Dilution of a mepivacaine-adrenaline solution in isotonic sodium bicarbonate for reducing subcutaneous infiltration pain in ambulatory phlebectomy procedures: A randomized, double-blind, controlled trial

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Background: Varicose veins are treated under local infiltration anesthesia. Literature shows that adding sodium bicarbonate reduces the pain associated with local infiltration anesthesia. Nonetheless, sodium bicarbonate is underused.

Objective: We sought to assess if the use of a solution of mepivacaine 2% plus adrenaline with sodium bicarbonate 1.4% results in less pain associated with local infiltration anesthesia preceding ambulatory phlebectomies, compared with standard preparation diluted with normal saline.

Methods: In all, 100 adult patients undergoing scheduled ambulatory phlebectomy were randomized to receive either a solution of mepivacaine chlorhydrate 2% plus adrenaline in sodium bicarbonate 1.4% or a similar solution diluted in normal saline 0.9%.

Results: Median pain scores associated with local infiltration anesthesia reported in the intervention and control groups were 2 (SD = 1.6) and 5 (SD = 2.0) ($P < .0001$), respectively. A general linear model with bootstrapped confidence intervals showed that using the alkalinized solution would lead to a reduction in pain rating of about 3 points.

Limitations: Patients were not asked to distinguish the pain of the needle stick from the pain of the infiltration. Moreover, a complete clinical study of sensitivity on the infiltrated area was not conducted.

Conclusions: Data obtained from this study may contribute to improve local infiltration anesthesia in ambulatory phlebectomy and other phlebologic procedures. (J Am Acad Dermatol 2014;71:960-3.)

Key words: alkalinized anesthesia; local infiltration anesthesia; phlebectomy; phlebology; reticular veins; varicose veins.

Outpatient surgery for varicose veins is generally performed under local infiltration anesthesia using an amide anesthetic diluted in normal saline 0.9% or lactated Ringer solution.[1,2] The infiltration of local anesthetic causes stinging pain in most patients, along with anxiety and uncooperative behaviors with forthcoming procedures.[3] Local anesthetics are usually marketed as acidic solutions, and this is one of the causes of the pain associated with local infiltration anesthesia.[4-6] Interestingly, sodium bicarbonate added in small concentrations can reduce the pain associated with

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local infiltration anesthesia.[4,7-12] Indeed, alkalinization of the anesthetic solution speeds the crossing of the neurilemma and, consequently, the clearance of local anesthetic from the interstitium, thus reducing pain.[13] However, the perceived risk of precipitation of the alkalinized anesthetic and tissue damage might limit the use of this solution.[14,15] The purpose of this randomized controlled trial was to assess whether a solution of mepivacaine 2% plus adrenaline diluted with sodium bicarbonate 1.4% compared favorably with an analogous anesthetic solution diluted with normal saline 0.9% in terms of safety and capacity to alleviate pain associated with local infiltration anesthesia in outpatient surgical treatment of varicose veins.

CAPSULE SUMMARY

- Buffering local anesthetics may ease pain during local infiltration anesthesia, yet this solution is underused.
- We present a randomized controlled trial to evaluate the balance between risks and benefits of using an alkalinized anesthetic solution in ambulatory phlebectomy procedures.
- Anesthetic solution diluted with sodium bicarbonate appears to reduce pain associated with local infiltration anesthesia.

METHODS

This was a monocentric, randomized, active-controlled, double-blind clinical trial with parallel assignment involving adult patients undergoing elective ambulatory phlebectomy. The study was approved by the local ethical committee, protocol number 18/12 PAR ComET CBM (Parere del Comitato Etico Campus Bio-Medico), and registered at ClinicalTrials.gov, number NCT01611324. Exclusion criteria were as follows: any acute disease; chronic kidney or liver disease; allergy to amide anesthetics; sinoatrial node disease or any degree of atrioventricular block; major psychiatric disorders; treatment with analgesics, monoamine oxidase inhibitors, or tricyclic antidepressants; and alcohol abuse. All patients with edema or skin lesions received dressing until adequate healing, and no patient presented alterations of the skin around the operating field that could enhance the perception of pain. The study took place at the phlebology service of University Campus Bio-Medico in Rome, Italy. After signing written informed consent, the patients enrolled were randomly assigned to 1 of the 2 groups in 1:1 ratio using a blocked randomization design with a fixed block size of 10. Study drugs were prepared as follows: in the experimental group, a solution of mepivacaine chlorhydrate 2% and adrenaline was diluted in sodium bicarbonate 1.4% (4 mL mepivacaine chlorhydrate 20 mg/mL with epinephrine 5 μg/mL [Carbosen 2%] diluted in 16 mL sodium bicarbonate 1.4%). The active comparator used in the control group was a solution of mepivacaine chlorhydrate 2% and epinephrine diluted in normal saline 0.9% (4 mL mepivacaine chlorhydrate 20 mg/mL with epinephrine 5 μg/mL diluted with 16 mL sodium chloride 0.9%). Subcutaneous infiltration of the skin was administered along the course of the vein to be removed, using a 20-mL syringe with a 26G needle measuring 19 mm (0.7 in). The investigator inspected syringes before performing anesthesia to detect any precipitate. The patient was prevented from viewing needle pricks.[16] The primary outcome measure was pain severity associated with local infiltration anesthesia, rated by the patient on an 11-point numeric rating scale (0 = no pain, 10 = worst imaginable pain) after the first 5 injections (placement of the needle plus administration of 2.5 mL of anesthetic solution). Considered as clinically significant, a difference of 1 point between the 2 groups' numeric rating scale score means, assuming a type I error rate of 5%, a sample size of 50 patients per group was deemed sufficient to give 80% statistical power to detect this difference.[17] The anesthetic syringe was prepared according to the allocation sequence by a nurse who was uninvolved in any other study procedure. Syringes were completely identical in appearance. Local infiltration anesthesia was performed using exactly the same brand and type of needle for each patient (Microlance 3, Becton Dickinson Labware, Franklin Lakes, NJ), and a single needle was used throughout the entire procedure. Statistical analysis was performed by an external party, blinded to the allocation, using the R 2.15 × 64 software (R Development Core Team, Vienna, Austria). To assess possible differences in pain ratings, preliminary bivariate analyses were performed. The pain level reported was crossed with age brackets ($\leq$ 49, 50–63, $\geq$ 64 years), gender, presence of diabetes, and type of anesthetic solution (alkalinized anesthetic solution [AAS] and non-AAS). Bivariate association significance was assessed using nonparametric tests. An ordinal logistic regression was therefore performed to verify the effect of all independent variables (gender, age brackets, type of anesthetic, and diabetes presence). Odds proportionality assumption was satisfied within the model (P = .36). The ordinal and vector generalized