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REPORTS OF ORIGINAL INVESTIGATIONS

Changes in sensory block level during a programmed intermittent epidural bolus regimen for labour analgesia: a prospective observational cohort study

Changements du niveau de bloc sensoriel au cours d'un schéma de bolus péridural intermittent programmé pour l'analgésie du travail : étude de cohorte observationnelle prospective

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Abstract

Purpose *In the context of a programmed intermittent epidural bolus (PIEB) regimen for labour analgesia, one can identify an upper sensory block level (USBL), defined as the highest dermatome with any altered sensation to cold, and a lower sensory block level (LSBL), defined as the highest dermatome with complete sensory block to cold. This study investigated whether and how these sensory block levels vary within PIEB cycles.*

Methods *We enrolled patients requesting epidural analgesia. An epidural catheter was placed at L2/L3 or L3/L4. A test dose of 3 mL of bupivacaine 0.125% with fentanyl 3.3 $\mu g \cdot mL^{-1}$ was administered, followed by 12 mL of the same solution as the loading dose. A PIEB plus patient-controlled epidural analgesia (PCEA) regimen was initiated 40 min after the loading dose, with bupivacaine 0.0625% with fentanyl 2 $\mu g \cdot mL^{-1}$: PIEB 10 mL, PIEB interval 40 min, PCEA 5 mL, lockout interval 10 min, maximum hourly 30 mL. As per institutional protocol, sensory block levels to ice were assessed 20 min after the loading dose and then hourly. Patients included in the study underwent eight extra assessments: immediately before the second and fourth PIEB and 10, 20, and 30 min after the second and third PIEB.*

Results *We studied 30 patients. The USBL and LSBL achieved their peak value 100 min after the loading dose. The median [interquartile range] USBL was T_8 [T_9–T_7] and T_6 [T_7–T_4] 20 and 100 min after the loading dose, respectively; LSBL was T_{10} [T_{11}–T_6] and T_8 [T_9–T_6], respectively. There was no significant variation in USBL or LSBL within the PIEB cycle between the second and the third or the third and the fourth PIEB.*

Conclusion *Once peak sensory block levels are established, there is no significant variation in the USBL and LSBL within the PIEB cycles.*

Study registration *www.clinicaltrials.gov (NCT04716660); registered 21 January 2021.*

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Résumé

Objectif *Dans le contexte du schéma de bolus périduraux intermittents programmés (PIEB) pour l'analgésie du travail, on peut identifier un niveau de bloc sensoriel haut (USBL) défini comme étant le dermatome le plus haut ayant une quelconque modification de la sensation au froid et un niveau de bloc sensoriel bas (LSBL) défini comme étant le dermatome le plus haut ayant un bloc sensoriel complet au froid. Cette étude a cherché à savoir si et comment ces niveaux de blocs sensoriels varient au cours des cycles de PIEB.*

Méthodes *Nous avons recruté des patientes demandant une analgésie péridurale. Un cathéter péridural a été placé au niveau L2/L3 ou au niveau L3/L4. Une dose test de 3 mL de bupivacaïne 0,125% avec fentanyl 3,3 $\mu g \cdot ml^{-1}$ était administrée, suivie de 12 mL de la même solution représentant la dose de base. Un protocole de PIEB plus analgésie péridurale contrôlée par la patiente (PCEA) a débuté 40 min après l'administration de la dose de base, comportant de la bupivacaïne 0,0625% et du fentanyl 2 $\mu g \cdot ml^{-1}$: PIEB 10 mL; intervalle de PIEB 40 min.; PCEA 5 ml; intervalle de verrouillage 10 min.; maximum par heure 30 mL. Conformément au protocole de l'établissement, les niveaux de bloc sensoriel à la glace ont été évalués 20 min après l'administration de la dose de base, puis toutes les heures. Les patientes incluses dans l'étude ont eu huit évaluations supplémentaires: immédiatement avant le deuxième et le quatrième PIEB et 10, 20 et 30 min après les deuxième et troisième PIEB.*
Résultats *Nous avons étudié 30 patientes. L'USBL et le LSBL ont atteint leur valeur pic 100 min après l'administration de la dose de base. L'USBL médian [plage interquartile] était T_8 [T_9–T_7] et T_6 [T_7–T_4], respectivement 20 et 100 min après la dose de base; Le LSBL était, respectivement, T_{10} [T_{11}–T_6] et T_8 [T_9–T_6]. Il n'y avait pas de variation significative de l'USBL ou du LSBL dans le cycle de PIEB entre le deuxième et le troisième ou le troisième et le quatrième PIEB.*
Conclusion *Une fois les niveaux maximums de blocs sensoriels établis, il n'y a pas de variation significative dans l'USBL et le LSBL dans les cycles de PIEB.*
Enregistrement de l'étude *www.clinicaltrials.gov (NCT04716660); enregistrée le 21 janvier 2021.*

Keywords epidural analgesia · labour analgesia · obstetric analgesia · programmed intermittent epidural bolus (PIEB) · sensory block-level testing

Epidural analgesia is widely used for managing pain during labour. Recent drug delivery systems allow the administration of programmed intermittent epidural bolus (PIEB) combined with patient-controlled epidural analgesia (PCEA).[1–5] Compared with continuous epidural infusion, PIEB produces a better spread of local anaesthetic solutions within the epidural space, resulting in less consumption of local anaesthetics, less motor block, better quality of analgesia, and increased maternal satisfaction.[6,7]

The spread of local anaesthetic solutions into the epidural space follows two distinct patterns. The first, closer to the injection site, is circumferential in nature, and it is thought to produce more effective analgesia. The second, farther from the injection site, is asymmetric and irregular.[8,9] De Souza Soares *et al.* have recently studied the distribution of sensory block to ice during labour analgesia and identified two different sensory block levels: 1) an upper sensory block level (USBL), defined as the highest dermatome with any detectable altered sensation to cold, and 2) a lower sensory block level (LSBL), defined as the highest dermatome with complete block to cold.[10] It is possible that the USBL and LSBL may be the expression of those two different patterns of local anaesthetic distribution. The clinical implication of these findings remains unclear, including the correlation of these block levels with the efficacy of labour analgesia and side effects, such as motor block and hypotension.

These two distinct sensory block levels to ice during labour epidural analgesia have only recently been described.[10] It is unknown whether and how they vary over time during maintenance of labour analgesia with a PIEB plus PCEA regimen. We hypothesized that both USBL and LSBL would change over time during a PIEB regimen, with higher levels soon after a given PIEB bolus and lower levels immediately before the subsequent PIEB bolus.

Methods

This study was approved by the Ethics Review Board, Mount Sinai Hospital, Toronto, Canada (REB 20–0309-E / January 2021) and registered at ClinicalTrials.gov (Trial number, NCT04716660; 21 January 2021; patient enrolment start, 2 February 2021).

Parturients who requested and had no contraindications to receive epidural analgesia were eligible for the study. We included parturients who were $\geq$ 18 yr old, were capable of understanding and signing the written informed consent, had no language barrier when responding to the sensory block assessment, had no medical condition that could compromise the body sensitivity to cold, and who responded satisfactorily to the administration of the loading dose. We considered a satisfactory response to the loading dose a verbal numeric rating score (VNRS) for pain $\leq$ 1 on a 0–10 scale 20 min after its administration. We excluded women who sustained an unintentional dural puncture, delivered before 160 min following the loading dose, required manual or PCEA boluses in the first 80 min after initiation of PIEB, or withdrew consent.

Upon the patient's request, an epidural catheter was placed at the L2/L3 or L3/L4 interspace, with the patient in the sitting position. A preprocedural ultrasound was used to facilitate the procedure. The anesthesiologist identified the epidural space with a 17G Tuohy needle using the loss of

resistance to saline or air and inserted a 19G multiport wire-reinforced epidural catheter (Arrow FlexTip plus; Arrow International Inc, Reading, PA, USA) 5 cm into the epidural space. After negative aspiration of the catheter, a 3-mL test dose of bupivacaine 0.125% plus fentanyl 3.3 $\mu g \cdot mL^{-1}$ was administered, followed by two aliquots of 6 mL of the same solution three minutes apart, for a total volume of 15 mL of the epidural mixture. Upon completion of the test and loading doses, patients were positioned in a semirecumbent position with a wedge under their right hip to alleviate aortocaval compression. Irrespective of the pain score at epidural request, patients who achieved a VNRS ≤ 1 at 20 min after the loading dose proceeded to the maintenance of analgesia with a PIEB plus PCEA regimen.

The maintenance solution was bupivacaine 0.0625% with fentanyl 2 $\mu g \cdot mL^{-1}$. The epidural pump (Cadd-Solis Ambulatory Infusion Pump; Smiths Medical ASD Inc, St. Paul, MN, USA) was programmed to deliver the first PIEB bolus 40 min after the loading dose. The maintenance settings were PIEB bolus 10 mL; PIEB interval 40 min; PCEA 5 mL; lockout 10 min; and maximum hourly 30 mL. Manual top-ups could be administered upon request by nurses and anesthesiologists if required.

The assessment of sensory block to ice was performed with an ice bag (10 $\times$ 20 cm plastic bag half-filled with ice chips) on each dermatome level, on the midclavicular line, bilaterally, from the anaesthetized to the nonanaesthetized area, starting at L1. Each participant was instructed to inform when they first felt any cold sensation caused by the bag of ice (LSBL) and subsequently when the cold felt the same as the control area (USBL). The control area was the C3–C5 dermatome above the clavicle and lateral to the sternocleidomastoid muscle.

As per institutional protocol, patients were assessed for the first time 20 min after the loading dose and then hourly. A recent study suggested that one to two hours is required for full establishment of the sensory block to produce consistent and reproducible assessments.[10] Therefore, for the purposes of the study, we started the additional sensory block-level assessments immediately before the second PIEB, 80 min after the loading dose. Patients included in the study underwent eight extra assessments of the sensory block level to cold (Fig. 1): immediately before the second and fourth PIEB; 10, 20, and 30 min after the second and third PIEB. The study was concluded after the fourth PIEB, 160 min after the loading dose.

In addition to the USBL and LSBL, patients were assessed for pain, using a VNRS ranging from 0 (no pain) to 10 (worst pain ever); satisfaction, using a VNRS ranging from 0 (not satisfied) to 10 (most satisfied possible); systolic blood pressure; and motor block, using a modified Bromage scale ranging from 0 to 3, as follows: grade 0 (no motor block); grade 1 (unable to raise extended legs but able to bend knees); grade 2 (unable to raise extended legs and bend knees, but able to dorsiflex feet); and grade 3 (complete motor block of the lower limbs).[11]

Sample size calculation and statistical analysis

Since there was no information reported in the literature on whether and how USBL/LSBL changed over time during PIEB cycles, we decided to enrol a convenience sample of 30 patients.

The study population was summarized using percentages (counts) and mean (standard deviation) for categorical data and normally distributed continuous data, respectively. For non-normally distributed continuous data, median and interquartile range (IQR) was used instead. The change in USBL and LSBL over time during PIEB cycles was assessed using a quantile regression model for repeated measures. Post hoc analyses using a similar method, but with time being treated as continuous, were used to test whether the increases in both USBL and LSBL from 20 to 100 min were statistically significant. Similarly, the same method was used to test whether both USBL and LSBL remained stable from 100 to 160 min. The data management and statistical analyses were performed using statistical software SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and R (https://www.r-project.org/). A two-sided P value of < 0.05 was used to determine statistical significance.

Results

The study was conducted between January and August 2021. We screened 64 patients for participation; 12 were not eligible for inclusion and 18 declined to participate. Of the 34 patients that agreed to participate, four were excluded: one delivered soon after the loading dose, one exhibited a high sensory block level, one developed hypotension that required changes in the PIEB settings, and one withdrew consent after the beginning of the study. Thirty individuals were included in the final analysis.

Patient demographics and obstetric data are shown in Table. The variation of USBL and LSBL over time, based on a quantile regression model for repeated measures, are shown in Fig. 2. We observed an increase in the median of both USBL and LSBL until 100 min after the loading dose. When sensory levels achieved their peak, they remained stable until the end of the study. The median [IQR] USBL was T_8 [T_9–T_7] and T_6 [T_7–T_4] at 20 and 100 min after the loading dose, respectively; LSBL was T_{10} [T_{11}–T_6] and T_8 [T_9–T_6] at 20 and 100 min after the loading dose, respectively. There was no significant variation in the USBL or LSBL within the second and third PIEB cycles ($P > 0.24$).

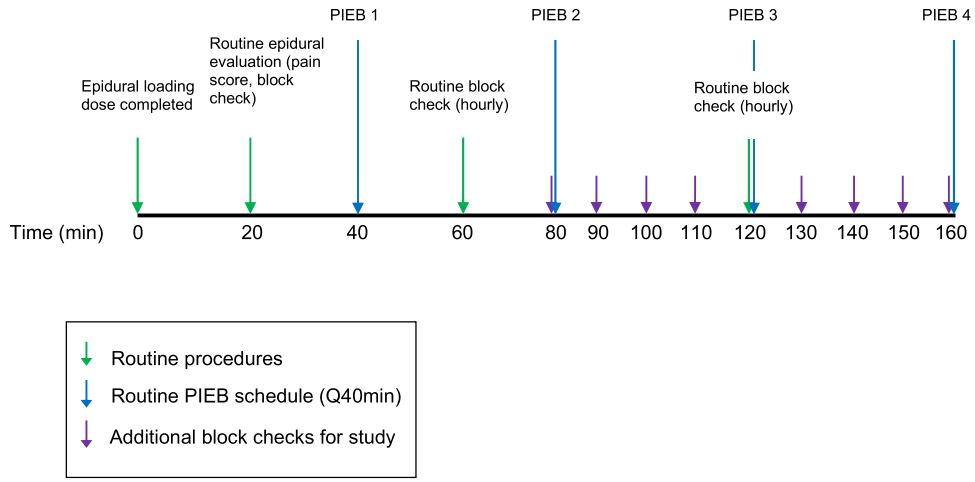

Fig. 1 Timeline of epidural procedures

Table Description of demographic and obstetric characteristics

Patient characteristics and obstetric data	
Age (yr), mean (SD)	34 (4.2)
Weight (kg), mean (SD)	79 (13.3)
Height (cm), mean (SD)	164.5 (6.3)
BMI ($kg \cdot m^{-2}$), median [IQR]	27.6 [26.1–32.2]
GA (weeks), mean (SD)	39.3 (1.0)
Nulliparas, *n*/total *N* (%)	11/30 (37%)
Cervical dilation at epidural request (cm), median [IQR]	4 [3, 4]
Number of contractions/ten minutes at epidural request, median [IQR]	3.5 [3–4.5]
Severe pain at epidural request *n*/total *N* (%)	22/30 (73%)

Severe pain was defined as a pain score > 7

BMI = body mass index; GA = gestational age; IQR = interquartile range; SD = standard deviation

All patients scored 0 on the Bromage scale during the study. No patient presented with hypotension or exhibited VNRS pain > 1 during the study. One patient activated the PCEA feature once and delivered a PCEA bolus. Patient satisfaction was high, with all patients scoring 8/10 or more on the satisfaction questionnaire.

Discussion

Our results confirm the presence of two levels of sensory block to ice during labour epidural analgesia—an USBL and a LSBL. Furthermore, our results suggest that both sensory block levels provided by our epidural regimen achieve their peak around 100 min after the loading dose and remain stable thereafter with no significant variation within the subsequent PIEB cycles.

The confirmation of two different levels of sensory block to ice is in keeping with a recent study by de Souza Soares et al.[10] The USBL and LSBL possibly reflect different densities or intensities of sensory block. Mowat *et al.* showed that the spread of the local anaesthetic solution within the epidural space shows a circumferential pattern closer to the injection site; however, it yields variable degrees of asymmetric and irregular spread as the anaesthetic solution travels away from the injection site.[8] These two different patterns of local anaesthetic distribution likely correspond to the USBL and LSBL, which in our study, ranged from two to three segments apart. The clinical implications of these two different sensory block levels remain to be determined. Our findings confirm the importance of a standardized definition of sensory block. Furthermore, future investigations are warranted to elucidate what sensory block level—USBL, LSBL, or both—anesthesiologists should monitor during epidural analgesia for labour. While the LSBL could in theory explain effective pain relief in labour, the USBL could perhaps be associated with side effects and also predict how successful a top up for a ceasarean delivery would be, should it be required.

Although we hypothesized that the upper and lower sensory block levels would be highest soon after the PIEB and lowest just preceding the subsequent PIEB, there was no significant variation in USBL and LSBL within each PIEB cycle once the peak sensory block levels were achieved around 100 min after the loading dose. The stability of the sensory block level suggests a steady state of the local anaesthetics in the epidural space, possibly associated with the efficacy of our PIEB regimen. We

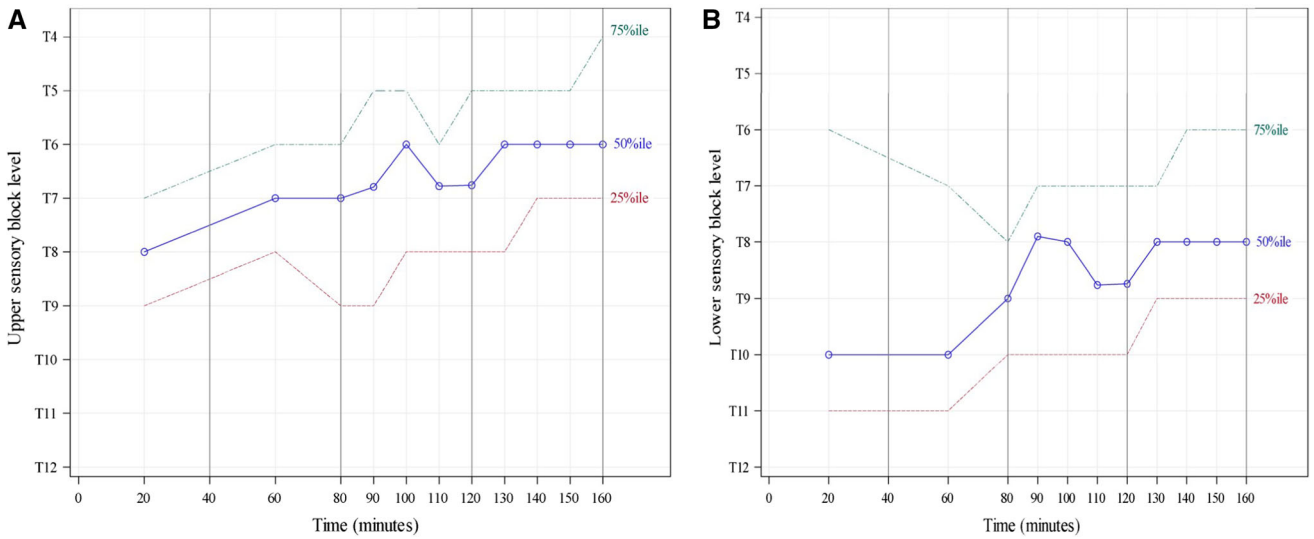

Fig. 2 Median, 25th, and 75th quartiles for the upper sensory block level (A) and lower sensory block level (B) over time. Programmed intermittent epidural boluses were administered 40, 80, 120, and 160 min after the completion of the loading dose (T_0). The median of the upper and the lower sensory block levels reached their peak around 100 min after the loading dose and remained stable thereafter

observed excellent pain control, with only one patient requesting one PCEA bolus, no motor block, and no haemodynamic instability, confirming findings from our previous studies.[12,13] Based on our results, we can recommend that, if this PIEB regimen is used, the assessment of the sensory block can be performed at any time during the PIEB cycle, once the peak sensory block has been established approximately 100 min after the loading dose.

There are some limitations to our study. First, we chose a convenience sample of 30 patients. The small sample size may be underpowered to assess the association of the sensory block level with the quality of the labour analgesia and adverse effects. Second, we only followed patients until the fourth programmed intermittent bolus. Even though the sensory block level is likely to remain stable throughout the first stage of labour, we did not investigate the sensory block level after 160 min from the loading dose or during the second stage of labour.

Conclusion

In conclusion, we confirmed the presence of two levels of sensory block levels to ice during our PIEB regimen. The USBL and LSBL achieved peak levels 100 min after the loading dose and remained stable within the subsequent PIEB cycles until the end of the study. Future studies are warranted to understand the clinical significance of these two different block levels.

Author contributions *Julia Fernandes Casellato*, *Kristi Downey*, and *Jose C. A. Carvalho* contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of data and writing the manuscript. *Xiang Y. Ye* contributed to study conception and design, analysis, and interpretation of data, and writing the manuscript.

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