

# The Influence Of Temperature On Spread Of Intrathecal Levobupivacaine

G Aydin, A Süslü, O Özlü, M Aksoy, R Polat

## Citation

G Aydin, A Süslü, O Özlü, M Aksoy, R Polat. *The Influence Of Temperature On Spread Of Intrathecal Levobupivacaine*. The Internet Journal of Anesthesiology. 2010 Volume 29 Number 2.

## Abstract

**Background:** The distribution of spinal anesthesia is affected by many factors such as the density and viscosity and temperature of the local anesthetics. We aimed to compare the effects of 37 °C plain %0.5 levobupivacaine versus 24°C levobupivacaine in regards of intraoperative anesthetic and postoperative analgesic conditions for patients undergoing arthroscopic meniscectomy. **Methods:** In this randomized, blind, prospective trial a total of fifty three patients aged 17-70 years (ASA I-II) scheduled to have elective ambulatory arthroscopic meniscectomy of the knee were randomly allocated into two groups. All patients received intrathecal 3 mL of plain % 0.5 levobupivacaine. Group 1 received the solution that had been previously equilibrated to 37 °C and group 2 received at room temperature(24°C) . Sensory blockade was assessed by loss of pinprick sensation and motor block was assessed using a modified Bromage scale. Readiness of surgery was defined as presence of adequate motor blockade (Bromage  $\geq$  2) and loss of pinprick sensation at L1 at the operative side. Visual analog scale was used to define patients degree of pain. **Results:** The mean time required to achieve readiness to surgery was  $5.07 \pm 0.39$  minutes in Group 1 and  $10.37 \pm 1.13$  minutes in Group 2 ( $p < .01$ ). The interval between intrathecal injection and bilateral loss of pinprick sensation was shorter in Group 1 than Group 2 ( $p < .01$ ). Time to complete block resolution was similar between the groups. Initial cephalad migration of block was faster in Group 1 than Group 2 at the 5th and 10th minutes ( $p < .01$ ,  $p = 0.037$ ). In two groups there was no difference in spread of sensory blockade at 20, 30, 40 minutes ( $p > 0.05$ ). **Conclusions:** We showed an increase in initial cephalad migration of block for the first 10 minutes by warming levobupivacaine % 0.5 from room temperature(24°C) to 37°C.

## INTRODUCTION

Spinal anesthesia is widely used for outpatient procedures because of its fast onset, effective sensory and motor blockade. (1,2). Levobupivacaine, the pure S(-) enantiomer for racemic bupivacaine, is a new long-acting local anesthetic that has recently been introduced in the clinical routine. Because of its significantly decreased cardiovascular and central nervous system toxicity, levobupivacaine seems to be an attractive alternative to bupivacaine (3).

The distribution of spinal anesthesia is affected by many factors such as the density and viscosity of the injectate that in turn, may be influenced by the temperature of the injectate. Warming plain bupivacaine solution to 37°C increases the distribution of spinal anesthesia performed in the sitting position, compared with bupivacaine at 25°C (4). We questioned whether temperature affects the spread of anesthesia with levobupivacaine. Up to date there is no study in current literature regarding the use of intrathecal injection of warmed levobupivacaine in spinal blockade for

arthroscopic meniscectomy. We therefore aimed to compare the effects of 37°C levobupivacaine versus 24°C levobupivacaine in regards of intraoperative anesthetic and postoperative analgesic conditions for patient undergoing arthroscopic meniscectomy.

## METHODS

In this randomised, blind, prospective trial a total of fifty three patients aged 17-70 years (ASA I-II) scheduled to have elective arthroscopic meniscectomy, were allocated into two groups by using a computer generated sequence of numbers and a sealed envelope technique. Patients with respiratory or cardiac disease, diabetes or peripheral neuropathy and patients receiving chronic analgesic therapy were excluded. Patients affected by coagulation disturbances and known hypersensitivity to amide local anesthetic were excluded from the study. Sample size was determined according to the previous studies and data was collected at Ministry of Health Diskapi Education and Research Hospital II. Anesthesiology and Reanimation Department.

Forty-five minutes before anesthesia patients were premedicated with midazolam (0.03 mg/kg), then a 20 gauge iv cannula had been inserted at the forearm, standard volume infusion of lactated Ringer's solution (7mL kg<sup>-1</sup>/hr) was given. Standard monitoring included noninvasive arterial blood pressure, electrocardiogram and pulse oximetry.

After obtaining informed written consent and the approval by the Institutional Ethics Committee, all patients received intrathecal 3 mL of plain levobupivacaine (5mg/ml Abbott, Norway). Group 1 received the solution that had been previously equilibrated to 37 °C for at least 24 hour at a stove (Heraeus®, Germany). Syringes used to administer the levobupivacaine solution were also equilibrated to 37 °C in Group 1. Group 2 received the solution at room temperature (24 °C). Room temperature of the operating rooms were fixed to 24°C. Levobupivacaine stored at room temperature for 24 hours. All patients were placed at the sitting position and dural puncture was performed with the midline approach at the L4-L5 interspace using a 22 gauge spinal needle. The study drug was withdrawn into the syringe within 20 seconds of retrieval from the stove in Group 1. Levobupivacaine was injected at a speed of 1 mL over 10 seconds without barbotage or aspiration by an anesthesiologist who did not know the aim of the present study. The patient was turned supine immediately after spinal injection and the operations were performed with the patients in the supine position.

Sensory blockade was assessed by loss of pinprick sensation (20 gauge needle) in the midclavicular line on both sides every minute till 15. minutes and 20,30,40,50,60 minutes after injection by a blinded investigator. Motor block was assessed using a modified Bromage scale by asking the patient to flex the limb at the hip, knee and ankle joints (0=no motor block, 1=hip blocked, 2= hip and knee blocked, 3=hip, knee and ankle blocked) at the time of injection and at every minute till 15. minutes and 20,25,30,40,50, and 60 minutes of anesthesia. The patient, surgeon and nursing staff taking care of the patients throughout the study were blinded to patient grouping. Clinically relevant hypotension is defined as the decrease in systolic arterial blood pressure >30% of baseline was initially treated with a rapid infusion of 200 mL of normal saline over 10 minutes. If this was ineffective, 5 mg of ephedrine was given intravenously. Bradycardia (decrease in heart rate to <45 bpm) was treated with 0,5 mg atropine intravenously. Readiness of surgery was defined as presence of adequate motor blockade (Bromage ≥ 2) and loss of pinprick sensation at L1 at the

operative side. The quality of spinal block was judged according to the need for supplementary iv analgesic and sedation: adequate spinal block= neither sedation nor analgesics were required to complete surgery; inadequate spinal block= need for additional analgesia (50 µg iv bolus of fentanyl) required to complete surgery; failed spinal block= general anesthesia required to complete surgery. The time to local anesthetic injection for spinal anesthesia to readiness of surgery and the spread of sensory blockade on both sides were recorded. The time from local anesthetic injection to complete resolution of sensory and motor blockades, heart rate, systolic, diastolic and mean arterial pressures every 5 minutes were also recorded during the anesthesia. After the operation, time to complete resolution of block (it was assessed by Bromage scale at 60, 120, 150, 180 minutes and subsequently at 10 minute intervals till complete resolution , urination time, necessity for bladder catheterization and pain treatment during the first 24 hours and readiness for home discharge were also recorded. All patients were asked to define their degree of pain during 24 hours postoperative period by means of visual analog scale (VAS) ranging from 0 (no pain at all) to 10 ( intolerable pain). The VAS scores of patients at rest and at flexion was recorded preoperatively and postoperatively at 2, 4, 8 and 24th hours. Rescue analgesia was obtained in case of VAS ≥ 4.

### **STATISTICAL ANALYSIS**

Statistical analysis were performed using SPSS software (Statistical Package for the Social Sciences, version 11 SPSS Inc., Chicago, IL, USA) for Microsoft Windows. Descriptive features were expressed as mean ± SEM (standard error of mean) or numbers (percentage). Chi-square test and t test were performed to compare descriptive features. T test was used to compare onset times of surgical blockade, surgery times, the level, distribution and resolution of block, visual analog scale score, hemodynamic variables and urination, readiness for home discharge, need for bladder catheterization and pain treatment. When there was a difference in the level of block between left and right, we used their mean as the achieved level. A p value ≤ 0.05 was considered statistically significant.

### **RESULTS**

All the participants were randomly assigned, received the treatment, completed the study protocol and analyzed for the study. The study was conducted between January 2008-September 2009. The two groups were comparable with regard to demographic variables (p>0.05) (Table I). The

anesthesia time and surgical time was similar between the groups ( $p>0.05$ )(Table II).

The mean time required to achieve readiness to surgery was  $5.07\pm0.39$  minutes in Group 1 and  $10.37\pm1.13$  minutes in Group 2 and the difference was statistically significant( $p<0.01$ )( Table III). The interval between intrathecal injection and bilateral loss of pinprick sensation was shorter in Group 1 than Group 2 ( $p<0.01$ )(Table III). Time to complete block resolution was similar between the groups ( $p=0.736$ )(Table III). Initial cephalad migration of block was faster in Group 1 than Group 2 at the 5th and 10th minutes ( $p<0.01, p=0.037$ ). In two groups there was no difference in spread of the sensory blockade at 20, 30, 40 minutes ( $p>0.05$ )(Figure 1). Warming levobupivacaine resulted in faster initial cephalad migration of block and also increased the speed of onset

There were no difference between the preoperative and postoperative VAS scores and hemodynamic variables between the groups ( $p>0.05$ ). Inadequate spinal blockade was not observed in any of the groups. None of the groups needed ephedrine to treat hypotension. First analgesic consumption, pain treatment during the first 24 hours, home discharge was similar between the groups ( $p>0.05$ ) and necessity of bladder catheterization was not required in any of the groups( $p>0.05$ ).

**Figure 1**

Table I: Demographic variables (mean  $\pm$  SD)

	Group I	Group II	p
Number of patients	26	27	
M/F	12/14	9/18	0.340
Age(year)	$44.42 \pm 10.94$	$41.37 \pm 14.01$	0.382

SD: Standard Deviation

**Figure 2**

Table II: Anesthesia and surgical times (mean  $\pm$  SEM)

	Group I	Group II	p
Anesthesia time(min)	$44.42 \pm 4.94$	$42.33 \pm 2.64$	0.708
Surgical time(min)	$38.19 \pm 4.73$	$32.22 \pm 2.03$	0.246

SEM: Standard Error of Mean

**Figure 3**

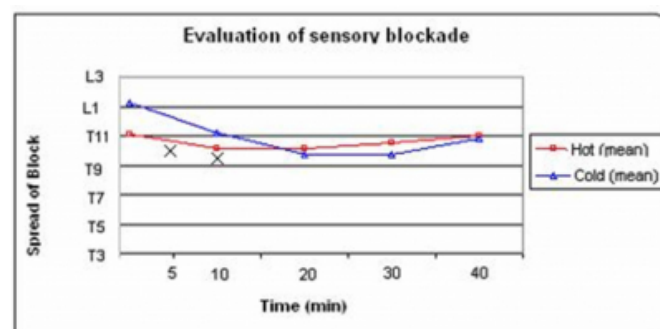
Table III: Characteristics of spinal block and readiness of surgery (mean $\pm$ SEM)

	Group I	Group II	p
Time between intrathecal injection to bilateral loss of pinprick sensation (min)	$4.92 \pm 0.35$	$9.29 \pm 0.65$	$<0.01$
Readiness of surgery (min)	$5.07 \pm 0.39$	$10.37 \pm 1.13$	$<0.01$
Time to complete block resolution (hour)	$4.11 \pm 0.20$	$4.22 \pm 0.23$	0.736

X= $p<0.05$

**Figure 4**

Figure 1: Evaluation of sensory blockade



## DISCUSSION

The density of an anesthetic solution is an important determinant of its spread in the cerebrospinal fluid (CSF) (5). Baricity is a measure of the relative density of local anesthetic solution with a density more than 3 standard deviations below human CSF density. Human CSF density is not uniform however, and varies according to age, sex, pregnancy and illness (6). CSF density ranges from 1.00028 to 1.00100 g/ml, defining the limits in most populations of hypo-hyperbaricity, respectively. Hyperbaric is the ratio more than 1.0 and hypobaric is a ratio less than 1.0 (7).

The density of plain levobupivacaine at 37°C is 1.00024 and at room temperature is 1.00419. Mean density of local anesthetic solution was higher at 23 °C compared with 37°C. The slope of the reduction in density with increasing temperature was equivalent for all plain local anesthetics. For every increase in temperature by 1°C between 23 and 37°C the density of all plain solutions fall by 0.0003 mg /ml. Warming reduces the viscosity and density of the solution which affects the distribution of spinal anesthesia (4).

The levobupivacaine warmed to 37°C led to greater cephalad spread of block assessed by the loss of pinprick sensation when injected into the subarachnoid space with the patient in the sitting position at the first 10 minutes time in our study.

Local anesthetics with a pKa closer to physiologic pH has a higher percentage of non-ionized free base (8). Kamaya et al(9) found that although lidocaine pKa is reduced by approximately 4.3% when warming the solution from 25°C to 38°C, bupivacaine pKa decreases only by approximately 2.9%. For both local anesthetics, a linear relation was found between pKa and solution temperature. Arai et al (10) demonstrated with intra-articular lidocaine that local anesthetic uptake by mammalian nerve increases with increased temperature, this speeds the onset of local anesthesia and improves the quality of block, in our study warming of levobupivacaine increased the speed of onset and resulted with faster initial cephalad migration of block. The change of thermal energy might have influenced the behaviour of the injectate into the subarachnoid space (4). Based on thermodynamics, temperature serves to gauge the intensity of the thermal energy, that is an actual energy of motion of the individually mobile particulate constituents of matter (11). Increased temperature indicates increased molecular kinetic energy and number of individually mobile particles increases by increased temperature (11). So, we hypothesized that an increase in motion of the anesthetic solution by warming might have extended the spread of spinal anesthesia at the 5th and 10th minutes of our study but there was not a difference in height of the sensory level at 20, 30, 40 minutes. Hypobaricity also has been proposed as a mechanism to explain postural effects on the extent of sensory block produced by hypobaric anesthetics (12).

Prewarming local anesthetic solutions is inherently safe provided certain precautions are observed. Local anesthetic ampules may be warmed to 43°C using a thermostatically controlled water bath or intravenous solution warmer. Dry heating may prevent the risk of undetected contamination by water from heating in a water bath, but it is important to ensure that overheating is not allowed to occur (13).

In Stienstra et al's study (14), injecting intrathecal bupivacaine 0.5% at 37 °C resulted a significantly higher cephalad spread than 20°C solution. They showed that the thermal equilibration in the cerebrospinal fluid and the temperature of the bupivacaine 0.5% solution is an important factor in determining sensory spread. They also suggest that using a solution that has been equilibrated previously to 37°C, predictability of the ensuing level of analgesia is good and if a high level of sensory blockade is desired, the solution should be equilibrated to 37°C (14). In our study heating 5% levobupivacaine resulted with faster initial cephalad migration of block.

Our limitation of the study is that we did not directly measure the temperature of the injectates. Although we did not measure the actual temperature of the injectates, in a study comparing the effect of two different temperatures (37°C and 25°C) of hyperbaric bupivacaine on the spread of spinal anesthesia, they found that the temperature was decreased to 36.9°C±0.0°C at 20 seconds after retrieval and decreased to 36.6 °C±0.2°C at 50 seconds after retrieval from the stove (4). We also administered warmed levobupivacaine in 20 seconds after retrieval from the stove.

In conclusion, we showed an increase in the cephalad level of spinal anesthesia by warming % 0.5 levobupivacaine from room temperature to 37°C. This might be caused by the result of decrease in density, viscosity of the injectates and increased molecular kinetic energy by increasing temperature of the local anesthetic solution. Warming levobupivacaine resulted in faster initial cephalad migration of block and also increased the speed of onset.

In busy operating rooms and in ambulatory surgery we suggest that warmed levobupivacaine might be preferable.

### References

1. Cappelleri G, Aldegheri G, Danelli G and colleagues. Spinal anesthesia with hyperbaric levobupivacaine and ropivacaine for outpatient knee arthroscopy: a prospective, randomized, double-blind study. *Anesth Analg*. 2005 Jul;101(1):77-82.
2. Casati A, Moizo E, Marchetti C and colleagues. A prospective, randomized, double-blind comparison of unilateral spinal anesthesia with hyperbaric bupivacaine, ropivacaine, or levobupivacaine for inguinal herniorrhaphy. *Anesth Analg*. 2004 Nov; 99(5):1387-92.
3. Glaser C, Marhofer P, Zimpfer G and colleagues. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. *Anesth Analg*. 2002 Jan; 94(1):194-8.
4. Arai YC, Ueda W, Takimoto E and colleagues. The influence of hyperbaric bupivacaine temperature on the spread of spinal anesthesia. *Anesth Analg*. 2006 Jan; 102(1):272-5.
5. Na KB, Kopacz DJ. Spinal chloroprocaine solutions: density at 37 degrees C and pH titration. *Anesth Analg*. 2004 Jan; 98(1):70-4.
6. McLeod GA. Density of spinal anesthetic solutions of bupivacaine, levobupivacaine, and ropivacaine with and without dextrose. *Br J Anaesth*. 2004 Apr;92(4):547-51.
7. Richardson MG, Wissler RN. Density of lumbar cerebrospinal fluid in pregnant and nonpregnant humans. *Anesthesiology* 1996;85:326-30.
8. Leykin Y, Nespolo R, Foltran F and colleagues. Anesthesia and postoperative analgesia after intra-articular injection of warmed versus room-temperature levobupivacaine: a double-blind randomized trial. *Arthroscopy*. 2009 Sep;25(9):1019-24.
9. Kamaya H, Hayes JJ, Ueda I. Dissociation constants of local anesthetics and their temperature dependence. *Anesth Analg* 1983;62:1025-1030.
10. Arai YC, Ikeuchi M, Fukunaga K and colleagues. Intra-articular injection of warmed lidocaine improves

intraoperative anesthetic and postoperative analgesic conditions. Br J Anaesth. 2006 Feb;96(2):259-61.

11. Stoner CD. Inquires into the nature of free energy and entropy in respect to biochemical thermodynamics. Entropy 2000;2:106-41.

12. Richardson MG, Wissler RN. Densities of dextrose-free intrathecal local anesthetics, opioids, and combinations measured at 37 degrees C. Anesth Analg. 1997 Jan;

84(1):95-913. 13. Jeffrey S, Plzak C, Wynn B and colleagues. Effect of temperature and ph adjustment of bupivacaine for intradermal anesthesia. Am J Emerg Med 1998;16:117-120.

13. Stienstra R, Poorten J.F. The temperature of bupivacaine 0.5% affects the sensory level of spinal anesthesia. Anesth Analg 1988;67:272-6.

**Author Information**

**Gözde Bumin Aydın, MD**

Anesthesiology and Reanimation Department, Ministry of Health Dıskapı Education and Research Hospital

**Asiye Süslü, MD**

Anesthesiology and Reanimation Department, Ministry of Health Dıskapı Education and Research Hospital

**Onur Özlü**

Associate Professor, Anesthesiology and Reanimation Department, Ministry of Health Dıskapı Education and Research Hospital

**Mustafa Aksoy, MD**

Anesthesiology and Reanimation Department, Ministry of Health Dıskapı Education and Research Hospital

**Reyhan Polat, MD**

Anesthesiology and Reanimation Department, Ministry of Health Dıskapı Education and Research Hospital