Can precise data improve a nonprecise anesthetic? [Letter]

Axel R. Heller, Thomas Rössel, R. J. Litz

Angaben zur Veröffentlichung / Publication details:

Heller, Axel R., Thomas Rössel, and R. J. Litz. 2007. "Can precise data improve a nonprecise anesthetic? [Letter]." *Anesthesiology* 106 (4): 882–83.
https://doi.org/10.1097/01.anes.0000264785.14855.ea.

Can Precise Data Improve a Nonprecise Anesthetic?

To the Editor:—The article by Heller *et al.*[1] was informative and adds precision to the effect of temperature on the baricity of local anesthetics. They provide interesting new data on the temperature at which local anesthetics used for spinal anesthesia are isobaric (the "isobaric temperature"). Clearly, the next question is, what is the clinical relevance of this added precision? The authors themselves state, "Whether this concept in fact improves patient safety in terms of hemodynamic stability or even allows dose reductions of local anesthetics must be confirmed in further clinical studies."

In 1989, Beardsworth and I published a simple study comparing the injection of 3 ml plain 0.5% bupivacaine at room temperature to an identical solution adjusted to 37°C (very close to but not precisely within the limits [34.3°–35.8°C] of the so-called isobaric temperature).[2] The injection was performed with the patients in the lateral decubitus position, and they were then immediately turned to the supine horizontal position. For the same reasons indicated by Heller *et al.*, we hypothesized that increasing the temperature of the bupivacaine would make it more isobaric and limit its spread. We found no difference in the extent of pinprick analgesia. However, the 37°C solution produced a more prolonged block, which we suggested was due to a decrease in pKa associated with the increased temperature.

Beardsworth's study compared but one dose of bupivacaine and one position after its injection. Other doses and patient positions will likely produce different results.

Heller's and Beardsworth's studies beg the question as to whether it is possible (with the exception of using a very hyperbaric solution for saddle or thoracic levels of block) to precisely control the level of spinal anesthesia. Although the temperature effect on the baricity of local anesthetics used for spinal anesthesia reported by Heller has achieved this pinnacle of precision, this effect will have to overcome the manifold factors that control the level of spinal anesthesia[3] to significantly impact clinical practice. Whether this can be accomplished will only be determined through clinical trials that will undoubtedly derive from Heller's publication. However, after 25 yr of studying, practicing, and watching spinal anesthesia, I suspect that the precise control of the level of spinal anesthesia will require more than simply adjusting the temperature of the injected local anesthetic.

Donald H. Lambert, Ph.D., M.D., Boston University Medical School, Boston, Massachusetts. donlam@fastmail.us or donald.lambert@bmc.org

References

1. Heller AR, Zimmermann K, Seele K, Rossel T, Koch T, Litz RJ: Modifying the baricity of local anesthetics for spinal anesthesia by temperature adjustment: Model calculations. Anesthesiology 2006; 105:346–53
2. Beardsworth D, Lambert DH: Warming 0.5% bupivacaine to 37°C increases duration of spinal anesthesia. Reg Anesth 1989; 14:199–202
3. Greene NM: Distribution of local anesthetic solutions within the subarachnoid space. Anesth Analg 1985; 64:715–30

In Reply:—We thank Dr. Lambert for his comments, which add interesting aspects to the discussion.

The difficulties of controlling local anesthetic (LA) spread during "isobaric" subarachnoid block in daily practice are well-known. As Dr. Lambert states, there is a manifold of influencing factors whereof several are unknown to the practitioner before LA injection (*e.g.*, lumbosacral cerebrospinal fluid volume).

Former studies have confirmed that pharmacokinetic action of cold and warm LA is quite different in the subarachnoid space[1–5] in terms of faster onset and higher maximum level of sensory block when using the warmed solution. Moreover, prolonged analgesia was reported by Dr. Lambert.[6]

After equilibration of the injected LA to cerebrospinal fluid (body) temperature, with the exception of articaine and mepivacaine, all commercially available LA solutions will behave hypobarically. This means that LA after injection at room temperature will initially descend and, after passing the isogravimetric point, ascend. This is supported by the fact that by keeping the patient in a sitting position during and after administration of warmed LA, a higher maximum level of sensory blockade is obtained.[3–5] Shortening the period of sitting or puncturing in the lateral decubitus position masks the hypobaric effect of warmed LA.[2] This may, likewise, be illustrated by Dr. Lambert's study,[6] where no difference in maximum level of sensory blockade was found in patients punctured in the lateral decubitus position and then immediately turned to the supine horizontal position. The clinical impact of positioning during "isobaric" subarachnoid block is further supported by the effect of (un)intended late posture change.[7,8] Further, cerebrospinal fluid density is lower in women.[9] Therefore, the absolute effect of warming LA on individual baricity must be considered smaller in females than in males at a given body temperature and may bias the results.[6]

From the available data, we conclude that the sitting position during puncture is a prerequisite for obtaining clinical impact of the hypobaricity concept of warmed LA solutions in terms of higher maximum level of sensory blockade, and a smaller variability of the number of blocked segments. Whether those observations are clinically transferable into lower doses of warmed LA in the sitting position must be evaluated in forthcoming trials.

With regard to puncturing in the lateral decubitus position, another point of view deserves discussion. Because the sensory nerves derive from the dorsal horn of the spinal cord and the roots are located posterior, in the supine position hypobaric (37°C) LA will ascend ventrally apart from these target structures and may even have less analgesic effect. In this regard, it would have been of particular interest if in his work[6] Dr. Lambert observed differences between anterior or posterior nerve roots. Because motor neurons and sudomotor output derive from the anterior roots, in their setting the usual difference of two segments between sensory and (sudo)motor block may have been lost in the hypobaric (37°C) group. This hypothesis is supported by data in a comparable setting (lateral decubitus puncture) from Higuchi *et al.*,[10] who found a trend to correlation between motor block onset and cerebrospinal fluid density—not, however, between time to peak sensory block level and cerebrospinal fluid density.

The discussion on pKa values of LA in conjunction with subarachnoid block, as already addressed elsewhere,[6,11] should not be overemphasized. LAs gain body temperature within 2 min[12] when injected at room temperature, and pKa values are then equilibrated with those LAs injected at 37°C. Therefore, the decreased pKa values of LAs

injected at 37°C[6] are comparatively effective for 2 min and may account for earlier onset of blockade but not, however, for the prolonged LA effects more than 2 h later.

Taken together, the discussed effects carry uncertainty for daily practice but may, besides others, explain the high interindividual ranges in maximum level of sensory blockade reported in many studies using "isobaric" solutions. *In vitro* studies and modeling as performed in our work[11] always observe and depict a limited part of reality. They never allow conclusions on the reality itself; rather, they may be hypothesis generating or may improve existing hypotheses, which then must be verified (or falsified) in reality. The problems associated with the complex physiology of subarachnoid block may not be solved with simple physics. The intention of our study was to identify isobaric temperatures and, thus, make the course of LA within the subarachnoid space more predictable to improve the *nonprecise anesthetic*.

Axel R. Heller, M.D.,* Thomas Roessel, M.D., Rainer J. Litz, M.D. *University Hospital Carl Gustav Carus, Dresden, Germany. axel.heller@uniklinikum-dresden.de

References

1. Callesen T, Jarnvig I, Thage B, Krantz T, Christiansen C: Influence of temperature of bupivacaine on spread of spinal analgesia. Anaesthesia 1991; 46:17–9

2. Kristoffersen E, Sloth E, Husted JC, Bach AB, Husegaard HC, Zulow I: Spinal anaesthesia with plain 0.5% bupivacaine at 19 degrees C and 37 degrees C. Br J Anaesth 1990; 65:504–7

3. Stienstra R, van Poorten JF: The temperature of bupivacaine 0.5% affects the sensory level of spinal anesthesia. Anesth Analg 1988; 67:272–6

4. Stienstra R, Gielen M, Van PF, Kroon JW: Spinal anesthesia with plain bupivacaine 0.5%: Regression of sensory and motor blockade with different temperatures of the anesthetic solution. Anesth Analg 1989; 69:593–7

5. Litz RJ, Reytan N, Vicent O, Wiessner D, Heller AR, Koch T: The influence of the temperature of bupivacaine 0.5% used for lumbosacral spinal anaesthesia (Taylor's approach) on onset and extent of block. Eur J Anaesthesiol 2005; 22:97

6. Beardsworth D, Lambert DH: Warming 0.5% bupivacaine to 37°C increases duration of spinal anesthesia. Reg Anesth 1989; 14:199–202

7. Niemi L, Tuominen M, Pitkanen M, Rosenberg PH: Effect of late posture change on the level of spinal anaesthesia with plain bupivacaine. Br J Anaesth 1993; 71:807–9

8. Vicent O, Litz RJ, Hubler M, Koch T: Secondary cranial extension after spinal anesthesia with isobaric 0.5% bupivacaine following postural change [in German]. Anaesthesist 2003; 52:1035–8

9. Schiffer E, Van GE, Gamulin Z: Influence of sex on cerebrospinal fluid density in adults. Br J Anaesth 1999; 83:943–4

10. Higuchi H, Hirata J, Adachi Y, Kazama T: Influence of lumbosacral cerebrospinal fluid density, velocity, and volume on extent and duration of plain bupivacaine spinal anesthesia. Anesthesiology 2004; 100:106–14

11. Heller AR, Zimmermann K, Seele K, Rossel T, Koch T, Litz RJ: Modifying the baricity of local anesthetics for spinal anesthesia by temperature adjustment: Model calculations. Anesthesiology 2006; 105:346–53

12. Davis H, King WR: Densities of common spinal anesthetic solutions at body temperature. Anesthesiology 1952; 13:184–8