Research Article

Volume of 4% sodium bicarbonate required to remove pain in tumescent anaesthesia for endovenous laser ablation of saphenous veins: a randomized, double-blind, controlled trial

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Bukina OV. Volume of 4% sodium bicarbonate required to remove pain in tumescent anaesthesia for endovenous laser ablation of saphenous veins: a randomized, double-blind, controlled trial. J Phlebol Lymphol. 2018;11(1): 3-6.

Background: Sodium bicarbonate in tumescent anaesthesia for endovenous laser ablation (EVLA) of saphenous varicose veins is underused.
Objective: To find the volume of 4% sodium bicarbonate required to significantly reduce intraprocedural pain.
Methods: Tumescent solution ingredients were determined by recalculating concentrations based on the Klein solution and was titrated to a slightly alkaline pH by buffering with 4% sodium bicarbonate. The outcome variable was the level of intraprocedural pain measured with a visual analogue scale.
Results: In total, 74 patients undergoing EVLA were randomized to receive either buffered solution at pH 7.1 (group A) or buffered solution at pH 6.63 (group B). Median pain scores (interquartile range) were significantly lower in patient group A than in group B (0.65 (0.2-1.38) versus 1.65 (0.87-3.5), $p<0.01$).
Conclusions: These results show that tumescent anesthesia for EVLA of saphenous veins is less painful if the local anesthetic is buffered prior to its infiltration. Nonetheless, the buffering may be inadequate. We advise adding 143 mL of 4% sodium bicarbonate to 1000 mL 0.08% lidocaine so that the pH of the solution is increased to 7.1 and the intraprocedural pain is reduced significantly.
Key Words: Tumescent anaesthesia, Infiltration pain, Endovenous laser ablation, Saphenous veins, Sodium bicarbonate.

INTRODUCTION

Endovenous laser ablation (EVLA) is the most popular surgical treatment for varicose veins in many countries. This procedure is often performed under local anaesthesia. However, subcutaneous injection of local tumescent anaesthetics may cause discomfort because of the acidity of the solution. Adding sodium bicarbonate reduces the pain associated with local infiltration anaesthesia [1-14].

Most dermatologists and surgeons use lidocaine with epinephrine to prolong the half-life of the anaesthetic, reduce toxicity, and provide haemostasis. Lidocaine with epinephrine is buffered with sodium bicarbonate to a slightly alkaline pH of 7.0 to 7.4 to reduce the pain on infiltration of the local anaesthetic solution. This mixture, including 8.4% sodium bicarbonate, was suggested by Klein [12]. In this study, we used a different concentration of sodium bicarbonate, 4%, because in our country we do not have 8.4% sodium bicarbonate.

OBJECTIVE

Our aim was to compare the level of pain associated with subcutaneous infiltration of the lidocaine solution with epinephrine at different pH levels and to find the optimal volume of 4% sodium bicarbonate to use in the tumescent solution.

METHODS

This study was designed as a prospective, double-blind, randomized, controlled trial in an outpatient department specializing in venous disease (more than 400 surgical procedures per year performed under local tumescent anaesthesia alone) in a multidisciplinary clinic. The study protocol was approved by the regional ethics committee (No.376-B, Ethics Committee of the Medical Faculty of Derzhavin Tambov State University).

The inclusion criteria called for patients with primary varicose veins and clinical, aetiologic, anatomic, and pathophysiologic (CEAP) clinical class C2–C5 venous disease; the criteria further called for patients aged 20-65 years, who were scheduled for EVLA during the period from November 1, 2015 to February 19, 2016. Each participant provided written informed consent to undergo the procedure and take part in the study. The patients were randomized into two groups using the method of envelopes. We performed the block randomization. Based on α of 0.05, it was determined that 32 patients in each group would yield 80% power to detect a median effect size at one point [11]. Given that the operation could be cancelled for any reason, we decided to include in the randomization the 80 patients who were included in the operational plan. Opaque envelopes containing the names of each patient were placed in a drum and mixed together. An employee who was not associated with the clinical work extracted 40 envelopes from the drum. We labelled these envelopes as group A. The remaining 40 envelopes were labelled group B. Due to concomitant diseases, six patients from group A were not operated on and were not included in the study.

A tumescent solution was prepared by the nurse before the procedure according to the group to which they were randomized. A commercially available solution of 10% lidocaine hydrochloride and 0.1% epinephrine was diluted with 1000 mL 0.9% NaCl. The pH of the 0.9% NaCl was 6.85. For buffering, 4% sodium bicarbonate with a pH of 7.87 was used. Concentrations were accordingly recalculated based on the Klein solution, and the solution was titrated to a slightly alkaline pH (7.1). The pH of the solutions was measured with an ABL 80 FLEX pH metre (Radiometer Medical ApS, Russia).

A surgeon (O.V. Bukina), experienced in EVLA techniques and varicose vein surgery, performed all the procedures. After laser fibre placement just distal to the orifice of the superficial epigastric vein in the GSV or at a site not contacting the tibial nerve distal to the deep vein junction in the SSV, local anaesthesia of the skin was performed in a projection of the GSV/SSV under ultrasound guidance using a small-bore needle (30

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Received: January 15, 2018, Accepted: January 29, 2018, Published: February 5, 2018

gauge). It was necessary to reduce the pain from needling using larger bore needles (21 gauge). Tumescent anaesthesia was performed without a pump for both groups.

In all patients, EVLA was supplemented by Varady phlebectomy. However, in view of the randomization and blinding we believe that phlebectomy influences pain in both groups equally, and we did not account for the phlebectomy in comparing groups.

The pain during injection of local anaesthetics was estimated with a visual analogue scale (VAS) that ranges from 0 (indicating no pain) to 10 (indicating the most extreme pain possible). The VAS was tested on each patient by a person independent of the physician after the operation. The physician paid attention to reports by each patient of the pain they felt at the stage of anaesthesia.

STATISTICAL ANALYSIS

Analyses were performed using the IBM SPSS Statistics v 20.0 software package. Qualitative characteristics of the samples were tested with the χ^2 test. For group comparisons of the quantitative values, the Mann-Whitney U test or Student's independent samples t-test was used. A p-value of <0.05 was considered to indicate statistical significance.

RESULTS

According to the recommendations of Jeffrey A. Klein, an addition of 12.5 mL 8.4% sodium bicarbonate to 1000 mL of the 0.05% lidocaine solution results in a concentration of sodium bicarbonate of ≈0.1%. We calculated it by the formula $p_2=p_1/(b/A + 1)$, where p_1-concentration of sodium bicarbonate before dilution, p_2-concentration of sodium bicarbonate after dilution, b-volume 0.9% NaCl, and A-volume of sodium bicarbonate before dilution. However, we used 4% sodium bicarbonate, which is why we added 25.6 mL 4% sodium bicarbonate to 1000 mL 0.05% lidocaine solution. We calculated it by the formula $A=b/(p_1/p_2-1)$, where p_1-concentration of sodium bicarbonate before dilution, p_2-concentration of sodium bicarbonate after dilution, b-volume 0.9% NaCl, and A-volume of sodium bicarbonate before dilution.

The concentration of sodium bicarbonate became 0.1%, but the pH reached only 6.9. In a separate solution, we used 0.08% lidocaine. When we added 26 mL 4% sodium bicarbonate to 1000 mL 0.08% lidocaine solution, the pH became 6.63. By means of titration, it was established that a pH of 7.1 was achieved by adding 143 mL 4% sodium bicarbonate to 1000 mL 0.08% lidocaine solution. Because of these results, we performed the trial by comparing two separate tumescent solutions that differed in their buffering. The pH of buffered solution A was 7.1, and the pH of buffered solution B was 6.63 (Table 1).

Table 1: Mixture and pH of the tumescent solution prepared by the nurse before the procedure.

	Solution A	Solution B
Cold NaCl 0.9% (4°C)	1000 mL	1000 mL
10% lidocaine	8 mL	8 mL
0.1% epinephrine	0.4 mL (1: 2,000,000)	0.4 mL (1:2,000,000)
4% sodium bicarbonate	143 mL	26 mL
pH	7.1	6.63

The patients were randomized into two groups: group A consisted of 34 patients who received the tumescent solutions with a pH of 7.1, and group B consisted of 40 patients who received the tumescent solutions with a pH of 6.63.

No significant differences were noted in terms of gender, mean age, CEAP classification, ratio of SSV/GSV and mean volume of solution injected during tumescent anaesthesia between the two groups (Table 2).

Table 2: Baseline patient characteristics.

	Group A (n=34)	Group B (n=40)	p
Mean age	44.8 ± 12.2	45.1 ± 9.5	p>0.5[a]
Gender (men/women)	25/9 73.5%/26.5%	33/7 82.5%/17.5%	p>0.5[b]
CEAP Clinical grade			
C2	29	32	
C3	4	6	p>0.5[b]
C4	1	1	
C5		1	
Mean volume of solution, mL	438.2 ± 153.7	432.5 ± 172.6	p>0.2[a]
Ratio of SSV/GSV	1/34 2.90%	5/40 12.50%	p>0.05[b]

[a]Student's independent samples t-test; [b]χ^2 test.

The median (interquartile range) pain score (VAS) in group A was 0.65 (0.2-1.38), whereas the pain score in group B was 1.65 (0.87-3.5) (Figure 1). According to the Mann-Whitney U test, the difference between the mean values for pain scores was statistically significant ($p<0.01$). Five of the 34 patients (14.7%) of group A felt no pain (pain score of 0) while in group B, there were no scores of 0 ($p<0.02$). We reasoned that severe pain was represented by a score of 5 or greater. In group A, there was only one score of 5 or greater (2.9%), and in group B there were six values of 5 or greater (15%); but the difference between the groups did not reach statistical significance, as measured by a χ^2 test ($p>0.05$) (Table 3). The maximum pain score was lower in group A (5.9) than in group B (8.7). In group A, most scores were between 0 and 1. In group B, there were fewer scores between 0 and 1 than in group A, and the distribution of points was uniform between 1.1 and 9. The pain scores from one patient (5.9) from group A and four patients (7.1-8.7) from group B differed greatly from those of the other participants. We believe that the severe pain of these patients was due to their extremely low pain threshold. No adverse events were reported.

Table 3: The pain score on the Visual Analog Scale (VAS) in group A and group B.

	Group A (n=34)	Group B (n=40)	p
Median pain score (interquartile range)	0.65 (0.2-1.38)	1.65 (0.87-3.5)	p<0.01[a]
No pain score	5/34 14.70%	0/40 0%	p<0.02[b]
Pain score 5 or greater	1/34 2.90%	6/40 15%	p>0.05[b]

[a]Mann-Whitney U test.

Complications and side-effect (systemic toxicity, CNS reactions, cardiovascular reactions, local tissue toxicity, and hypersensitivity reactions including anaphylaxis) was not detected in each group.

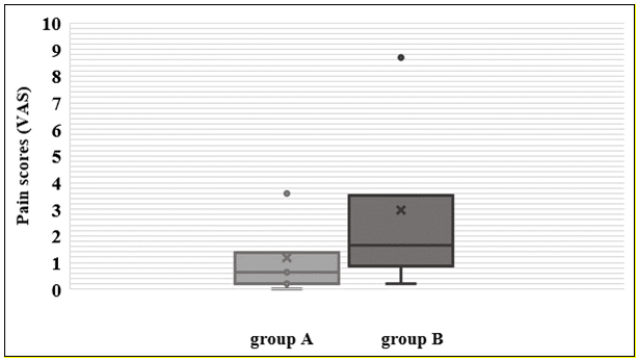

Figure 1: Pain scores (VAS) in groups A and B.

DISCUSSION

We believe that the level of pain experienced by patients during tumescent anaesthesia depends on the amount of sodium bicarbonate that is part of the solution. With the use of small doses of sodium bicarbonate the pH of the solution does not reach alkaline values, and thus patients feel uncomfortable [1,4]. This fact can explain the results of some previous studies in which the difference in pain between groups of patients treated with buffered and unbuffered solution was insignificant. The pH of the buffered solution in this studies was 7.05 [1,4]. In more recent studies, researchers have used Klein's solution in which the volume of the buffer was 2 times more than in the earlier studies. In later studies, the difference in the pain between buffered and unbuffered solutions was significant [7,8,13].

In most studies the median score for pain in groups in which patients received anaesthesia with a buffered solution were in the range of 1.75 to 2.11 [11]. This is slightly above the median score for pain in patients in group A in our study. Perhaps this is due to the fact that immediately prior to infiltration by anaesthetic under the skin we anesthetized the skin with a small diameter needle.

Different countries produce sodium bicarbonate in various concentrations: 4%, 5%, 7%, 8.4%, and 10%. According to the recommendation of J. Klein, a 0.1% solution is obtained by dilution of 12.5 mL 8.4% sodium bicarbonate in 1000 mL tumescent solution [12].

If 4% sodium bicarbonate is used for buffering and the concentrations of the solutions are recalculated to make a 0.1% solution, the desired alkaline pH values will not be achieved. This is because the buffer capacity depends on the concentration of the solution, but is not directly proportional to it. But Klein's solution contains 0.05% lidocaine. If a concentration of more than 0.05%, for example 0.08%, is applied to the same lidocaine, the pH will be even lower.

Therefore, for solutions containing different amounts of lidocaine it is necessary to determine the exact amount of sodium bicarbonate required to achieve slightly alkaline pH values close to physiological levels. We found an optimal volume of 4% sodium bicarbonate, which was able to bring the pH of 0.08% lidocaine and epinephrine to 7.1 and greatly ease the pain during anaesthesia. However, we calculated the amount of sodium bicarbonate only for the amount of lidocaine and epinephrine, which are used in our practice. If a different concentration of lidocaine or sodium bicarbonate is used, it is necessary to titrate the amount of sodium bicarbonate to a pH of 7.1.

Although the pH of the solution in our study was slightly alkaline and did not reach physiological values (7.35-7.45), the pain score did not differ significantly from data obtained in a recent study in which a buffered solution with pH 7.4 was used for tumescent anaesthesia in the EVLA [13]. The pH of commercial lidocaine, epinephrine and 0.9% NaCl can differ considerably and be more alkaline than that used in our study.

In clinical practice, we do not determine the pH of all the components of the tumescent solution. We can easily be wrong and prepare a solution with a pH more than 7.4. Too much alkalization can lead to precipitation of the anaesthetic, rendering it unsafe for use (may lead to tissue necrosis) [15]. Therefore, there is no need to bring the pH of the tumescent solution to physiological values; it is sufficient to use a solution with a pH in the range of 7.1 to 7.35.

Among our patients there were some with hyperalgesia. They are unable to comfortably receive any form of local anaesthesia. This is a small group which requires the use of sedative drugs during an operation.

Limitations to the study

1. We compared the pain associated with local infiltration anesthesia by two buffered solutions with different pH but we did not compare with the pain score of unbuffered solution.
2. The pH of commercial lidocaine, epinephrine and 0.9% NaCl can differ considerably and be more alkaline or acid than that used in the present study.
3. We calculated the amount of sodium bicarbonate only for 0.08% lidocaine.
4. Randomization using the method of envelopes is not the best method of randomization.
5. Pain assessment was performed after surgery but not immediately after anesthesia.
6. Phlebectomy could influence the assessment of pain. But randomization equalizes the influence of phlebectomy in the two groups.

CONCLUSIONS

The tumescent anesthesia for EVLA of saphenous veins is less painful if the local anesthetic is buffered prior to its infiltration. Nonetheless, the buffering may be inadequate. We believe that no need to bring the pH of the tumescent solution to physiological values; it is sufficient to use a solution with a pH in the range of 7.1 to 7.35. We advise adding 143 mL of 4% sodium bicarbonate to 1000 mL 0.08% lidocaine so that the pH of the solution is increased to 7.1 and the intraprocedural pain is reduced significantly. If a different concentration of lidocaine or sodium bicarbonate is used, it is necessary to titrate the amount of sodium bicarbonate to a pH of 7.1.

ACKNOWLEDGMENTS

I thank Alexander Viktorovich Baranov, Candidate of Medical Sciences and a Professor and head of the Department of Faculty Surgery of the Medical Institute at Derzhavin Tambov State University, Tambov, Russia. Dr. Baranov served as scientific advisor.

I thank Iraida Sergeevna Shchegoleva, nurse at the Department of Ambulatory Vascular Surgery, Regional Hospital, Tambov, Russia, for help with preparation of solutions.

I thank Vera Evgenevna Provotorova, biologist at the Clinical Diagnostic Laboratory, Regional Hospital, Tambov, Russia, for help with measurement of the pH of the solutions.

I thank Ulia Alekseevna Kiseleva, assistant surgeon at the Department of Ambulatory Vascular Surgery, Regional Hospital, Tambov, Russia, for help with assessing pain.

CONFLICT OF INTEREST/FUNDING

None

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