segment where we performed EVCA embolization with the catheter-mediated continuous injection with an injector containing second generation NBCA, and tried to ensure closure through polymerization in our patient group. Despite using continuous injection technique and the agent called Venablock, which is a second generation NBCA, the phlebitis rate detected during the early controls was 10.9%. We think that it is not easy to apply compression at the correct moment onto the correct spot with sufficient severity in technical terms, since the vein segment where EVCA embolization is performed cannot be easily localized from the outside. We also think that before starting continuous injection for EVCA embolization, bringing patients to Trendelenburg position and reducing the blood within the GSV lumen will decrease the risk for thrombus formation secondary to the agent-blood reaction and thus, the development of phlebitis.

There are some limitations of our study in terms of small sample size, retrospective design, and absence of control group.

Conclusion

In our opinion, while EVCA embolization is a treatment option with similar success rates to EVTA, it should be kept in mind that there may be a possibility of developing thrombophlebitis and NBCA extension or thrombus extension to the deep veins depending on the properties of the agent used, the technique of administration, and correct and adequate compression.

Acknowledgments

None.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contribution

SY: Idea, study design, evaluation; FK: Data collection; SZ: Writing; MK: Data analysis and statistical analysis; IC: Editing and literature search.

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