ORIGINAL ARTICLE

Buffered versus non-buffered lidocaine with epinephrine for subcutaneous implantable venous access devices insertion reduces pain: A randomized trial

Lidocaïne tamponnée versus non tamponnée avec épinéphrine pour la réduction de la douleur lors de la pose de dispositifs d'accès veineux implantables sous-cutanés: Un essai randomisé

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Abstract

Introduction: Implantable ports (Port-a-Caths) are a mainstay in the treatment of cancer patients. While these devices improve patient experience, their insertion can be painful.

Aim: To compare the analgesic efficacy of buffered and non-buffered lidocaine with epinephrine in reducing pain during Port-a-Caths insertion in cancer patients.

Methods: This study was a prospective, randomized, double-blind, controlled trial. One hundred twenty cancer patients scheduled for Port-a-Cath placement under local anesthesia were randomized to receive either buffered (pH=7.33) or non-buffered lidocaine with epinephrine (pH=3.50). The primary outcome was pain assessed during five procedural steps using a standardized 100-mm visual analog scale (VAS). Secondary outcomes included sensory block onset time and patient satisfaction.

Results: One hundred twenty patients were enrolled in this study, with sixty patients in each group. Mean pain scores during local anesthesia infiltration were significantly lower in the buffered lidocaine group (15.7 ± 7.6 mm) compared to the control group (46.9 ± 12.3 mm; $p < 0.001$). Mean VAS satisfaction scores were significantly higher in the buffered lidocaine group (95.75 ± 8 mm) compared to the control group (70.2 ± 20.1 mm; $p < 0.001$). Sensory block onset time, as determined by pinprick test, was significantly shorter in buffered lidocaine group (3.25 ± 1.3 min) compared to control group (5.5 ± 1.3 min; $p < 0.001$).

Conclusion: Alkalinizing lidocaine with epinephrine significantly reduced pain during Port-a-Cath placement in cancer patients, improving anesthesia quality and patient satisfaction.

Key words: Vascular Access Devices; pain ; Anesthesia ; neoplasms

Résumé

Introduction: Les chambres à cathéters implantables (Port-a-Caths) sont couramment utilisées en oncologie. Bien que ces dispositifs améliorent l'expérience des patients, leur insertion peut être douloureuse.

Objectif: Comparer l'efficacité analgésique de la lidocaïne tamponnée et non tamponnée avec épinéphrine pour réduire la douleur lors de l'insertion de Port-a-Caths chez les patients cancéreux.

Méthodes: Cette étude était un essai prospectif, randomisé, en double aveugle, contrôlé. Cent vingt patients cancéreux ont été randomisés pour recevoir de la lidocaïne tamponnée ou non tamponnée avec épinéphrine. Le critère principal était la douleur évaluée lors de cinq étapes procédurales à l'aide d'une échelle visuelle analogique (EVA) standardisée de 100 mm. Les critères secondaires étaient le délai de début du bloc sensoriel et la satisfaction du patient.

Résultats: Cent vingt patients ont été inclus dans cette étude, avec soixante patients dans chaque groupe. Les scores de douleur moyens pendant l'infiltration de l'anesthésique local étaient significativement plus faibles dans le groupe lidocaïne tamponnée (15,7±7,6mm) par rapport au groupe contrôle (46,9±12,3 mm). Les scores de satisfaction EVA moyens étaient significativement plus élevés dans le groupe lidocaïne tamponnée (95,75±8 mm) par rapport au groupe contrôle (70,2±20,1 mm). Le délai de début du bloc sensoriel, était significativement plus court dans le groupe lidocaïne tamponnée (3,25±1,3 min) comparé au groupe contrôle (5,5 ±1,3 min).

Conclusion: La lidocaïne tamponnée avec épinéphrine réduit significativement la douleur lors de la pose de Port-a-Caths chez les patients cancéreux, améliore la qualité de l'anesthésie et la satisfaction des patients.

Mots clés: Dispositifs d'accès vasculaire ; douleur ; anesthésie ; néoplasmes

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Introduction

Repeated venipuncture for administering cytotoxic and supportive therapies is a significant source of discomfort and inconvenience for cancer patients. The physical discomfort, along with the psychological impact of repeated needle sticks, can negatively affect patients' quality of life and adherence to treatment. Subcutaneous implantable venous access devices, such as Port-a-Caths, offer a safe and effective alternative. Typically inserted under local anesthesia, Port-a-Caths provide a convenient and reliable method for delivering chemotherapy and other medications (1).

While local infiltration of epinephrine-containing anesthetic can reduce superficial bleeding associated with Port-a-Cath placement, it can also increase injection pain due to its acidic nature (2,3). Although some studies suggest that adding sodium bicarbonate to lidocaine can alleviate this pain, others have found no benefit (4–6). The efficacy of buffered lidocaine remains controversial (6–10). To the best of our knowledge, no research has examined the effect of adding sodium bicarbonate to epinephrine-containing lidocaine on injection pain during Port-a-Cath insertion in cancer patients.

Therefore, this study aims to compare the analgesic efficacy of buffered and non-buffered lidocaine with epinephrine in reducing pain during Port-a-Cath insertion in cancer patients.

Methods

Study design

This study was a prospective, randomized, controlled, double-blinded study (NCT03628430, updated: August 9, 2018) conducted in the Anesthesia and Resuscitation Department of Farhat Hached Teaching Hospital in Sousse, Tunisia. The Research and Ethics Committee of Farhat Hached Teaching Hospital, Sousse, Tunisia, (IRB00008931, Office for Human Research Protection—US Department of Health and Human Service) approved the study. Before entering this study, a written informed consent was obtained from each patient by the investigators.

Participants

All adult cancer patients scheduled for Port-a-Cath placement under local anesthesia between January 1 and June 30, 2017, were eligible for inclusion.

Exclusion criteria included pregnancy, known allergy to study drugs, current opioid or benzodiazepine use, neuropathy, history of thoracic or cervicofacial radiotherapy, and severe respiratory or cardiovascular compromise. These conditions were excluded due to their potential impact on pain perception and response.

Randomization and Masking

Patients were randomized in a double-blind manner (using computer-generated allocation numbers sealed in brown envelopes) to receive either:

- **Buffered lidocaine group**: Patients in this group received 5 mL of 4.2% sodium bicarbonate added to 10 mL of 2% lidocaine with epinephrine 0.005 mg/mL (Lidocaine adrenaline; Aguettant, France).
- **Control group**: Patients in this group received 5 mL of 0.9% NaCl added to 10 mL of 2% lidocaine with epinephrine 0.005 mg/mL (Lidocaine adrenaline; Aguettant, France).

pH Measurements

pH measurements were obtained using a pH meter (PH-meter/millivoltmeter 3510 JENWAY) at the study's outset. The control group's pH was 3.5, while the buffered lidocaine group's pH was 7.33.

Protocol

To maintain double blinding, a member of the anesthesia team, blinded to group allocation, prepared the local anesthetic solutions in advance. After preparation, solutions were labeled with unique identification codes by an investigator independent of the study team. These pre-filled syringes were then equilibrated at room temperature for 30 minutes before the procedure. Both the anesthesiologist performing the procedure and the patient were blinded to group assignment. The anesthesiologist received syringes with identical labels and administered the randomly assigned local anesthetic without knowledge of its composition.

Vital signs (heart rate, blood pressure, oxygen saturation, respiratory rate) were monitored upon patient arrival in the operating room. Strict aseptic technique was maintained. The insertion site was prepared with depilation, cleansing, rinsing, drying, antiseptic application, and sterile draping. No preoperative sedation, topical anesthesia, or other pain management techniques were administered prior to local anesthetic injection.

Ultrasound was used to confirm the suitability of the target subclavian vein. The operator received a syringe containing one of the randomly assigned local anesthetics. Under ultrasound guidance, 3 mL of local anesthetic was injected directly superficial to the subclavian vein over 10 seconds, maintaining a consistent injection angle. Subsequently, 12 mL was injected to infiltrate the skin and deep tissue of the target area on the anterior chest wall. A 7 Fr non-tunneled catheter was inserted.

Outcome measurements

Pain and Satisfaction Assessment: Patients rated pain and satisfaction using a standardized 100-mm visual analog scale (VAS) (Figure 1). A score of 0 indicated no pain (very satisfied) and 100 represented the worst possible pain (not satisfied) .

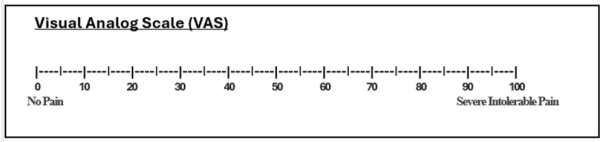

Figure 1. The visual Analog Scale used in the study

Primary Outcome: Pain was assessed on the VAS during five procedural steps: 1) local anesthetic infiltration, 2) central vein cannulation, 3) skin incision, 4) deep tissue dissection and pocket formation, and 5) skin closure.
Secondary Outcomes: Sensory block onset time (determined by pinprick test) and patient satisfaction assessed immediately following the procedure.

Sample size

The required sample size was calculated based on the expectation of a 30 mm decrease in VAS score during local anesthetic injection following alkalinization. With a power of 90%, a two-sided alpha level of 5%, and an estimated standard deviation of 42, a sample size of 42 patients per group was determined. To account for potential missing data or protocol deviations, the sample size was increased to 60 patients per group.

Statistical Analyses

Data were collected on customized data collection sheets and analyzed using IBM SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at a p-value of 0.05. Quantitative variables were presented as mean ± standard deviation and compared using the Student's t-test. Qualitative variables were described as frequencies and percentages and compared using the Chi-square test.

Results

During the study period, 186 patients were scheduled for Port-a-Cath placement. Of the 137 eligible patients approached for participation, 17 (12.4%) declined. All 120 enrolled patients completed the study protocol. No complications, including local reactions or systemic adverse events, were observed in either study group (Figure 2).

There were no significant differences in age, gender, or cancer type between the two randomized groups (Table 1).

Pain scores differed significantly between groups during various procedural steps. Mean VAS satisfaction scores were 83 ± 19.94 mm for the overall population, 95.75 ± 8 mm for the buffered lidocaine group, and 70.2 ± 20.1 mm for the control group ($p < 0.001$) (Table 2).

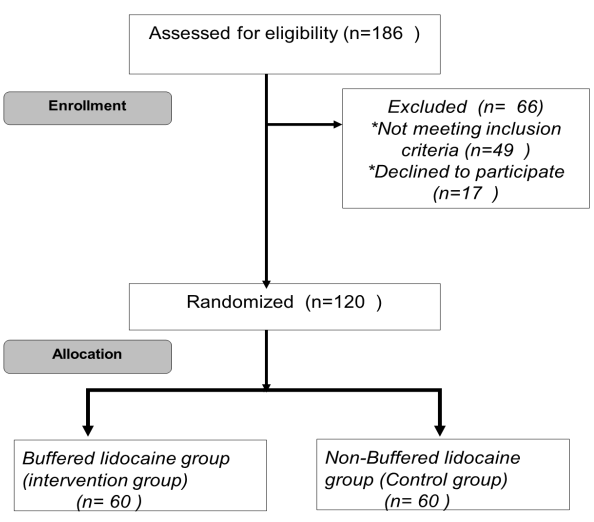

Figure 2. Stydy flow diagram

Table 1. Comparison of sociodemographic characteristics and neoplastic pathology origin in both groups

	Buffered lidocaine group (n=60)	Control group (n=60)	p
Age (mean ± SD)	51.5 ± 12.7	50.2 ± 12.6	0.51
Gender (%)			0.35
Man	22 (36.7)	27 (45)	
Woman	38 (63.3)	33 (55)	
Cancer localization (%)			0.53
Breast	24 (40)	28 (46.7)	
Ovary	1 (1.6)	4 (6.7)	
Colorectal	19 (31.7)	17 (28.3)	
Gastric	4 (6.7)	3 (5)	
Other	12 (20)	8 (13.3)	

Table 2. Comparison of pain scores and patient satisfaction during Port-a-Cath placement between buffered lidocaine and control groups

	Buffered lidocaine group (n=60)	Control group (n=60)	p
Pain scores (mm on VAS)			
Local anesthetic infiltration	15.7±7.6	46.9±12.3	<0.001
Central vein cannulation	8.5±7	14.4±9.7	<0.001
Skin incision	4.9±6.6	10.8±7.6	<0.001
Deep tissue dissection and pocket formation	12.8±9.9	35±20.4	<0.001
Skin closure	3.6±7.7	7.4±8.1	0.008
Patient satisfaction (mm on VAS)	95.75±8	70.2±20.1	<0.001

VAS: Visual Analog Scale; data are presented as mean ± standard deviation; **p**: p-value for between-group comparison

Discussion

Our findings demonstrate that alkalinizing lidocaine with epinephrine effectively reduces Port-a-Cath placement pain and enhances cancer patient satisfaction. Additionally, the onset of anesthesia was accelerated.
These results align with previous studies suggesting that the pain associated with local anesthetic infiltration is related to its acidic pH and alkalinizing lidocaine may provide analgesic benefits (2–6,11–13). Furthermore,

an improved anesthesia quality and increased patient satisfaction have also been reported in the literature (6,14–18). For instance, Yiannakopoulos' study (19) on carpal tunnel decompression found that 55% of patients in the control (non-buffered lidocaine) group would refuse to undergo the same anesthetic technique again, compared to only 18% in the intervention (buffered lidocaine) group.

However, some studies have not demonstrated benefits from lidocaine alkalinization (7,20–22). These results should be interpreted cautiously as many of these studies involved patients with infection or acute inflammation, which can interfere with local acid-base balance and render alkalinization rather random. Moreover, fluctuations in pain characteristics and intensity during inflammation can complicate pain assessment. Notably, several studies have been conducted in pediatric populations undergoing central venous catheterization, which may not accurately represent the general population due to specific pain perception and evaluation in children (23). Culp et al. (24) employed a similar administration protocol (needle size, injection speed, angle, and ultrasound guidance) but they did not observe a reduction in pain related to local anesthetic injection following lidocaine alkalinization. This discrepancy might be attributed to the use of different local anesthetic concentrations.

According to the Henderson-Hasselbalch equation (log [base]/[acid] = pH - pKa), an anesthetic with a low pH predominantly exists in a cationic form, limiting the availability of the free base to penetrate the nerve membrane, and consequently delaying onset of action. Alkalinizing the anesthetic solution can accelerate this process (25). Fuchsjäger-Mayrl et al. compared the corneal permeability of buffered and non-buffered lidocaine (26). They demonstrated that a buffered solution at pH 7 exhibited increased penetration, resulting in a shorter onset time, prolonged duration of action, and reduced local irritation and lacrimation. Furthermore, a double-blind randomized study involving 44 volunteers showed that a buffered 1% lidocaine solution provided a longer anesthetic effect compared to the non-buffered formulation (27).

Lidocaine topical anesthetic has demonstrated antibacterial effects against various microorganisms, which are not compromised by alkalinization (28). A retrospective review of 63 patients (59 fingers and 4 toes) undergoing Mohs micrographic surgery for basal cell carcinoma between October 2002 and January 2009 was conducted to assess the association between local anesthesia (0.5% buffered lidocaine with 1:200,000 epinephrine) and postoperative complications, including infection or necrosis. No cases of digital ischemia or infection were reported (29).

Conclusion

The present study demonstrates that alkalinizing lidocaine with epinephrine can effectively reduce pain intensity during Port-a-Cath placement in cancer patients and improve anesthesia quality, leading to greater patient satisfaction. Given their vulnerability, cancer patients often experience heightened sensitivity to pain. This simple intervention, characterized by low cost, safety, and minimal pharmacological impact, warrants consideration for routine clinical practice in this vulnerable population.

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