Can J Anesth/J Can Anesth (2020) 67:617–618
https://doi.org/10.1007/s12630-019-01549-8

CORRESPONDENCE

Effect of temperature on the density, local anesthetic, and glucose concentrations of 0.75% hyperbaric bupivacaine for spinal anesthesia

Shih-Chieh Huang, MD · Anthony Chau, MD, FRCPC, MMSc · Aaron Shapiro, PhD, F-ABFT · Christopher Prabhakar, MD, FRCPC

Received: 26 July 2019 / Revised: 6 November 2019 / Accepted: 8 November 2019 / Published online: 16 December 2019

To the Editor,

Spinal anesthesia is an effective regional block modality with widespread surgical applications. Although backflow of cerebrospinal fluid (CSF) into the spinal needle is a clear endpoint indicating successful entry into the subarachnoid space, the subsequent injection of local anesthetic (LA) still results in spinal block failure in approximately 3.2% of cases.[1] These failures may lead to repeated neuraxial interventions or conversion to general anesthesia with the potential for increased morbidity, as well as decreased patient satisfaction, and even medico-legal consequences.[2] The underlying etiology of a failed spinal anesthetic block is likely multifactorial. Nevertheless, one potential mechanism may be that subarachnoid entry is incomplete with only a part of the needle's bevelled opening being sited in the subarachnoid space. As a result, despite aspiration of CSF, some injectate may be lost into the epidural or subdural space.[2] While many other factors might also contribute to spinal block failure, when failure does occur, the efficacy of the LA solutions is often questioned.[3,4] Exposure of the LA to extremes of hot or cold temperatures during product transport have been suggested as one possible contributor to this diminution of drug efficacy.[3] After experiencing a series of unexplained spinal anesthetic block failures at our institution, we sought to determine the influence of extreme storage temperatures on the density and glucose and drug concentrations of 0.75% hyperbaric bupivacaine.

This *in vitro* study was conducted at St. Paul's Hospital in Vancouver, Canada. We randomly allocated 12 2-mL ampules of 0.75% hyperbaric bupivacaine with 82.5 $mg \cdot mL^{-1}$ glucose (Bupivacaine HCl/Dextrose, preservative free; Hospira Inc., Lake Forest, IL, USA) in a 1:1:1 ratio to one of three temperature groups: -20°C (cold), 20°C (ambient), and 65°C (heated). All samples were from the same lot (Hospira 730163A) that was associated with at least three failed spinal anesthetics at our institution. The cold group samples were stored in a temperature-controlled and monitored biomedical freezer (Sanyo; PHCBi, Wood Dale, IL, USA), the heated group samples were stored in a temperature-controlled and monitored blanket and solution warming cabinet (Imperial Surgical, Scarborough, ON, Canada), and the ambient temperature samples were left at room temperature in the operating room area. After 72 hr of storage, all ampules were then brought to ambient temperature.

The numbered samples were sent to the British Columbia Provincial Toxicology Center and the St. Paul's Department of Pathology and Laboratory Medicine to be processed and analyzed using liquid chromatography-mass spectrometry. Precision for detection and quantitation of bupivacaine is 2.4% while accuracy is measured with a positive bias of 6.79% at 1000 $mg \cdot L^{-1}$. All laboratory technicians and analysts involved with the analysis were

S.-C. Huang, MD
University of British Columbia, Vancouver, BC, Canada

A. Chau, MD, FRCPC, MMSc · C. Prabhakar, MD, FRCPC (✉)
Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada
e-mail: c.prabhakar@ubc.ca

Department of Anesthesia, St. Paul's Hospital, Vancouver, BC, Canada

A. Shapiro, PhD, F-ABFT
BC Provincial Toxicology Centre, Provincial Health Services Authority, Vancouver, BC, Canada

Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

TABLE Density, local anesthetic, and glucose concentrations of hyperbaric 0.75% bupivacaine samples after 72-hr storage in three temperature conditions

	Cold (−20°C) ($n = 4$)	Ambient (20°C) ($n = 4$)	Heated (65°C) ($n = 4$)	P value
Density ($g \cdot mL^{-1}$)	1.022 (0.00003)	1.022 (0.00004)	1.024 (0.00007)	0.94
Bupivacaine concentration ($mg \cdot mL^{-1}$)	7.87 (0.55)	7.94 (0.07)	7.68 (0.22)	0.56
Glucose concentration ($mmol \cdot L^{-1}$)	435.5 (63.2)	442.2 (8.9)	430.8 (37.6)	0.07

Data are represented as mean (standard deviation)

blinded to the group assignment. One-way analysis of variance was used to determine between-group differences with a $P < 0.05$ indicating significance.

We found there was no significant difference in bupivacaine concentration, glucose concentration, or density between the groups (Table). In addition, no bupivacaine degradation products were identified. These data suggest that temperatures under condition of this study have no significant influence on the quality of 0.75% hyperbaric bupivacaine solutions. Our results were consistent with the findings of Wasan et al. who also showed no significant change in bupivacaine concentration with 72-hr storage at 4 or −20°C in comparison with 23°C.[5] Further study should explore the impact of extreme temperatures on dextrose degradation and other physicochemical parameters affecting LA (e.g., pH, pKa), and the subsequent *in vivo* effect of these solutions.

Conflicts of interest None.

Funding statement Departmental.

Editorial responsibility This submission was handled by Dr. Hilary P. Grocott, Editor-in-Chief, *Canadian Journal of Anesthesia.*

References

1. *Fuzier R*, *Bataille B*, *Fuzier V*, *et al*. Spinal anesthesia failure after local anesthetic injection into cerebrospinal fluid: a multicenter prospective analysis of its incidence and related risk factors in 1214 patients. Reg Anesth Pain Med 2011; 36: 322-6.
2. *Fettes PD*, *Jansson JR*, *Wildsmith JA*. Failed spinal anaesthesia: mechanisms, management, and prevention. Br J Anaesth 2009; 102: 739-48.
3. *Smiley RM*, *Redai I*. More failed spinal anesthetics with hyperbaric bupivacaine. Int J Obstet Anesth 2004; 13: 131-4.
4. *Wood M, Ismail F*. Inadequate spinal anaesthesia with 0.5% Marcain Heavy (Batch 1961). Int J Obstet Anesth 2003; 12: 310-1.
5. *Wasan EK*, *Sacevich C*, *El-Aneed A*, *et al*. Investigation into spinal anesthetic failure with hyperbaric bupivacaine: the role of cold exposure on bupivacaine degradation. Can J Anesth 2019; 66: 803-12.