Effect of Epidural Infusion Bolus Delivery Rate on the Duration of Labor Analgesia

A Randomized Clinical Trial

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ABSTRACT

Background: Programmed intermittent boluses of local anesthetic have been shown to be superior to continuous infusions for maintenance of labor analgesia. High-rate epidural boluses increase delivery pressure at the catheter orifice and may improve drug distribution in the epidural space. We hypothesized that high-rate drug delivery would improve labor analgesia and reduce the requirement for provider-administered supplemental boluses for breakthrough pain.

Methods: Nulliparous women with a singleton pregnancy at a cervical dilation of less than or equal to 5 cm at request for neuraxial analgesia were eligible for this superiority-design, double-blind, randomized controlled trial. Neuraxial analgesia was initiated with intrathecal fentanyl 25 μg. The maintenance epidural solution was bupivacaine 0.625 mg/ml with fentanyl 1.95 μg/ml. Programmed (every 60 min) intermittent boluses (10 ml) and patient controlled bolus (5 ml bolus, lockout interval: 10 min) were administered at a rate of 100 ml/h (low-rate) or 300 ml/h (high-rate). The primary outcome was percentage of patients requiring provider-administered supplemental bolus analgesia.

Results: One hundred eight women were randomized to the low- and 102 to the high-rate group. Provider-administered supplemental bolus doses were requested by 44 of 108 (40.7%) in the low- and 37 of 102 (36.3%) in the high-rate group (difference −4.4%; 95% CI of the difference, −18.5 to 9.1%; P = 0.67). Patient requested/delivered epidural bolus ratio and the hourly bupivacaine consumption were not different between groups. No subject had an adverse event.

Conclusions: Labor analgesia quality, assessed by need for provider- and patient-administered supplemental analgesia and hourly bupivacaine consumption was not improved by high-rate epidural bolus administration. (ANESTHESIOLOGY 2018; 128:745-53)

What We Already Know about This Topic
• There are theoretical reasons to believe that programmed intermittent boluses of epidural local anesthetic with high-rate delivery might be preferable to low-rate delivery of boluses

What This Article Tells Us That Is New
• Two hundred and twenty laboring women were randomized to intermittent boluses with high versus low delivery rate
• Analgesia and the need for supplemental local anesthetic injections were similar in each group
• Programmed high-rate epidural injections do not appear superior to low-rate epidural injections

The earliest reports of neuraxial analgesia for labor pain were published in 1900; since that time there has been a substantial evolution in the use of epidural catheters and the development of pumps to provide continuous labor analgesia to parturients. Today, neuraxial labor analgesia is usually maintained by the injection of local anesthetic combined with opioid through a catheter placed in the lumbar epidural space. Administration of anesthetic solution into the epidural space is usually accomplished by a combination of continuous infusion, provider-administered supplemental boluses, and patient-administered boluses (patient-controlled epidural analgesia [PCEA]). While the ideal combination of administration methods for maintaining labor analgesia is unknown, an optimal analgesic regimen would provide adequate analgesia, while minimizing motor weakness.

Studies suggest that programmed intermittent epidural boluses (PIEB) provide superior maintenance of labor analgesia with less need for provider intervention, lower local anesthetic consumption, and less motor block than maintenance with a continuous infusion. Epidural infusion pumps capable of delivering PIEB with PCEA are commercially available. Many units have implemented PIEB for labor analgesia, but an optimum regimen (drug concentration, bolus dose and interval, bolus delivery rate) has yet to be determined. Studies evaluating variations in PIEB regimens to improve labor analgesia have been focused on varying the...
pump-administered bolus volume and interval between the programmed boluses,5–7 yet have not studied varying bolus delivery rates. Bolus delivery rates are programmable, but whether the delivery rate influences the quality of analgesia is unknown. High-rate delivery of epidural bolus does increase delivery pressure at the catheter orifice and may improve drug distribution in the epidural space compared with low-rate bolus administration.8,9 We hypothesized that patients whose labor analgesia is maintained using a high-rate PIEB and PCEA will have less breakthrough pain, require fewer provider-administered supplemental boluses, have decreased total hourly bupivacaine consumption, and reduced PCEA request-to-delivery ratios, compared with women maintained with a low-rate PIEB and PCEA regimen.

Materials and Methods

The study was approved by the Northwestern University Institutional Review Board (STU00100819) and the protocol was registered at ClinicalTrials.gov (NCT02340806) on December 29, 2014. This manuscript adheres to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. Term, nulliparous, English-speaking patients with singleton vertex pregnancies who were 18 yr or older and presented to the Labor and Delivery Unit of Prentice Women’s Hospital of Northwestern Memorial Hospital (Chicago, Illinois) in spontaneous labor or for induction of labor were eligible to participate in the study. Exclusion criteria before randomization included a history of chronic opioid analgesic use, previous opioid administration during labor, refusal of a vaginal examination before initiation of combined spinal-epidural (CSE) analgesia, or the presence of contraindications to neuraxial analgesia, such as coagulopathy or sepsis. Patients with cervical dilation greater than 5 cm at the request for an epidural analgesia and women that were dilated greater than 5 cm upon presentation to the labor and delivery unit were not approached for inclusion in the study; patients were excluded from the study after randomization if request for provider-administered supplemental bolus, or delivery, occurred within 90 min of intrathecal injection, or if there was a need for epidural catheter replacement during labor.

A convenience sample of eligible women was screened; women who met the inclusion criteria were recruited shortly after admission and provided written informed consent to participate. Recorded baseline maternal characteristics included age, height, weight, gravidity/parity, gestational age, and race/ethnicity. A cervical examination was performed at the time of request for labor analgesia. If cervical dilation was less than or equal to 5 cm, the parturient was randomized to receive PIEB with PCEA with either a low rate (100 ml/h) or high rate (300 ml/h).

Before the study commencement, two-group 1:1 block randomization using randomly select block sizes of 4, 8, and 12 was performed by one of the investigators (P.C.F.) using a computer-generated allocation list.10 Group allocations were concealed in sequentially numbered opaque envelopes that were opened by a research nurse following cervical examination at request for labor analgesia. This research nurse was not blinded to group allocation. All other study personnel, including the anesthesiologist, research nurses performing follow-up assessments, and the study participants, were blinded to group allocation. Similarity of the intervention was made by using high-flow tubing (CADD High-Volume Administration Sets, Smiths Medical, USA), regardless of infusion rate.

A baseline visual analog scale (VAS) pain score was obtained using a 100-mm unmarked line with the endpoints labeled “no pain” and “worst pain imaginable” before the initiation of CSE analgesia. Analgesia was initiated in the sitting position at the estimated L3 to L4 or L4 to L5 interspace. A loss-of-resistance technique was used with a 17-gauge Tuohy needle to identify the epidural space. Intrathecal fentanyl 25 μg (concentration: 50 μg/ml) was administered through a 27-gauge spinal needle (Sprotte, Pajunk, USA). The initiation of analgesia was defined as the time of intrathecal fentanyl administration. A single orifice 19-gauge epidural catheter (Flex Tip Plus, Arrow International, Inc., USA) was threaded and secured 4 to 5 cm in the epidural space and an epidural test dose (1.5% lidocaine with epinephrine 5 μg/ml, 3 ml) was injected. The unblinded research nurse programmed the epidural pump and the bolus rate. The maintenance epidural solution was bupivacaine 0.625 mg/ml with fentanyl 1.95 μg/ml delivered using high-flow tubing (CADD High-Volume Administration Sets, Smiths Medical), regardless of infusion rate to maintain blinding. The PIEB volume was 10 ml administered every 60 min; the first bolus was administered 30 min after intrathecal injection. The bolus was delivered over 6 min (100 ml/h) in the low-rate group and over 2 min (300 ml/h) in the high-rate group. In addition to the programmed bolus, patients were able to self-administer PCEA boluses of 5 ml every 10 min to a maximum of 15 ml/h (three PCEA boluses in a 1-h period, with a lockout period of 10 min) at the same rate as the programmed bolus. The CADD-Solis Pain Management System v3.0 with Programmed Intermittent Bolus (PIB) Model 2110 (Smiths Medical) was used for all study patients.

Fifteen minutes after the intrathecal dose, a VAS pain score, the upper dermatome sensory level of analgesia to ice bilaterally, and a modified Bromage score (0: no motor paralysis; 1: inability to raise extended leg, but able to move knee and foot; 2: inability to raise extended leg and to move knee, but able to move foot; 3: inability to raise extended leg or to move knee and foot) were obtained. These assessments were repeated hourly after the intrathecal dose until the patient reached complete cervical dilation or required cesarean delivery. If a patient requested supplemental analgesia for breakthrough pain, the time of request, medication used for provider-administered supplemental bolus, dose,
and pain scores before and 15 min after the provider-administered supplemental bolus were recorded.

The type of labor (spontaneous, induction) and duration of labor from the initiation of analgesia to delivery as well as the mode of delivery were recorded. Pump utilization data downloaded from the CADD-Solis pumps included the number of PCEA demands and delivered boluses, and the total amount of local anesthetic delivered via the pump. After delivery, the patient reported a final VAS pain score as well as an overall satisfaction with labor analgesia using a 100-mm unmarked line (the left end labeled “not satisfied at all” and the right end labeled “extremely satisfied”).

The primary outcome was the proportion of subjects in each group who had breakthrough pain requiring a provider-administered supplemental bolus by the anesthesia providers. Secondary outcomes were bupivacaine consumption per hour (total amount administered by the pump, as well as in provider-administered supplemental boluses), requested and delivered PCEA boluses, and the request-to-delivery PCEA ratio.

Exploratory analyses included: the time to first request for supplemental analgesia with a provider-administered supplemental bolus, the weighted mean pain score (measured by the area under the VAS-time curve calculated using the trapezoidal integration divided by the duration of labor analgesia), total number of requested provider-administered supplemental boluses, the frequency of motor block, and highest cephalad spread of analgesia to ice during labor. The study was conducted in accordance with the original protocol with the following exception: the criteria for inclusion was changed from a cervical dilation of less than or equal to 4 cm to less than or equal to 5 cm shortly after study recruitment (1 month). This change was made to increase the eligibility of women requesting neuraxial analgesia.

Statistical Analysis

Standardized differences in patient and labor characteristics were calculated for interval data using Hedges’s g, and for ordinal data using Cliff’s delta. The proportion of subjects with breakthrough pain requesting a provider-administered supplemental bolus was compared between low-rate and high-rate programmed bolus groups using a chi-squared statistic with continuity correction. Total hourly bupivacaine consumption requested and delivered PCEA boluses, and the request-to-delivery PCEA ratio were compared between groups using the log-rank test. The weighted mean pain score and hourly bupivacaine consumption were compared between groups stratified by the request for a provider-administered supplemental bolus using the Kruskal Wallis H test, with post hoc comparisons made using Dunn’s test. Motor block was converted to a binomial outcome (Bromage score 0 vs 1, 2, or 3) and the sign test was used to compare the presence of a motor block compared to the baseline. Comparison of motor block between groups were made using a chi-squared statistic with continuity correction. Hourly sensory levels were compared between groups at same time points in labor using the Mann-Whitney U test, and between the 1-h and subsequent time periods using the Wilcoxon signed rank test. Confidence intervals for differences in proportions were calculated using the Pearson-Klopper method, and for the difference in medians using a 10,000 sample bootstrap. Data were analyzed per protocol. Statistical analysis was performed using RStudio version 1.0.153 (Integrated Development for R. RStudio, Inc., USA; http://www.rstudio.com/) and R version 3.4.1, release date June 30, 2017 (The R Foundation for Statistical Computing, Austria).

In previous studies that have used programmed intermittent boluses for maintenance of labor analgesia, the percentage of patients who have required supplemental manual boluses of local anesthetic has ranged between 30 and 50%.6,11 Using a superiority design assuming that 50% of the patients in the 100 ml/h group will require supplemental analgesia and 30% of patients in the 300 ml/h group will require supplemental analgesia, 106 patients per group is required to achieve a power of 80% at an alpha of 0.05 using a two-sided Fisher exact test. To account for study drop-outs, 259 patients were recruited. Sample size calculations were made using Stata SE (version 12, StataCorp, USA).

Results

Four hundred and five parturients were approached for study participation between February 2015 and January 2017; 259 patients consented to participate and 220 patients were randomized to either the low-rate (n = 112) or high-rate (n = 108) group (fig. 1). Ten subjects were excluded from the analysis after randomization as described in figure 1. There were no clinically important differences between groups in age, gestational age, race/ethnicity, body mass index, labor type, cervical dilation, or VAS pain score at time of request for labor analgesia, or mode of delivery and indications for cesarean delivery (table 1).

Analgesia outcomes are shown in table 2. A request for supplemental provider-administered supplemental bolus occurred in 44 of 108 (40.7%) in the low-rate and 37 of 102 (36.3%) in the high-rate group (difference, −4.4%; 95% CI of the difference, −18.5 to 9.1%; P = 0.69). Median (quartile) hourly bupivacaine consumption was 10.8 mg/h (8.6 to 11.4 mg/h) in the low-rate group and 9.9 mg/h (8.1 to 11.4 mg/h) in the high-rate group (difference in medians, 0.9 mg/h; 95% CI of the difference, −0.1 to 1.8 mg/h; P = 0.08). The number of requests and deliveries of PCEA analgesia was not different between groups, with a median request/delivery ratio of 1.5 (1.2 to 2.1) in the low-rate and 1.4 (1.2 to 2.1) in the high-rate group.
Epidural Bolus Rate and Quality of Labor Analgesia

The median time to first request for supplemental analgesia was 302 min in the low-rate group and 357 min in the high-rate group (difference in medians, –55 min; 95% CI of the difference, –162 to 142 min; P = 0.92; fig. 2).

The median weighted mean pain score in the low-rate group was 6.9 mm (3.7 to 15.0 mm) and 9.0 mm (3.9 to 17.2 mm) in the high-rate (difference in medians, –2.1 mm; 95% CI of the difference, –5.3 to 3.0 mm; P = 0.58). When stratified by patients requesting provider-administered supplemental bolus analgesia, there was an increase in the weighted mean pain score and bupivacaine consumption per hour in patients who requested supplemental analgesia within each group, but no differences between groups in patients who did not or did request supplemental bolus analgesia (fig. 3). Median patient satisfaction scores for labor analgesia were 98 of 100 mm in both low- and high-rate groups.

The upper sensory level of anesthesia to ice and motor block are shown in figure 4. Motor weakness, defined as Bromage score greater than 0, occurred in 8 (7%) of patients receiving the low rate and 11 (11%) of patients receiving the high rate (difference, 4%; 95% CI, –5 to 13%; P = 0.31). One patient in the high-rate group had a Bromage score of 3, suggestive of complete motor block. There was no difference in the incidence of motor weakness/block between groups at any time. The median sensory level was T6 at 1 h for both groups (low-rate quartiles T7 to T5; high-rate quartiles T7 to T5). At the end of epidural infusion both groups also had median T6 levels. Sensory levels did not differ between groups at any time during the study.

Discussion

The important finding of this study was that there was no difference in the frequency of requests for supplemental provider-administered analgesia when providing PIEB labor analgesia.
Table 1. Patient and Labor Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Low Delivery Rate (n = 108)</th>
<th>High Delivery Rate (n = 102)</th>
<th>Standardized Difference* (95% CI of the Difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>31 [29 to 33]</td>
<td>32 [29 to 33]</td>
<td>0.01 (–0.26 to 0.28)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>40 [39 to 41]</td>
<td>40 [39 to 41]</td>
<td>0.05 (–0.22 to 0.32)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29 [27 to 33]</td>
<td>29 [27 to 33]</td>
<td>–0.04 (–0.32 to 0.22)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>–0.11 (–0.22 to 0)</td>
</tr>
<tr>
<td>White</td>
<td>79 (73)</td>
<td>86 (84)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>7 (7)</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>9 (8)</td>
<td>5 (5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>13 (12)</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>Labor type</td>
<td></td>
<td></td>
<td>0.01 (–0.11 to 0.14)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>35 (32)</td>
<td>31 (30)</td>
<td></td>
</tr>
<tr>
<td>Induction</td>
<td>73 (69)</td>
<td>71 (70)</td>
<td></td>
</tr>
<tr>
<td>Cervical dilation at request for epidural (cm)</td>
<td>2 [2 to 4]</td>
<td>2 [2 to 3.5]</td>
<td>–0.10 (–0.37 to 0.17)</td>
</tr>
<tr>
<td>VAS pain score (mm) at request for analgesia</td>
<td>73 [62 to 84]</td>
<td>75 [63 to 87]</td>
<td>0.17 (–0.10 to 0.44)</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td>–0.01 (–0.14 to 0.12)</td>
</tr>
<tr>
<td>Vaginal</td>
<td>71 (66)</td>
<td>69 (68)</td>
<td></td>
</tr>
<tr>
<td>Assisted vaginal</td>
<td>13 (12)</td>
<td>9 (9)</td>
<td></td>
</tr>
<tr>
<td>Cesarean</td>
<td>24 (22)</td>
<td>24 (23)</td>
<td></td>
</tr>
<tr>
<td>Indications for cesarean delivery</td>
<td></td>
<td></td>
<td>0.30 (–0.01 to 0.57)</td>
</tr>
<tr>
<td>Arrest of dilation</td>
<td>14 (58)</td>
<td>7 (30)</td>
<td></td>
</tr>
<tr>
<td>Arrest of descent</td>
<td>5 (21)</td>
<td>8 (33)</td>
<td></td>
</tr>
<tr>
<td>Fetal intolerance</td>
<td>5 (21)</td>
<td>9 (37)</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as N (%) or median [25th to 75th percentiles].

*Standardized differences reported as Hedge’s g for interval data and Cliff’s delta for dichotomous data.

VAS = Visual Analog Scale.

Table 2. Analgesia Outcomes and Patient Satisfaction

<table>
<thead>
<tr>
<th></th>
<th>Low Delivery Rate (n = 108)</th>
<th>High Delivery Rate (n = 102)</th>
<th>Difference (95% CI of the Difference)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requests for provider-administered supplemental bolus</td>
<td>43 (40)</td>
<td>37 (36)</td>
<td>4 (–10 to 18)</td>
<td>0.67</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine consumption (mg/h)</td>
<td>10.8 [8.6 to 11.4]</td>
<td>9.9 [8.1 to 11.4]</td>
<td>0.9 (–0.1 to 1.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>PCEA doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requests</td>
<td>17 [10 to 31]</td>
<td>14 [6 to 27]</td>
<td>3 (–3 to 8)</td>
<td>0.21</td>
</tr>
<tr>
<td>Delivered</td>
<td>10 [7 to 17]</td>
<td>9 [5 to 18]</td>
<td>1 (–2 to 4)</td>
<td>0.14</td>
</tr>
<tr>
<td>Request/delivery ratio</td>
<td>1.5 [1.2 to 2.1]</td>
<td>1.4 [1.2 to 2.1]</td>
<td>0.1 (–0.2 to 0.3)</td>
<td>0.66</td>
</tr>
<tr>
<td>Exploratory outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to provider-administered supplemental bolus (min)</td>
<td>302 [148 to 559]</td>
<td>357 [215 to 525]</td>
<td>–55 (–162 to 142)</td>
<td>0.92</td>
</tr>
<tr>
<td>Weighted mean pain score (mm)</td>
<td>6.9 [3.7 to 15]</td>
<td>9.0 [3.9 to 17.2]</td>
<td>–2.1 (–5.3 to 3.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>Stage of labor at redose request</td>
<td></td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>First</td>
<td>40 (93)</td>
<td>34 (92)</td>
<td>1 (–7 to 9)</td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td>3 (7)</td>
<td>3 (8)</td>
<td>–1 (–9 to 6)</td>
<td></td>
</tr>
<tr>
<td>Number of redoses</td>
<td></td>
<td></td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>1</td>
<td>31 (72)</td>
<td>27 (73)</td>
<td>–1 (–14 to 12)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6 (14)</td>
<td>5 (13.5)</td>
<td>0.5 (–10 to 11)</td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>6 (14)</td>
<td>5 (13.5)</td>
<td>0.5 (–10 to 11)</td>
<td></td>
</tr>
<tr>
<td>Satisfaction with labor analgesia</td>
<td>98 [88-100]</td>
<td>98 [86-100]</td>
<td>0 (–2 to 4)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Data presented as N (%) or median [25th to 75th percentiles].
PCEA = patient-controlled epidural analgesia.
analgesia with the high rate (300 ml/h) compared with the low rate (100 ml/h). In addition, bupivacaine consumption, patient request for epidural boluses and deliveries, and the ratio of requests to boluses were not different, suggesting that the quality of labor analgesia was not associated with the change in epidural delivery rate. Exploratory analysis showed no differences in weighted mean pain scores, the number of re-doses, and satisfaction scores, further suggesting no improvement in labor analgesia quality between groups. Although not statistically different, there was an increase in the median time to request for supplemental provider-administered analgesia of 55 min in the high-rate group. While this difference could be clinically significant, given the wide CIs, no definitive conclusions can be made.

There are also important cost implications to our findings. To achieve optimal flow dynamics with PIEB when using higher rates of infusion (greater than 250 ml/h), a high-flow tubing (CADD High-Volume Administration Sets, Smiths Medical) is required. When conventional tubing (CADD Administration Set, Smiths Medical) is utilized with high-programmed infusion rates, the pump will sense high delivery pressures and may not deliver the volume accurately. The high-flow tubing set comes at an additional cost when compared to the conventional tubing set. As either delivery rate should be acceptable in this patient population, and the high-rate group offers no evidence of benefit in terms of clinical outcomes or clinical workload, the avoidance of high-flow tubing by utilizing a lower infusion rate may provide significant cost savings. Because the high-flow tubing set was utilized in both infusion rate groups in this study to maintain blinding, we cannot comment on different infusion rates utilizing the conventional tubing.

In vitro studies have demonstrated that increasing the bolus delivery rate is associated with higher delivery pressures; however, it is unknown if this same relationship is seen in vivo. Higher delivery pressures could result in greater spread of local anesthetic within the epidural space. Kaynar and Shankar, in an in vitro experiment, demonstrated that intermittent boluses were associated with a greater surface area of diffusion than continuous infusion. Similarly, in

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**Fig. 2.** Duration of analgesia until first request for provider-administered supplemental bolus in subjects randomized to receive low-rate programmed intermittent epidural boluses (PIEB) at 100 ml/h or high-rate PIEB at 300 ml/h. The initiation of labor analgesia defined as intrathecal fentanyl administration is time 0. Times are censored at time of first request for provider-administered bolus analgesia or time of delivery. Circles and triangles represent first time patient requested supplemental bolus analgesia. Median (quartiles) duration until first request supplemental bolus request was 302 min (148 to 559 min) in the low-rate group and 357 min (216 to 525 min) in the high-rate group (P = 0.92).

**Fig. 3.** Box plots of weighted mean pain score (upper panel) and hourly bupivacaine consumption (both from the pump as well as the provider-administered supplemental boluses; lower panel) stratified by the request for a provider-administered supplemental bolus. The horizontal line is the median, the box ceiling and floor are the 25th to 75th percentiles, and the whiskers are the 10th and 90th percentiles. Weighted mean pain scores and bupivacaine consumption per hour were increased in patients that requested supplemental analgesia within each group. The weighted mean pain score and bupivacaine consumption per hour in patients that did or did not request supplemental bolus analgesia were not different between the low- and high-rate groups. †Different from no requested provider-administered supplemental bolus(es) within low- or high-rate group; P < 0.05 adjusted for 6 comparisons.
continuous infusions for maintenance of labor analgesia.3
programmed intermittent epidural bolus administration and
uous epidural infusion shown in a meta-analysis comparing
as the difference between PIEB administration and continu-
cadaver study, Hogan found dye injected at high pressures
had more uniform spread throughout the epidural space
supporting the concept of intermittent epidural injection
providing superior analgesia.e This improved spread of
local anesthetic has been the hypothesized mechanism for
improved clinical outcomes with PIEB, such as improved
algesia and lower bupivacaine consumption.11,13
In our study, there was a decrease in the median bupiva-
caine consumption of 0.9 mg/h (95% CI of the difference,
–0.1 to 1.8 mg/h) in the high-rate group compared with the
low-rate group, and although this difference was not statisti-
cally different, over the course of labor this difference could
result in considerable decreases in total bupivacaine adminis-
tered. In addition, the reduction in median bupivacaine con-
sumption per hour observed in this study (1.2 mg/h [95%
CI, 0.3 to 2.2 mg/h]) was on the same order of magnitude
as the difference between PIEB administration and continu-
ous epidural infusion shown in a meta-analysis comparing
programmed intermittent epidural bolus administration and
continuous infusions for maintenance of labor analgesia.3
Therefore, we cannot entirely rule out differences in epidural
distribution of local anesthetic solution between the low-
and high-rate groups.
We observed no differences in the mode of delivery, high-
est cephalad sensory level, or incidence of motor blockade
between low- and high-rate groups. Capogna et al. com-
pared PIEB to continuous infusions and demonstrated a
reduction in total local anesthetic consumption, as well as
motor block, and fewer instrumental vaginal deliveries
in the PIEB group; however, two differing concentrations
of local anesthetic were used for maintenance and PCEA,
possibly accounting for this difference.13 A systematic review
of PIEB to continuous infusions did not find any difference
in motor block; however, PIEB is associated with higher
sensory levels than continuous infusions.5,14 Our study
found that the median sensory level was high (T6), which is
considerably more cephalad than the T10 sensory level nec-
essary to achieve adequate labor analgesia. Yet, the majority
of patients in our study did not experience a motor blockade.
In the literature, six variables have differed among stud-
ies comparing PIEB to continuous epidural infusion tech-
niques: choice of local anesthetic, local anesthetic dose and
concentration, epidural catheter design (single- vs. multi-
orifice), and bolus delivery rate, volume, and interval. The
commercially available pumps with PIEB and PCEA allow
for adjustment of three of these parameters; thus, provid-
ers will need to make several decisions regarding pump
programming and the choice of anesthetic solution in an
try to optimize maintenance of neuraxial labor analge-
sia. Bolus delivery rates have varied significantly in previous
studies examining PIEB infusion rates.6 Wong et al. used a
delivery rate of 400 ml/h and single-orifice epidural catheter
in their initial PIEB paper demonstrating decreased local
anesthetic consumption and improved patient satisfaction
when compared to continuous infusions.11 In a follow-up
study by the same group, the median hourly bupivacaine
consumption was 8.8 mg using a 10 ml bolus delivered every
60 min at 400 ml/h, which is slightly less than the 9.9 mg
observed in the current study using a bolus rate of 300 ml/h.6
In contrast, both Chua and Fettes were able to demonstrate
longer duration of adequate labor analgesia and improved
pain scores using PIEB at lower delivery rates, 100 ml/h and
120 ml/h, respectively;14,15 however, these studies were con-
ducted using multiorifice catheters, which in vitro generate
higher pressures with higher delivery rates than single-orifice
catheters.9
Our study should only be interpreted with respect to its
limitations and may be underpowered for certain outcomes.
We limited our study to nulliparous patients in early labor in
an effort to obtain longer durations of labor analgesia. Lim-
iting our study subjects to nulliparous patients in early labor
could have led to a cohort that was more prone to dysfunc-
tional labor, and these results could be different in multiparous
women with shorter labors. In addition, our study used single-
orifice catheters, which may have resulted in different anes-
thetic spread dynamics than a multiorifice catheter9; therefore,
the results of this study cannot be extrapolated to multiorifice
studies. Furthermore, it is unknown if different bolus volume
with different pressures would result in differences in provider-
administered supplemental bolus rates or time to request for
supplemental analgesia. Our method of motor and sensory
assessment may not have been sensitive enough to detect sub-
tle changes in the extent or density of motor block. We only
assessed cephalad sensory levels, and not caudal sensory levels.
The high rate chosen for this study was chosen because higher
delivery rates have been associated with occlusion alarms (of

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Fig. 4. Box plot of hourly upper sensory levels to cold from
the initiation of labor analgesia, defined as intrathecal fentanyl
administration. The horizontal line is the median, the box ceil-
ing and floor are the 25th to 75th percentiles, and the whis-
kers are the 10th and 90th percentiles. There were no differ-
ences between the low- and high-rate groups.
which we did not experience any),

but it is possible that a difference exists in analgesia between the highest maximum rate settings and that our high rate was too low to detect it.

The data are limited in regard to the location of breakthrough pain, as this was not collected at the time of request for provider-administered supplemental bolus. It is possible that subsets of women may benefit from higher delivery rates, such as those with analgesic “windows” or asymmetric blocks, as the high rate might facilitate better drug distribution. In addition, we cannot exclude the potential benefit of high-rate infusion to parturients with anatomic barriers to optimal drug distribution in the epidural space. We varied not only PIEB, but also the PCEA bolus infusion rates between groups. While it is unlikely that using the different PCEA infusion rates instead of a standard infusion rates would have altered our overall results, we cannot eliminate the possibility. Finally, although our institution uses a standard range of provider-administered supplemental boluses with regard to choice of local anesthetic, volume and concentration, in our study they were not protocolized. This may have altered the subsequent comfort of the parturient.

In conclusion, our study did not find epidural bolus delivery rates are associated with differences in labor analgesia quality, assessed by need for supplemental analgesia, hourly bupivacaine consumption, and PCEA requests and demands. As clinical outcomes were similar between the groups, either bolus delivery rate should be acceptable for clinical care; however, these results might be different with different catheter, drug choice/concentration, bolus volume, and patient population. Future work is needed to determine the optimal delivery rate when other pump and solution parameters are optimized.

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**Competing Interests**

The authors declare no competing interests.

**Reproducible Science**

Full protocol available at: elizabeth.lange@northwestern.edu. Raw data available at: elizabeth.lange@northwestern.edu.

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Dibucaine, Cinchocaine, or Nupercaine? CIBA's Trademarked Long-acting Amide Local Anesthetic

In 1930, pioneering British surgeon-anesthetist W. Howard Jones published his clinical experiences with a long-acting amide local anesthetic related to “butyloxychinocinonic acid diethylylendiamide.” That lengthy chemical designation would be abbreviated to dibucaine in the United States and cinchocaine internationally (“cincho” reflecting the chemical similarity to quine). Dr. Jones published articles about this anesthetic initially under the brand name Percaine, but he predicted that Americans would brand it as Nupercaine. Indeed, from Summit, New Jersey, CIBA Pharmaceuticals would eventually distribute the 5g bottles (above) bearing the trademark “Nupercaine.” (Copyright © the American Society of Anesthesiologists’ Wood Library-Museum of Anesthesiology.)

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