

Topical Lidocaine 2% Gel for Analgesia and Patient Comfort during Interscalene Brachial Plexus and Axillary Blocks: A Noninferiority Randomized Trial

Bouts Cédric¹, Van Boxtael Sam¹, Vandepitte Catherine¹, Leunen Ine², Hassanin Jalil³, Louage Sofie⁴, Kuroda Maxine M⁵, Alexander Vloka⁶ and Hadzic Admir^{1*}

¹Department of Anesthesiology, Intensive Care, Emergency Medicine and Algology, Ziekenhuis Oost-Limburg (ZOL), Genk, Belgium.

²Department of Anesthesiology and Intensive Care Medicine, AZ Turnhout, Turnhout Belgium.

³Department of Anesthesiology, Intensive Care, Jessa Ziekenhuis, Hasselt, Belgium.

⁴Department of Anesthesiology and Intensive Care Medicine, AZ Glorieux, Ronse, Belgium.

⁵New York School of Regional Anesthesia (NYSORA), SciMedBE, Leuven, Belgium.

⁶Research Student, Belgium.

*Correspondence:

Admir Hadzic, MD, PhD, Director NAICE (North American Institute of Continuing Education), President, Scientific Medical (SciMedGlobal), 2753 Broadway STE 183, New York. Consultant - Anesthesiology ZOL, Genk, Belgium, Address: 2753 Broadway STE 183, New York, NY 10025; Tel: +1-212-665-1400, E-mail: admir@nysora.com.

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ABSTRACT

Aim: Skin infiltration with local anesthetic is commonly used to decrease patient discomfort during the administration of peripheral nerve blocks. Topically applied local anesthetic gel could provide analgesia while eliminating the need for additional injections of local anesthetics prior to placing the blocks. The primary objective of this study was a noninferiority comparison of the analgesia achieved for needle insertion and injection pain by applying a topical local anesthetic gel or by infiltrating a local anesthetic to the area for placement of an interscalene or axillary brachial plexus block.

Methods: Thirty subjects undergoing surgery of the upper limb were randomized into three treatment groups. Group 1 received 10 g (10 mL) topical lidocaine 2% gel applied to the skin surface over the brachial plexus, Group 2 received a skin infiltration in the same area with 3 cc lidocaine 2%, and Group 3 received aqueous non-medicated ultrasound gel applied over the interscalene space. These treatments were applied 5 min prior to placement of the nerve block. Primary outcome variables were Visual Analogue Scale (VAS) pain scores during needle insertion and injection. Fearfulness of the nerve block was by verbal report on a 5-point Likert scale.

Results: Topical lidocaine 2% gel was found to be noninferior to lidocaine infiltration in improving pain during needle insertion and injection of the interscalene and axillary brachial plexus blocks.

Conclusion: Analgesia conferred by application of lidocaine gel is noninferior to that of infiltration with lidocaine 2% for pain during needle insertion and injection of the interscalene and axillary brachial plexus blocks.

Keywords

Lidocaine, Patient comfort, Peripheral nerve blocks, Premedication.

Introduction

The interscalene and axillary brachial plexus blocks are common anesthetic methods for upper limb surgery [1,2]. While ultrasound

has improved the quality and safety of these peripheral nerve blocks, needle insertion and manipulation during the blocks may cause substantial discomfort that can reduce patient compliance and increase anxiety, fear and dissatisfaction with anesthesia care [3-6]. To decrease pain, some practitioners infiltrate the skin with lidocaine 2% prior to the nerve block. However, this involves extra needle insertions and injections that can result in patient discomfort and increase the risk for intraneural or intravascular trauma.

Gel is used as an acoustic coupling medium for ultrasound-guided nerve blocks. Although a non-medicated water-based gel is the most common choice for this purpose, a water-based lidocaine 2% gel is also widely used, and its cost is similar to that of the non-medicated gel. When applied topically, the gel containing lidocaine may reduce discomfort during needle insertion and injection and can even be time-saving as the gel base can serve as an acoustic coupling medium for ultrasound imaging [6-10]. Thus lidocaine gel would eliminate the need for additional injections to infiltrate local anesthetic into the tissues and the time required to apply more sterile gel for ultrasound conduction.

This trial examined whether topical lidocaine gel 2% applied prior to an interscalene or axillary brachial plexus block provides noninferior patient comfort for the procedure compared to skin infiltration with 3cc lidocaine 2%. We hypothesized that mean pain scores during peripheral nerve block needle insertion and injection using topical lidocaine gel are no worse than mean pain scores using lidocaine infiltration by our prespecified margin of noninferiority. The effect of patient fearfulness of the block on reported pain during needle insertion and injection were also assessed. It was hypothesized that fear of the block differs between subjects given an application of gel and subjects given an infiltration with a needle. It was further hypothesized that fearfulness and pain are positively correlated.

Methods

Study design

This was a single center, noninferiority randomized controlled trial comparing analgesia during interscalene and axillary brachial plexus blocks administered for upper extremity surgery. Noninferiority trials are often performed to assist in finding new treatments that have approximately the same efficacy while offering benefits that the standard (reference) treatment may not provide [11,12]. In this study, peripheral nerve block safety would be enhanced by eliminating the need for additional injections for infiltration that increase risks for tissue and nerve damage, hematoma and/or patient discomfort. Moreover, since lidocaine gel can serve as an acoustic coupling medium, there is no need for additional sterile gel, which is normally used during ultrasound imaging.

This trial is registered with www.clinicaltrials.gov (NCT03206320). After local ethics committee approval (B371201628396) and informed consent, 30 adult subjects were randomized by the method of sealed envelopes in a 1:1:1 ratio to one of three groups: Group 1 subjects received 10 g (10 mL) of topical lidocaine 2% gel applied over the block needle insertion site 5 min prior to their

nerve block (new treatment). Group 2 subjects received 3 mL of lidocaine 2% for skin infiltration 5 min prior to their nerve block (reference treatment). Group 3 subjects received 10 g sterile ultrasound gel prior to their nerve block, and serve to inform the analyses on level of fearfulness among subjects receiving the usual, non-medicated, non-infiltration preparation for ultrasound-guided peripheral nerve blocks.

Inclusion criteria were age 18 years or older, ASA I-III physical class and scheduled for interscalene or axillary brachial plexus block for upper limb surgery. Exclusion criteria were any contra-indication to the use of local anesthetic, existing baseline neurological deficit, inability to assess sensory distribution or communicate with staff, coagulation disorders, infection at the block site, opioid therapy, drug or alcohol abuse, or pregnancy. Staff who performed the blocks were not blinded to the treatment arm, however they did not conduct any of the subject assessments. Conversely, research associates who collected the outcome data were not permitted to view the gel application or infiltration procedures that took place 5 min prior to the blocks.

Primary outcome variables were Visual Analogue Scale (VAS) pain scores marked by the subject on a 100 mm line from 0 “no pain” to 100 “worst imaginable pain” for both needle insertion and injection. Needle insertion VAS represents the pain reported by the subject at the moment of skin puncture with the block needle. Injection VAS represents the pain reported by the subject during the injection of local anesthetic around the neural structures. As no measure of injection fear or anxiety that is suitable for use in the busy clinical setting has been validated [13], a simple Likert scale was devised to assess fear of the nerve block procedure from “1” (no fear) to “5” (very fearful) and was reported by the subject immediately before the block procedures were initiated (gel or infiltration) to avoid confounding block pain with pain reported from the infiltration needle sticks.

Clinical procedure

Prior to performing the nerve blocks, subjects had an intravenous line placed and standard ASA monitoring was maintained throughout the procedure. No premedication was given. All blocks were performed in a designated block room outside the operating room.

The blocks were performed preoperatively using ultrasound guidance, nerve stimulator and injection pressure monitoring. Subjects were placed comfortably in a semi upright position with the head facing the contralateral side. The skin was disinfected with an alcohol solution of chlorhexidine combined with azorubicin. Group 1 received 10 g of topical lidocaine 2% gel applied as a 2-3 mm thick film over the block area for both block anesthesia and ultrasound conduction. Group 2 received a skin infiltration with 3 cc lidocaine 2% (27-gauge needle) and 10 g sterile ultrasound gel (2-3 mm thick film) for ultrasound conduction. Skin infiltration was performed to ensure coverage of the block needle insertion site. Group 3 received 10 g sterile non-medicated ultrasound gel applied as a 2-3 mm thick film over the block area for ultrasound conduction only.

For the interscalene and axillary brachial plexus blocks, the needle was inserted into the brachial plexus sheath using ultrasound and nerve stimulator guidance; evoked motor response <0.5 mA (0.1 msec) was avoided. After negative aspiration and an opening injection pressure below 15 psi, an ultrasound-guided perineural injection of 15 mL bupivacaine 0.5% was administered.

Statistical analysis

Sample size for the noninferiority comparison was based on a noninferiority margin of 25 for each primary outcome (needle insertion and injection VAS) with standard deviation of 15, Type I error (α) 0.05, and power ($1-\beta$) 0.90. If there is truly no difference between the reference and new treatment, then 21 subjects (7/group) are required to be 90% sure that the lower limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) will be above the noninferiority limit of -25 [14,15]. Noninferiority would be declared if the mean needle insertion and injection pain scores for lidocaine 2% gel were no worse than the mean pain scores for lidocaine 2% infiltration, within statistical variability, by a margin of 25 units. Our choice of noninferiority margin was based on the smallest effect size that lidocaine would reasonably and reliably provide when compared with placebo (normal saline) [16]. Sample size parameters were based on the lidocaine infiltration literature [17], but the calculated size of 21 (7/group) was increased to 30 subjects (10/group) to accommodate the analyses assessing the potential impact of patient fearfulness of the block on their subjective reports of pain during needle insertion and injection.

Continuous variables are presented as mean \pm standard deviation or as median [interquartile range]; nominal and ordinal (discrete) variables as n (%) or as ratios.

Lidocaine gel was deemed noninferior to lidocaine infiltration when the lower limit of the confidence interval between the new and reference treatments was above the lower noninferiority limit [18]. Noninferiority comparisons were concluded for pain during needle insertion and for pain during injection, separately.

Differences in needle insertion and injection pain scores by study group were analyzed by one-way ANOVA [19]. Group differences in fearfulness were analyzed by the Mann-Whitney U or Kruskal-Wallis H test, as appropriate. The association of fearfulness with pain was assessed by the nonparametric correlation coefficient, tauB. P-values <0.05 were considered statistically significant. Analyses were conducted using the Statistical Package for the Social Sciences (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

Results

Demographic characteristics and clinical features did not differ among the groups (Table 1). All nerve blocks were successful (Figure 1). One subject who had an interscalene block developed Horner's syndrome, which was self-limiting. Although we did not formally study the quality of ultrasound images among the groups, ultrasound anatomy was easily identified in all subjects. There was

no perceptible difference in image quality.

	Lidocaine gel (n = 10)	Lidocaine infiltration (n = 10)	Non-medicated gel (n = 10)
Age (y)	51 \pm 19	49 \pm 14	49 \pm 14
Gender (M:F)	6 : 4	4 : 6	6 : 4
BMI (kg/m ²)	25 \pm 5	25 \pm 3	28 \pm 3
Laterality (R:L)	7 : 3	5 : 5	7 : 3
Baseline function*	2.5 [1, 4.3]	3 [1, 5]	2.5 [2, 4.3]
Block (Interscalene: Axillary)	7 : 3	5 : 5	4 : 6
Baseline VAS pain	42 \pm 30	52 \pm 29	40 \pm 28

Table 1: Demographic characteristics and clinical features of 30 subjects undergoing interscalene or axillary plexus blocks for upper extremity surgery. Data are mean \pm standard deviation or median [interquartile range] for continuous variables; n (%) for ordinal and nominal (categorical) variables. Gender, laterality, and block type are ratios.

* Baseline function score from 0 (inability to do any activity with the arm) to 5 (normal activity with the arm).

The lower limit of the one-sided 95% confidence interval for the comparison of lidocaine gel with lidocaine infiltration was above the prespecified margin for noninferiority (-25) for needle insertion and injection VAS pain scores [-8.2, 95% CI lower bound -23] and 5.4 (95% CI lower bound -13), respectively] (Figure 2).

Fear of block was distributed evenly across groups (Table 2) and did not differ between the two groups that received gel and the group that received skin infiltration (Mann-Whitney U p-value = 0.131). Fearfulness was positively correlated with both insertion and injection VAS (tauB = 0.337, p = 0.019 and tauB = 0.275, p = .053, respectively).

	Lidocaine gel (n = 10)	Lidocaine infiltration (n = 10)	Non-medicated gel (n = 10)	p-value (overall test)
Pain on needle insertion (VAS)*	23.5 \pm 16.2	15.3 \pm 14.4	17.8 \pm 14.5	ns
Pain during injection (VAS)*	19.1 \pm 15.7	24.5 \pm 18.6	25.1 \pm 21.1	ns
Fearfulness**	2.2 \pm 1.2	1.9 \pm 1.4	3.1 \pm 1.4	0.104

Table 2: Pain on needle insertion, pain during injection, and fearfulness during interscalene and axillary brachial plexus blocks for upper extremity surgery. Data are mean \pm standard deviation.

*VAS pain scores rated from 0 (no pain) to 100 (worst imaginable pain); p-values from 1-way ANOVA.

**Fearfulness rated from 1 (no fear) to 5 (very fearful); p-value from Kruskal-Wallis test by ranks.

Discussion

Noninferiority trials are often performed to help find new treatments that have approximately the same efficacy while offering benefits that the standard treatment may not [11,12]. For instance, using lidocaine gel eliminates the need for additional injections that increase risks for tissue and nerve damage, hematoma and/or patient discomfort. Moreover, lidocaine gel can serve as an acoustic coupling medium, thus avoiding the need for additional

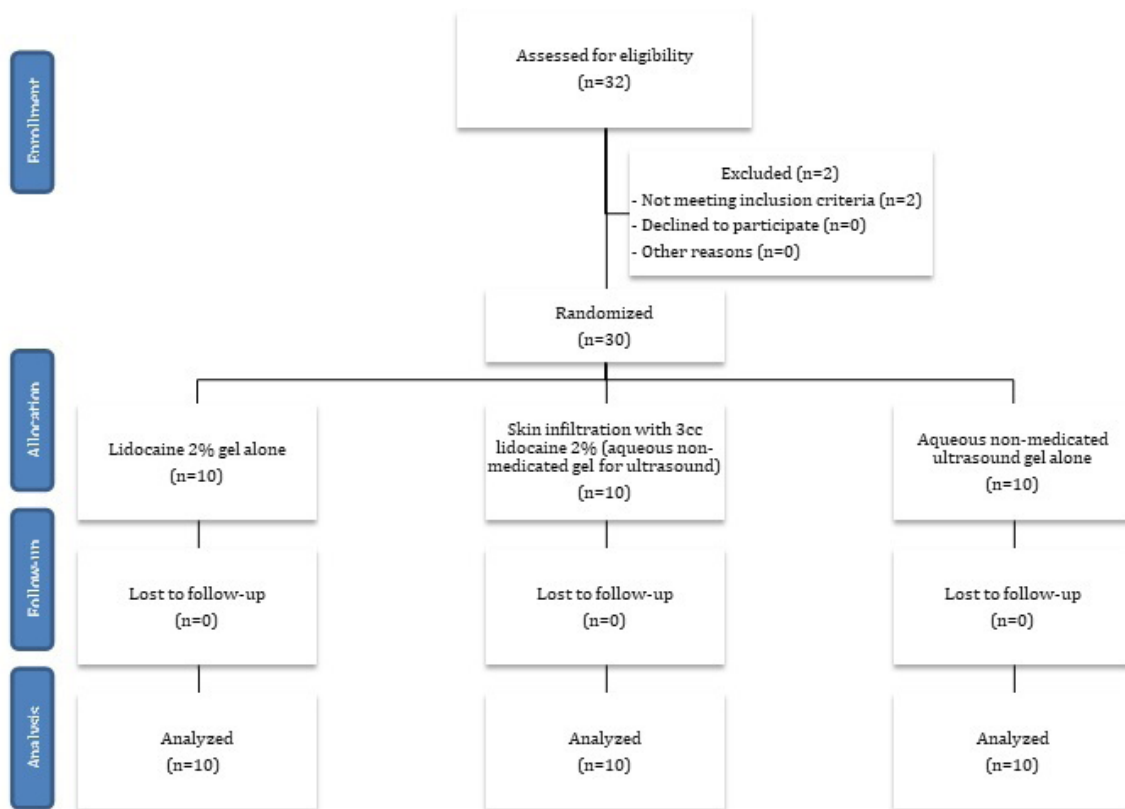


Figure 1: CONSORT diagram of participant flow.

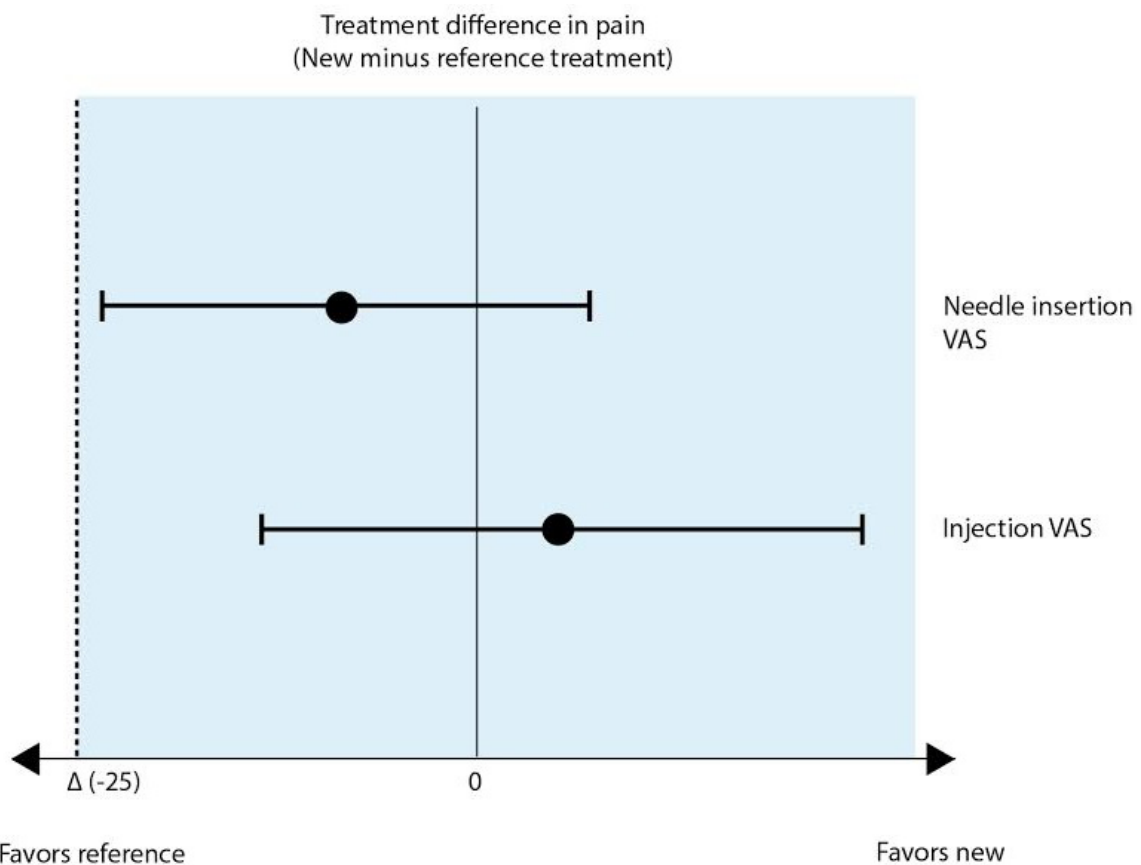


Figure 2: Noninferiority demonstrated by lower bound of 95% confidence intervals for needle insertion and injection VAS pain scores.

sterile gel, which is typically used during ultrasound imaging.

Under the conditions of our study, lidocaine 2% gel did not confer inferior analgesia to lidocaine 2% infiltration for needle insertion or for injection pain during interscalene or axillary brachial plexus blocks. Lidocaine gel could be more effective when applied for a longer period before block performance, comparable to previous studies with different topical agents [7,9,10,20].

However, this could result in its drying, and the advantage of ultrasound conduction may dissipate. Moreover, application of gel as acoustic coupling medium in the practice of peripheral nerve blocks occurs immediately prior to the procedure, i.e., less than 5 minutes before the block. Hence, although lidocaine gel could confer more skin analgesia if left for a longer period of time (e.g., 30 min or more), we chose to apply the lidocaine gel for 5 min, which is more consistent with actual clinical practice.

Our study did not compare different application times or types of ultrasound transmission gel. Other media for ultrasound transmission may be useful, as for example, Sutton et al. used hand sanitizer as an alternative to ultrasound transmission gel [21]. Currently, we are testing higher concentrations of water-based lidocaine gel, e.g., the 5% gel that is available to examine its analgesic effect on needle insertion and injection pain.

Conclusion

Lidocaine 2% gel is noninferior for analgesia during interscalene and axillary brachial plexus blocks compared to infiltration with lidocaine 2% while eliminating the need for additional injections.

References

1. Fredrickson MJ, Krishnan S, Chen CY. Postoperative analgesia for shoulder surgery: A critical appraisal and review of current techniques. *Anaesthesia*. 2010; 65: 608-624.
2. Ranganath A, Srinivasan KK, Iohom G. Ultrasound guided axillary brachial plexus block. *Med Ultrason*. 2014; 16: 246-251.
3. Fredrickson MJ, Kilfoyle DH. Neurological complication analysis of 1000 ultrasound guided peripheral nerve blocks for elective orthopaedic surgery: A prospective study. *Anaesthesia*. 2009; 64: 836-844.
4. Hadzic A, Sala-Blanch X, Xu D. Ultrasound guidance may reduce but not eliminate complications of peripheral nerve blocks. *Anesthesiology*. 2008; 108: 557-558.
5. Marhofer P. Ultrasound guidance in regional anaesthesia. *Br J Anaesth*. 2004; 94: 7-17.
6. Hu P, Harmon D, Frizelle H. Patient comfort during regional anesthesia. *J Clin Anesth*. 2007; 19: 67-74.
7. Raveh T, Weinberg A, Sibirsky O, et al. Efficacy of the topical anaesthetic cream, EMLA, in alleviating both needle insertion and injection pain. *Ann Plast Surg*. 1995; 35: 576-579.
8. Eidelman A, Weiss JM, Lau J, et al. Topical anesthetics for dermal instrumentation: A systematic review of randomized, controlled trials. *Ann Emerg Med*. 2005; 46: 343-351.
9. Speirs AF, Taylor KH, Joanes DN, et al. A randomised, double-blind, placebo-controlled, comparative study of topical skin analgesics and the anxiety and discomfort associated with venous cannulation. *Br Dent J*. 2001; 190: 444-449.
10. Brenner SM, Rupp V, Boucher J, et al. A randomized, controlled trial to evaluate topical anesthetic for 15 minutes before venipuncture in pediatrics. *Am J Emerg Med*. 2013; 31: 20-25.
11. Piaggio G, Elbourne DR, Altman DG, et al. CONSORT Group for the reporting of noninferiority and equivalence randomized trials. *JAMA*. 2006; 295: 1152-1160.
12. Gupta SK. Non-inferiority clinical trials: Practical issues and current regulatory perspective. *Indian J Pharmacol*. 2011; 43: 371-374.
13. Noble LM, Farquharson L, O'Dwyer NA, et al. The impact of injection anxiety on education of travelers about common travel risks. *J Travel Med*. 2014; 21: 86-91.
14. Julious SA. Tutorial in biostatistics: Sample sizes for clinical trials with normal data. *Stat Med*. 2004; 23: 1921-1986.
15. <https://www.sealedenvelope.com/power/continuous-noninferior/>
16. Lee JS, Hobden E, Stiell IG, et al. Clinically important change in the Visual Analog Scale after adequate pain control. *Acad Emerg Med*. 2003; 10: 112-130.
17. Krause RS, Moscati R, Filice M, et al. The effect of injection speed on the pain of lidocaine infiltration. *Acad Emerg Med*. 1997; 4: 1032-1035.
18. Kaul S, Diamond GA. Good enough: A primer on the analysis and interpretation of noninferiority trials. *Ann Intern Med*. 2006; 145: 62-69.
19. Dexter F, Chestnut DH. Analysis of statistical tests to compare visual analog scale measurements among groups. *Anesthesiology*. 1995; 82: 896-902.
20. Zempsky WT, Robbins B, McKay K. Reduction of topical anesthetic onset time using ultrasound: A randomized controlled trial prior to venipuncture in young children. *Pain Med*. 2008; 9: 795-802.
21. Sutton E, Bullock WM, Khan T, et al. Hand sanitizer as an alternative to ultrasound transmission gel. *Reg Anesth Pain Med*. 2016; 41: 655-656.