The Relationship between Pain and ABO Blood Type During Saphenous Vein Ablation using N-Butyl Cyanoacrylate

N-Butil Siyanoakrilat Kullanılarak Safen Ven Ablasyonunda Oluşan Ağrı ile ABO Kan Grubu Arasındaki İlişki

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ABSTRACT

Aim: The aim of this study was to investigate whether there is a relation between ABO blood groups and pain levels during venoblock procedure to vena saphena magna using N-butyl cyanoacrylate (NBCA), as well as need of analgesics in the postoperative period in patients with venous insufficiency.
Materials and Methods: Fifty patients from each of the A, B, AB and O blood groups were included in the study. The severity of pain during ablation with NBCA was measured using the Visual Analogue Scale (VAS) score. In addition, all patients were asked how many days they used analgesics after the procedure at the fifth day visit. VAS scores and postoperative analgesic requirements were evaluated according to ABO blood groups.
Results: Both VAS scores and the days of analgesics need after procedure in the B and AB blood groups were significantly higher than in the A and O blood groups ($p < 0.001$), however, were not different between B and AB blood groups. They were significantly higher in blood group 0 were than in blood group A ($p < 0.001$) but were significantly lower thanB and AB blood groups ($p < 0.001$). The VAS scores and days of analgesics need of patients with A blood group were the lowest among all blood groups ($p < 0.001$).
Conclusion: We demonstrated that pain levels occurred during venablock procedure and postoperative analgesic need were related to ABO blood group. Accordingly, the relationship between pain and blood group may contribute to pain management for both diagnostic and therapeutic purposes.

Key Words:N-butyl cyanoacrylate, ABO blood groups, Pain, Primary venous insufficiency, Visual Analogue Scale, Venous ablation.

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ÖZET

Amaç: Bu çalışmanın amacı venöz yetmezlikli hastalarda vena safena magnaya N-bütil siyanoakrilat (NBCA) verilerek uygulanan venablock tedavisi esnasında oluşan ağrının ve postoperatif dönemde analjezik gereksiniminin ABO kan grubu ile olan ilişkisini araştırmaktır.
Yöntem: Çalışmaya vena safena magnaya venablock tedavisi uygulanan A, B, AB ve O kan gruplarından 50'şer adet hasta alındı. Tedavi olarak kullanılan N-butyl cyanoacrylate ile ablasyon yöntemi sırasında oluşan ağrının şiddeti vizuel analog skala (VAS) skoru ile ölçüldü. İşlem sonrası ne kadar ağrı kesici ihtiyacı olduğu 5. gün kontrole çağırılıp soruldu. VAS değerleri ve ağrı kesici kullanımı ABO kan gruplarına göre değerlendirildi.
Bulgular: Gruplar VAS skoru ve işlem sonrası ağrı kesici ihtiyacı olan gün sayısına göre değerlendirildiğinde B ve AB kan grupları A ve O kan grubuna göre anlamlı oranda daha yüksekti ($p<0,001$). B ve AB kan grubu arasında anlamlı bir fark yoktu. O kan grubu A kan grubundan anlamlı oranda daha yüksekti ($p<0,001$), B ve AB kan grubundan anlamlı oranda daha düşüktü ($p<0,001$). A kan grubu tüm kan gruplarından anlamlı oranda daha düşüktü ($p<0,001$).
Sonuç: Çalışmamızda venablock tedavi işlemi esnasında oluşan ağrı ve sonrasında ağrı kesici gereksinimi ile ABO kan grubu arasında ilişki olduğu gösterilmiştir. Bu çalışma sonucuna göre gösterilen ağrı ile kan grubu arasındaki ilişki hem tanı hem de tedavi amacıyla ağrı yönetimine katkıda bulunabilir.

Anahtar Sözcükler: N-butyl cyanoacrylate, ABO kan grubu, Ağrı, Primer venöz yetmezlik, Vizual analog skala,Venöz ablasyon.

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INTRODUCTION

Primary venous insufficiency (PVI) is a health problem affecting a significant part of the population. Previously, surgical procedures such as stripping or ligation techniques, which requires general or spinal anesthesia, were applied to the vena saphena magna (VSM). In the last decade, various methods have been developed for treatment of PVI. Of these, endovenous ablation techniques have become increasingly common and replacedsurgical treatment. Endovenous thermal ablation techniques (laser or radiofrequency) have been shown to be effective and safe according to the results of long-term follow-up (1). In these two ablation techniques, the need for tumescent anesthesiaduring the procedure and tight bandage wrapping after the procedure lead to discomfort and serious painfor the patients. To reduce these complaints, N-butyl cyanoacrylate (NBCA) ablation method, which does not require the use of tumescent anesthesia or thermal ablation, was started to use and its safety and efficacy have been demonstrated in previous studies (2,3). During this procedure, NBCA, a caustic chemical agent, is given to VSM by a special catheter method, which may cause pain in some patients for approximately 30 seconds.In this study we used Venablock Venous Closure System (Invamed, Ankara, Turkey).

The ABO blood group system consists of four blood groups: A, B, AB and O. The gene that determines ABO blood type is found on chromosome 9q34.1 and 9q34.2 and is called ABO glycosyltransferase (4). ABO blood group has been shown to be associated with various diseases such as vascular diseases, colorectal adenocarcinoma, coronary artery disease and diabetes mellitus, and related with cardiovascular disease risk and survival after heart transplantation (5-10). In addition, the relationship between pain and ABO blood group has been shown in previous studies (11). Pain response varies according to gender, race and ethnic differences (12, 13).

The aim of this study was to investigate the relationship between pain levels during venablock treatment with NBCA administration to VSM, as well as postoperative analgesic need,and ABO blood type in patients with PVI.

MATERIALS and METHODS

Study protocol

This study was conducted between February 2019 and November 2019 at KahramanmaraşSütçü İmam University Faculty of Medicine. Fifty patients from each of the A, B, AB and O blood groups who were treated with venablock for VSM were included in the study. Study patients were between 21-70 years of age and were in the C2-C4 groups according to CEAP (C: Clinical, E: Etiological A: Anatomical P: Pathophysiological) classification.

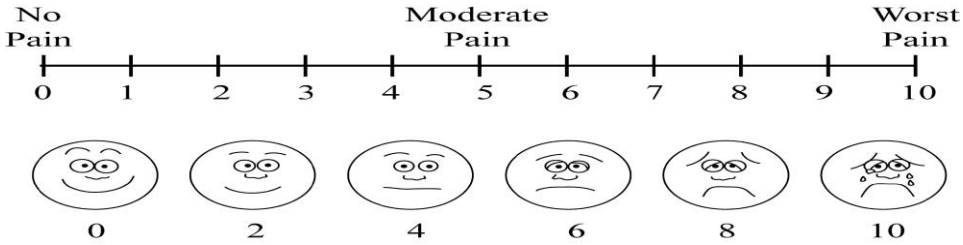


Figure 1: Visual analogue scale (VAS)

Statistical analysis

The Statistical Program for Social Sciences version 22 was used for all statistical calculations. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Kruskal Wallis H test was used to compare the groups for non-normally distributed variables. Dunn-Sidak and Bonferroni tests were used for post-hoc tests. The $\chi 2$ test wasused for comparison of categorical variables between groups.Statistical significance was defined as $P < 0.05$.

The patients who underwent venablock had a VSM diameter of at least 5.5 mm and had avenousinsufficiency of at least 2 seconds. Visual AnalogueScale (VAS) score was used to assess the severity of pain according to the responses of the patients during the procedure. All patients included in the study were mentally competent to report the degree of pain and were able to attend follow-up. Exclusion criteria of the study were active cancer, history of deep vein thrombosis, current or previous thrombophlebitis, pregnancy, peripheral arterial disease, immobilization, cynoacrylate sensitivity and previous saphenous vein treatment.

The study was approved by the Institutional Ethics Committee (approval date: February 2019, document number: 10). Before participation in the study, informed written consent was obtained from each subject after explaining the protocol.

Venablock procedure

All procedures were performed under local anesthesia with standard sterile techniques. A 6-F sheath was inserted to VSM percutaneously. The Venablock catheter was advanced through the sheath and placed approximately 3 cm proximal of the saphenofemoral junction. The saphenous vein in the saphenofemoral junction area was compressed with a doppler ultrasound probe to ensure no blood flow. Every 5 s push on the gun trigger delivered 0.3 ml NBCA with a pullback rate of 2 cm/s applied on every 10 cm until the vein segment was fully supplied with NBCA. At the end, 0.03 ml of NBCAwas applied on every 1 cm of VSM. Finally, manual compression was applied on the puncture site after the catheter and the sheath were removed, and an elastic bandage was wrapped. No additional procedures were performed during the same session.

Assessment

The study was described to all subjects who gave informed consent before the beginning of the study. The blood types of the patients were examined from the samples obtained by routine intravenous vascular access before the procedure. Pain level during the procedure was evaluated according to the Visual Analogue Scale (VAS), whichis the standard method (Figure 1). VAS is used to convert some values that cannot be measured quantitatively to the numerals andis the most commonly used method among pain scales (14). VAS consists of a scale with numbers between 0 and 10. The point where there is no pain is indicated by 0 and the point where the pain is unbearable is indicated by the number 10 (15). The patient either marks or says anappropriate number according to what he or she feels. The test has been used for a very long time. It is an easily applicable, safe and accepted test all over the world (16). The pain level during the procedure was asked to the patients and their responses were recorded.After the procedure, the patients were prescribed paracetamol 500 mg as an analgesic and were told to take it 4 times a day. On the 5th day after the procedure, the patients were called for control and asked how many days they needed pain medication.

RESULTS

A total of 200 study patients were divided into 4 groups according to A, B, AB and O blood groups, each consisting of 50 patients.The age and gender characteristics of the patients are shown in Table 1. There was no significant difference among the groups in terms of gender or age ($p > 0.05$). The VSM diameters, the depth of the VSM from the skin, CEAP stages, VAS values and the number of days of analgesic requirement after the procedure of the patients are given in Table 2. Of these, VSM diameters, CEAP stages and depth of VSM from the skin were not significantly different between groups.

When VAS scores of the groups were examined, the VAS values in the B and AB blood groups were significantly higher than in the A and O blood groups (p <0.001). VAS scoreswere notdifferent between B and AB blood groups. VAS values in O blood group were significantly higher than the A blood group (p <0.001) but were significantly lower than the B and AB blood groups (p <0.001). VAS scores of patients with A blood group were the lowest among all blood groups (p <0.001) (Figure 2).The mean days of analgesics need after procedure were 4 days in patients with B and AB blood groups, 2 days in patients with 0 blood group and 1 day in patients with A blood group. When the groups were compared in terms of postoperative analgesic need, there was no significant difference between B and AB blood groups. It was significantly higher in patients with B and AB blood groups than patients with A and O blood groups (p <0.001). Analgesic use in patients with 0 blood group was higher than in patients with A blood group, but was significantly lower than those in B and AB blood groups (p <0.001). Patients with the least analgesic requirement were those with A blood group (p <0.001).

Table 1: Age and gender characteristics of patients according to blood groups

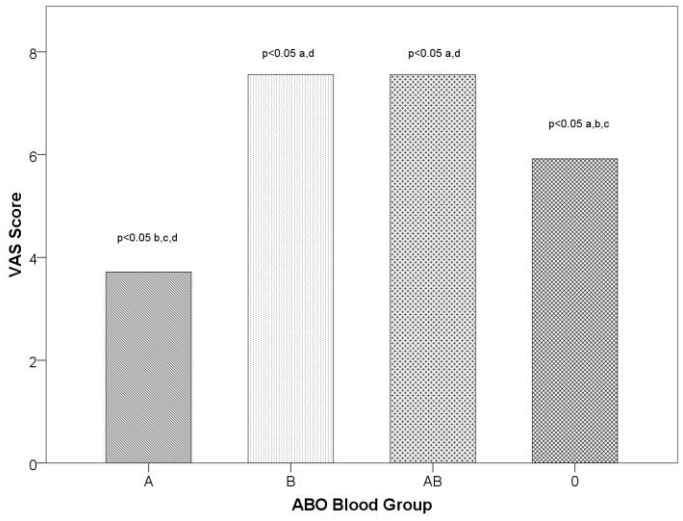
			Blood groups				
			A	B	AB	0	P
Age		Median(Q1-Q3)	46(38-52)	48(41-54)	46.50(38-52)	48.50(38-54)	0.499[a]
Gender	Male	N(%)	16 (25.8)	14 (22.6)	10 (16.1)	22 (35.5)	0.071[b]
	Female	N(%)	34 (24.6)	36 (26.1)	40 (29)	28 (20.3)	

[a]Kruskal Wallis H test; [b]Chi-Squaretest;a:0.05

Table 2: Relation between clinical characteristics and VAS score

	Blood groups A Median(Q1-Q3)	 B Median(Q1-Q3)	 AB Median(Q1-Q3)	 0 Median(Q1-Q3)	p
VSM diameters (mm)	6.7(6.1-7.5)	6.7(6.3-7.2)	6.5(6.1-7.7)	6.9 (6.2-7.4)	0.805
CEAP stages	2(2-3)	3(2-3)	3(2-3)	3(2-3)	0.074
Number of days in need of analgesics after procedure	1(1-2)[b,c,d]	4(4-5)[a,d]	4(3-5)[a,d]	2(2-3)[a,b,c]	**0.001***
Depth of the VSM (mm)	17 (16-18)	17(14-19)	18(16-19)	18(16-19)	0.131
VAS score	4(3-5)[b,c,d]	8(7-8)[a,d]	7(7-8)[a,d]	6(6-6)[a,b,c]	**0.001***

[a]Kruskal Wallis H test;a:0.05; *Statistically significant; Post-hoc: Dunn-Sidaktest;Bonferroni test; [a]Significantly different from group A; [b]Significantly differentfrom group B; [c]Significantly differentfrom group AB;[d]Significantly differentfrom group O.



[a]Significantly different from group A; [b]Significantly differentfrom group B; [c]Significantly differentfrom group AB;[d]Significantly differentfrom group O.

Figure 2: Relation between ABO blood group and VAS score

DISCUSSION

The main purpose of this study is to investigate whether the levels of pain in patients with PVI treated with venablocktherapy differed between blood types. Venablock treatment procedure is one of the most reliable methods of saphenous vein ablation in patients with venous insufficiency and is perhaps the most comfortable treatment way for patients that does also not lead to labor loss.

This study investigated the relationship between pain sensation during venoblock procedure as well as the need of analgesics in the postoperative period and the ABO blood type in patients with PVI without additional disease.This procedure causes pain of varying severity among patients due to the burning effect of NBCA at the saphenous vein territory. The effects of NBCA on the vessels have been shown by Wang et al. When histopathologic changes after the injection of cynoacrylate into the vessel wall of adult rabbits were examined, following rapid polymerization of NBCA, an acute inflammatory effect was observed in the tissue in the second week. At the end of the second month, chronic granulomatous tissue was formed and eventually progressed to fibrosis. In addition, there was inflammation and necrosis without hyperplasia of elastic fibrils in the venous wall (17).On the other hand, no toxicological, carcinogenic or mutagenic effects of NBCA have been demonstrated previously (18,19).

The most current definition ofpain is made by the International Association for the Study of Pain (IASP). As reported by IASP, pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (20).

According to this definition, pain is always subjective because of being an individual sensation of an undesirable condition. Therefore, when evaluating thepain experience, as well as its physical dimension, subjectivity should be taken into consideration and the patient's pain reporting should be taken as a basis because of perception, description and behavioral reactions to pain will vary individually. Since the pain is a personal symptom, it requires getting to know the patient in all aspects and taking the appropriate history, making continuous observations and using appropriate methods in the assessment of pain.

There are many studies showing the relationship between ABO blood group and various diseases (21-23). On the other hand, studies showing the relationship between pain and ABO blood group are limited. Simino et al. investigated the relationship between pain and ABO blood type with an experimental method. In this study, participants were asked to put their non-dominant hands into an ice bucket in the temperature range of 1-4 °C. Participants were asked to keep their hands in ice water for 2 minutes and to gradethe pain severity according to the VAS score every 10 seconds.

Additionally, the pain severity was measured by an algometer probe when the pressure was felt as pain by applying pressure to the masseter, temporalis and deltoid muscles. When the results obtained from these tests were analyzed according to ABO blood groups, neither pain caused by exposure to ice water nor pain caused by pressure on muscles was found to be related to blood groups. However, it was noticed that pain sensitivity was increased only in AB blood type participants who subjected to pressure test after cold water test (11). In our study, it was found that patients with blood group B and AB were most susceptible to pain, patients with blood group 0 were less sensitive, and patients with blood group A were most resistant to pain. Our study findings were consistent with the study of Simino et al. and showed that patients with AB blood type were the most sensitive group to pain. However, in our study, it was observed that patients with B blood group had similar senseof pain intensity like patients with AB blood group and pain perception severity showed a ranking such as B = AB> O> A in terms of blood groups. Lausten et al. investigated the association between postoperative pain and ABO blood type in patients undergoing anterior cruciate ligament reconstruction and no significant difference was found between blood groups and analgesic use, but it was shown that patients with 0 blood type were more likely to use analgesics (24). In another study investigating the effect of blood groups on pain perception, male students kept their dominant hands in 4-6 ° C cold water. After the subjects had put their hands in cold water, the first time they felt pain and the time they had taken their hands from the water were recorded. When these measured durations were evaluated according to blood groups, there was no significant difference between ABO blood groups and pain sensation, but the sensitivity of the AB blood group to pain was found to be higher (25). Although no significant relationship was demonstrated between ABO blood group and pain in these two studies, the authors stated that there may be higher sensitivity to pain in AB and O blood groups and recommended further studies with increased number of subjects (24, 25). Our findings are consistent with these studies in terms of the relationship between AB blood group and pain sensitivity. We found that there was a significant relationship between ABO blood groups and pain which was evaluated according to VAS score during venablock treatment in patients with venous insufficiency. In addition, there is a significant relationship between ABO blood groups and the need for analgesics in the postoperative first 5 days.

CONCLUSION

The number of articles investigating the relationship between ABO blood group and pain is very limited. In our study, it was clearly seen that pain occurred during venablock treatment and postoperative analgesic need were related to ABO blood group in patients with PVI. Accordingly, the relationship between pain and blood group may contribute to pain management for both diagnostic and therapeutic purposes. However, more comprehensive studies are needed to understand the interaction between ABO phenotype and pain perception.

Conflict of interest

No conflict of interest was declared by the authors.

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