Journal of Regional Anesthesia & Pain Medicine

Open Mind Analysis

doi: 10.39127/2021/JRAPM:1000103
Kodali BS, et al. J Reg Anes Pain Med: JRAPM-103

# An In-Vitro Flow Model Comparing Programmed Intermittent Epidural Boluses Versus Continuous Epidural Infusions with Patient Activated Boluses Commonly Used for Labour Analgesia

***(Running title: Is PIEB better than PCEA? -In vitro model evaluation)***

**Bhavani Shankar Kodali MD*, Professor of Anesthesiology, Michael Wong MD, Fellow in Obstetric Anesthesiology, Shobana Bharadwaj M.B.B.S, Assistant Professor of Anesthesiology**

Department of Anesthesiology, University of Maryland School of Medicine, Maryland, Baltimore, Maryland, United States

***Corresponding author:** Bhavani Shankar Kodali MD, University of Maryland Medical Center, University of Maryland School of Medicine, 22 S Greene Street, Baltimore, MD 21201, United States. Tel: 4103284229; Email: bkodali@som.umaryland.edu

**Citation:** Kodali BS, Wong M, Bharadwaj S (2021) An In-Vitro Flow Model Comparing Programmed Intermittent Epidural Boluses Versus Continuous Epidural Infusions with Patient Activated Boluses Commonly Used for Labour Analgesia. J Reg Anes Pain Med: JRAPM-103.

**Received Date:** 07 June, 2021; **Accepted Date:** 11 June, 2021; **Published Date:** 18 June, 2021

## *Abstract*

***Background:*** *Clinical studies have conflicted over superiority of Programmable Intermittent Epidural Bolus (PIEB) and Continuous Epidural Infusion with Patient Controlled Epidural Analgesia (CEI/PCEA) modes for labour analgesia. We designed an in vitro model to analyse how epidural infusate spread is influenced by currently used epidural labour analgesia modes, gravity, and resistance to flow within the epidural space.*

***Methods:*** *The epidural model consisted of 1¾ inch diameter polyvinyl carbonate tubing wrapped with absorbable paper and placed in a 2-inch diameter clear polycarbonate tube. An epidural catheter was placed inside the simulated epidural space and connected to CADD®-Solis pump to deliver methylene blue: PIEB (9 ml delivered every (q) 45 min, and boluses 10 ml q10 min, ceiling 48 ml/hr), CEI/PCEA-8 (8 ml/hr infusion/hr, 8 ml q 15 min boluses, ceiling 32 ml/hr), CEI/PCEA-6 (6 ml/hr infusion, 6 ml q15 min boluses, ceiling 24 ml/hr), and continuous epidural analgesia (CEA-12 ml/hr). The distribution of the dye was photographed and measured. We also studied the effect of gravity and the influence of decreased epidural space resistance. A hypothetical CEI/PCEA-12 (12 ml/hr infusion, 10 ml q15min boluses, ceiling 42 ml/hr) mode was also tested.*

***Results:*** *The area of dye spread ranged from 221.9 cm2 (PIEB) to 58.5 cm2 (CEA) with CEI/PCEA-8 and -6 interposed between them. Dye spread was volume-dependent, such that CEI/PCEA-12 had a similar spread as PIEB. Gravity favoured spread in the dependent area (75-80% area below catheter in in both modes). Decreasing resistance in the space also increased area of dye spread.*

***Conclusions:*** *This in vitro model demonstrates that while PIEB mode may be associated with a greater spread of infusate, CEI/PCEA can match this spread if the total infusate volume is similar in both modes. This simple model may be used to further study novel epidural pump modes and parameters.*

***Clinical trials Number:*** *Not applicable as this is in vitro study*

*Presented at Society of Obstetric Anesthesiology and Perinatology Meeting 2019, Phoenix, Arizona, United States, May 1st to 5th, 2019*

***Keywords:*** *Epidural, Labour analgesia, In vitro model.*

## Background

Continuous epidural infusion with patient-activated bolus epidural analgesia, or patient-controlled epidural analgesia, (CEI/PCEA) and programmed intermittent epidural analgesia (PIEB) are two popular modes of delivering local anaesthetic during labour neuraxial analgesia [1-4]. These two techniques have replaced traditional continuous epidural infusion without patient-activated boluses, known as continuous epidural analgesia (CEA). This transition was initially spurred by in-vitro observations of infusate spread and subsequent clinical studies demonstrating improved analgesia with PIEB over CEI/PCEA [2-6]. However, a recent study by Ojo and colleagues had conflicting conclusions regarding the

superiority of PIEB or CEI/PCEA for labour analgesia [7]. We propose a simple in vitro epidural simulation model to demonstrate flow dynamics for each mode of epidural labour analgesia (i.e., CEA, CEI/PCEA, PIEB), which may also help to explain why apparent discrepancies in the clinical literature are observed.

## Methods

An epidural space of 3 to 4 mm was simulated by interposing a 1¾-inch diameter polyvinyl carbonate (PVC) tube into a 2-inch diameter clear polycarbonate (PC) tube. The PVC tube was wrapped with two layers of Bounty® absorbable paper towel with wavy pattern, to simulate areas of noncontinuous epidural space and absorption of infusate by fat and vasculature (Figure 1AB). In addition, holes simulating intervertebral foramina (28 $mm^2$ area) were drilled laterally on each side of the outer PC tube, spaced 30 mm apart. The model was placed horizontally on a level surface with the upper aspect of the outer PC tube designated as upper (anterior), and the lower aspect of the PC tube as lower (posterior). A uniport Arrow Flex® catheter (Arrow International Inc, Reading, Pennsylvania, USA) was placed inside the simulated epidural space with the catheter tip positioned in the centre of the posterior wall of the outer PC tube, thus simulating epidural catheter placement in a supine patient. The epidural catheter was connected to a CADD Solis pump (Smiths Medical ASD Inc, St. Paul, Minnesota, USA) programmed to deliver methylene blue (5 mg in 250 mL normal saline) in various modes used in clinical practice for labour analgesia. The distribution of the dye on paper towel was analysed using SketchAndCalc® area calculation software (https://www.SketchAndCalc.com), taking the average of three measurements. Trial runs to test the reproducibility of methylene blue spread using the same flows found the spread was within 7% between different trials.

Four common modes for labour analgesia were analysed: PIEB (9 ml delivered automatically every 45 min, plus 10 ml switch-activated boluses with 10 min lockout, ceiling 48 ml/hr), CEI/PCEA -8 (8 ml/hr continuous infusion, 8 ml switch-activated bolus with 15 min lockout, ceiling 32 ml/hr), CEI/PCEA -6 (6 ml/hr continuous infusion, 6 ml switch activated bolus, with 15 min lockout, ceiling 24 ml), and CEA (12 ml/hr with no switch activated boluses). The simulations were terminated when ceiling dose was achieved (45 minutes, except CEA to an hour), and all permissible switch activated boluses were used. Three additional scenarios were also analysed (i.e., decreasing resistance to flow within the simulated epidural space; comparing hand-delivered vs. pump-delivered bolus; uniport vs. multiport epidural catheter; Table 1A).

| | |
|---|---|
| 1 | Hypothetical CEI/PCEA-12 mode (continuous infusion 12 ml/hr, and switch activated bolus 10 ml with 15 min lockout, ceiling 42 ml/hr |
| 2 | The effect of gravity on the infusate spread. Done by rotating the model 90° to simulate lateral position in PIEB and CEI/PCEA -6 modes. |
| 3 | The effect of decreased flow resistance within the simulated epidural space. Done by using one layer of paper instead of two in PIEB and CEI/PCEA -6 modes. |
| 4 | The effect of hand-delivered bolus. Tested using 20 ml of infusate delivered from a 20 ml syringe by hand versus the same volume delivered by the CADD Solis pump. |
| 5 | Simulating, as closely and logistically feasible, the hourly infusate consumption used in a study by Ojo et al. [7] comparing PIEB and CEI/PCEA. A PIEB of 6 ml and one switch activated bolus 8 ml (total 14 ml), was compared to CEI/PCEA simulation, 8 ml/hr continuous infusion with one switch activated bolus of 8 ml (total 14 ml, 6 ml in 45 min) in this model. |

**Table 1: A:** Additional simulated modes tested in the model.

## Results

Table 1B and Figure 1C show the area and circumference of infusate spread with each mode. The area of spread varied from 221.9 (PIEB) to 58.5$cm^2$ (CEA). Similarly, the circumference of spread was also greater for PIEB compared to CEA. The area of spread of CEI/PCEA-8 and CEI/PCEA-6 were in between PIEB and CEA. The total infusate volume used was 48 ml in PIEB, 32 ml in CEI/PCEA 8, 24ml in CEI/PCEA 6 and 12 ml in CEA. A hypothetical test mode CEI/PCEA-12 behaved similarly to PIEB in the spread of the infused fluid (211.6 versus 221.9 $cm^2$, Figure 1: C1 and C5).

| Mode | Area ($cm^2$) | Circumference (cm) | Length (cm) | Width (cm) | Area left ($cm^2$)/ Circumference (cm) | Area right ($cm^2$)/ Circumference (cm) |
|---|---|---|---|---|---|---|
| PIEB 9/45/10/10/48 | 221.9 | 84.2 | 38 | 9.92 | 108 /79 | 110/81.3 |
| CEI/PCEA 8/8/15/32 | 162.5 | 69.2 | 32.9 | 9.07 | 76.1/67.5 | 75.5/68.2 |
| CEI/PCEA 6/6/15/24 | 124.2 | 51.9 | 21.6 | 8.75 | 64.5/46.5 | 56.4/48 |

| | | | | | | |
|---|---|---|---|---|---|---|
| CEA 12 | 58.5 | 35.6 | 11.82 | 7.6 | 30.5/29.2 | 28.3/30.3 |
| PCEA 12/10/15/42 | 211.6 | 85.9 | 40.5 | 9.8 | 101.7/82.7 | 108.5/82 |

**Table 1B:** Area measured in each mode.

CEA: Continuous epidural infusion; CEI/PCEA: Patient controlled epidural analgesia+continuous infusion; PIEB: Programmed intermittent epidural bolus, with 9 ml bolus every 45 min, 10 ml activated bolus every 10 min, ceiling 48 ml/h. CEI/PCEA-8: 8 ml/h continuous infusion, 8 ml activated bolus every 15 min, ceiling 32 ml/h. CEI/PCEA-6: 6 ml/h continuous infusion, 6 ml activated bolus every 15 min, ceiling 24ml/h. CEA: Continuous epidural analgesia: 12 ml/h. Area left and right are from the position of catheter tip.

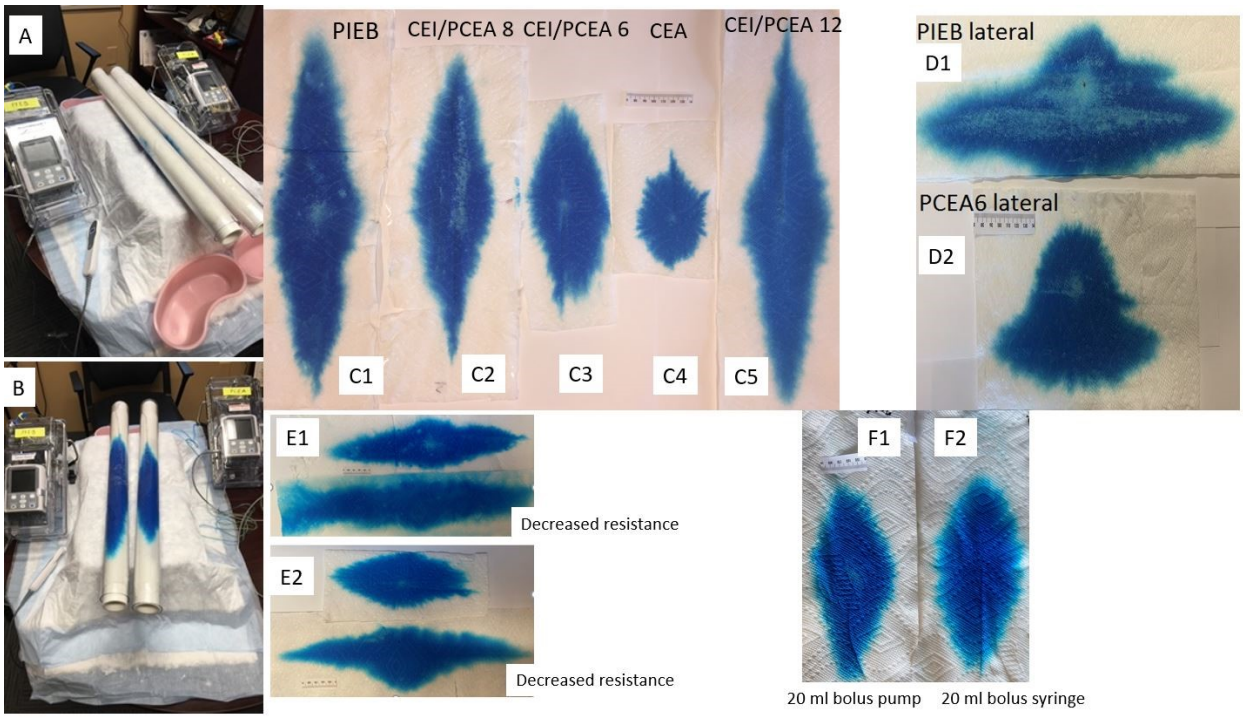


**Figure 1**

**A:** Shows the polyvinyl tube (PVC) wrapped with Bounty paper, placed in a polycarbonate tube (PC) tube.
**B:** A completed simulation showing spread of the dye.
**C:** Comparative areas of spread for (C1) programmed intermittent epidural bolus (PIEB), (C2) continuous epidural infusion with switch activated bolus (CEI/PCEA-8 8/8/15/32), (C3) continuous epidural infusion with switch activated bolus (CEI/PCEA-6 6/6/15/24), (C4) continuous epidural analgesia (CEA 12), and (C5) hypothetical test dose CEI/PCEA 12/10/15/42.
**D:** Effect of gravity on the spread of infusate, in (D1) PIEB and (D2) PCEA 6 modes.
**E:** Effect of decreasing resistance on the spread of infusate in (E1) PIEB and (E2) CEI/PCEA modes.
**F:** Spread of infusate with (F1) 20 ml pump-delivered bolus, and (F2) hand-delivered 20 ml bolus via syringe.

In simulated lateral position, gravity favoured spread of the infusate to the dependent area in both studied modes (Figure 1: D1 and D2); seventy-five to eighty percent of area was below the catheter tip (in PIEB 71.4 $cm^2$ upward versus 324 $cm^2$ downward spread, in CEI/PCEA-6 53.7 $cm^2$ upward versus 175 $cm^2$ downward, Figure 1D).

In our simulation of Ojo and colleagues' study comparing PIEB versus CEI/PCEA, after 45 min the area of spread for the two modes were similar (PIEB: 98.4 $cm^2$, circumference 36.5 cm; CEI/PCEA: 97.79 $cm^2$, circumference 38.8 cm).

Decreasing flow resistance of the simulated epidural space by removing the second sheet of paper increased the area of distribution, in supine position (in PIEB from 221.9 to 421 $cm^2$, in CEI/PCEA-6 from 124.2 to 196 $cm^2$; Figure 1E).

A hand-delivered bolus showed marginally increased spread than pump-delivered bolus (hand-delivered bolus 142.7 $cm^2$, circumference 49 cm vs. pump-delivered bolus 129 $cm^2$, circumference 49 cm; Figure 1F).

Finally, we did not find a difference in the spread of infusate via a multiport catheter (B.Braun, Perifix, Bethlehem, Pennsylvania, USA) using PIEB (9 ml delivered automatically every 45 min, plus 10 ml switch-activated boluses with 10 min lockout, ceiling 48 ml/hr) mode as compared to the infusate spread via uniport catheter (Multiport catheter: area 229 $cm^2$, circumference 81 cm; Uniport catheter: area 232 $cm^2$, circumference 86 cm).

## Discussion

The in vitro epidural space model demonstrated greater spread of fluid with PIEB than CEI/PCEA-8, CEI/PCEA-6, or CEA modes. This is in agreement with clinical observations favouring PIEB over CEI/PCEA, or CEA [8,9]. However, if the infusate volume is similar between PIEB and CEI/PCEA, the spread should be comparable; in our model, the hypothetical CEI/PCEA 12 mode infused a similar total volume as PIEB and also resulted in a similar area of spread. Thus, similarities in total infusate volumes may explain why some studies do not find a clinical difference between Programmed Intermittent Epidural Boluses and Patient Controlled Epidural Analgesia modes of labour analgesia [7].

Ojo et al compared PIEB (6 ml every 45 min, 8 ml optional patient-activated boluses with 10 min lockout) and CEI/PCEA (8 ml/hr continuous infusion, 8 ml optional patient-activated boluses with 10 min lockout) but found no difference in clinical outcomes except less motor block in patients receiving PIEB [7]. They infused approximately a total of 12 ml/hr including one patient activated bolus in each group. Our closely matched simulation using total of 14 ml/hr of infusate in each group, which also included one switch-activated bolus, did not find an apparent difference in the spread of infusate. These observations are likely because, in continuous mode, CADD®-Solis pump is not truly a slow continuous dribble, but that the infusate is rather pushed at 125 ml/hr in a pulsatile fashion in tiny, fractionated boluses, or pulses.

We also demonstrated in vitro the effect of gravity on infusate spread for both PIEB and CEI/PCEA-6 modes (Figure 1D). Labouring patients often complain of discomfort on their nondependent side, which is relieved on turning the patient to the other side and administering a clinician bolus. The literature downplays the effect of gravity or position during epidural analgesia, but lack of effect may be due to small epidural infusate volumes and short duration of observation [10].

When flow resistance within the epidural space was decreased by removing one sheet of paper in the model, infusate spread was increased (Figure 1E). This may vary unpredictably among patients and may be another likely cause of variability among studies [7,11].

A hand-delivered bolus resulted in a marginally greater infusate spread compared to CADD®-Solis pump-delivered bolus (Figure 1F). Many clinicians use hand boluses for epidural initiation as well as top-ups, and this is effective when automatic pumps are unavailable. Furthermore, the longitudinal spread of infusate after both hand- and CADD®-Solis pump-delivered boluses was approximately 12 cm or 4 vertebral levels heights. With the catheter tip at the level at L3/L4, or L2/L3, the proximal spread could extend up to T11/T12, or T10/T11, and with a corresponding spinal segmental block at a T8 level. These observations from our simulation reinforces the clinical observation that a manual epidural bolus of 20 ml leads to excellent analgesia during labour [7].

Our study of a simple in vitro resistance model has several limitations. The model did not study the effect of epidural contents (e.g., blood vessels, adipose and connective tissue), drug absorption by epidural fat, drug clearance by epidural vasculature, shape of the epidural space (i.e., more triangular in vivo), or infusate migration through intervertebral foramina into paravertebral spaces. Clinically important outcomes such as patient analgesia and adverse reactions could not be assessed. Cadaveric human or animal models have also been used for studying epidural infusate spread; however, these models are relatively laborious and expensive, and similarly do not directly allow observation of clinical effect. Additionally, animal models have imperfect generalizability to humans given species differences. For instance, porcine models have previously been used to demonstrate epidural infusate spread. Infusate spread in porcine models is relatively higher than our findings and those generally observed in clinical practice for comparable boluses; this discrepancy may in part be due to wider spinal canal and higher vertebral height in humans compared to pigs [12-15].

## Conclusion

Our in vitro model offers a simple and accessible opportunity to demonstrate epidural fluid dynamics with commonly used infusion modes. Using our simulated epidural space, Programmed Intermittent Epidural Boluses mode may be associated with a greater spread of infusate, but Patient Controlled Epidural Analgesia can match this spread if the total infusate volume is similar in both modes.

## Declaration

**Ethics approval and consent to participate**; Not applicable

**Consent for publication:** Not applicable

**Availability of data and material:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing Interests:** The authors declare that they have no competing interests

**Funding:** No external funding

**Author contributions**

BSK conceptualized the idea, performed the study and prepared the manuscript.
MW performed the study and prepared the manuscript.
SB performed the study and prepared the manuscript.

## References

1. Halpern SH, Carvalho B. Patient-controlled epidural analgesia for labor. Anesth Analg. 2009;108(3):921-8.
2. Carvalho B, George RB, Cobb B, McKenzie C, Riley ET. Implementation of Programmed Intermittent Epidural Bolus for the Maintenance of Labor Analgesia. Anesth Analg. 2016;123(4):965-71.
3. Gupta S, Partani S. Neuraxial techniques of labour analgesia. Indian J Anaesth. 2018;62(9):658-66.

4. Pandya ST. Labour analgesia: Recent advances. Indian J Anaesth. 2010;54(5):400-8.
5. Kaynar AM, Shankar KB. Epidural infusion: continuous or bolus? Anesth Analg. 1999;89(2):534.
6. Roofthooft E, Barbe A, Schildermans J, Cromheecke S, Devroe S, Fieuws S, et al. Programmed intermittent epidural bolus vs. patient-controlled epidural analgesia for maintenance of labour analgesia: a two-centre, double-blind, randomised study. Anaesthesia. 2020.
7. Ojo OA, Mehdiratta JE, Gamez BH, Hunting J, Habib AS. Comparison of Programmed Intermittent Epidural Boluses With Continuous Epidural Infusion for the Maintenance of Labor Analgesia: A Randomized, Controlled, Double-Blind Study. Anesth Analg. 2020;130(2):426-35.
8. Wong CA, Ratliff JT, Sullivan JT, Scavone BM, Toledo P, McCarthy RJ. A randomized comparison of programmed intermittent epidural bolus with continuous epidural infusion for labor analgesia. Anesth Analg. 2006;102(3):904-9.
9. George RB, Allen TK, Habib AS. Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: a systematic review and meta-analysis. Anesth Analg. 2013;116(1):133-44.
10. Norris MC, Dewan DM. Effect of gravity on the spread of extradural anaesthesia for caesarean section. Br J Anaesth. 1987;59(3):338-41.
11. Sia AT, Leo S, Ocampo CE. A randomised comparison of variable-frequency automated mandatory boluses with a basal infusion for patient-controlled epidural analgesia during labour and delivery. Anaesthesia. 2013;68(3):267-75.
12. Cole JH, Fishback JE, Hughey SB. Cadaveric Porcine Spines as a Model for the Human Epidural Space. Comp Med. 2019;69(4):308-10.
13. Sheng SR, Wang XY, Xu HZ, Zhu GQ, Zhou YF. Anatomy of large animal spines and its comparison to the human spine: a systematic review. Eur Spine J. 2010;19(1):46-56.
14. Mowat I, Tang R, Vaghadia H, Krebs C, Henderson WR, Sawka A. Epidural distribution of dye administered via an epidural catheter in a porcine model. Br J Anaesth. 2016;116(2):277-81.
15. Busscher I, Ploegmakers JJ, Verkerke GJ, Veldhuizen AG. Comparative anatomical dimensions of the complete human and porcine spine. Eur Spine J. 2010;19(7):1104-14.