Brazilian Journal of Anesthesiology xxxx;xxx(xx):xxx–xxx

Sociedade Brasileira de Anestesiologia

Brazilian Journal of ANESTHESIOLOGY

CLINICAL RESEARCH

Comparison of standing stability with different doses in epidural fentanyl among post-cesarean delivery women: a prospective trial

Masayuki Oshima [a,*], **Kazuyoshi Aoyama** [b]

[a] *Department of Anesthesia, Kobari General Hospital, Chiba, Japan*
[b] *The Hospital for Sick Children, Department of Anesthesia and Pain Medicine, Toronto, Canada*

Received 20 August 2020; accepted 26 June 2021

KEYWORDS
Cesarean section;
Analgesia;
Epidural;
Standing position;
Postural balance;
Early ambulation

Abstract
Background: The study purpose was to determine the safety and efficacy of different doses of epidural fentanyl plus local anesthetics on ambulation for patients who had elective cesarean delivery.
Methods: A prospective study at a single community hospital used posturography to compute Sway area for assessment of standing stability [ISRCTN14517337]. Continuous epidural infusion of 0.2% ropivacaine containing either 2.5 mcg.mL^{-1} (Group 1, n = 8) or 5 mcg.mL^{-1} fentanyl (Group 2, n = 8) was randomly assigned to an individual and started at a rate of 5 mL.h^{-1} postoperatively and continued for 48 hours after cesarean delivery in addition to standing acetaminophen and ibuprofen. Posturography measured with SYMPACK^{TM} was used to compute Sway area for investigation of standing stability. The unpaired *t*-test was used to compare continuous variables between groups. Analysis of variance (ANOVA) was used to assess differences of Sway area measured repeatedly within groups.
Results: Participants' demographics, pain status, and leg motor function one day after cesarean delivery were not different between groups. Sway area in Group 1 was not different across three repeated measurements. Sway area of Group 2 on postoperative day 1, with epidural analgesia, was significantly higher than at the baseline (4.1 ± 2.8 vs. 3.1 ± 1.1 cm^2, $p < 0.05$).
Conclusions: Because both low and high concentrations of epidural fentanyl allowed participants to ambulate with the same pain effect, the lower concentration of continuous epidural fentanyl (2.5 mcg.mL^{-1} at 5 mL.h^{-1}) is warranted to avoid potential adverse events during ambulation after cesarean delivery.

* Corresponding author.
E-mail: oshimasayuki@gmail.com (M. Oshima).

https://doi.org/10.1016/j.bjane.2021.06.022

Please cite this article as: M. Oshima and K. Aoyama, Comparison of standing stability with different doses in epidural fentanyl among post-cesarean delivery women: a prospective trial, Brazilian Journal of Anesthesiology, https://doi.org/10.1016/j.bjane.2021.06.022

Background

Epidural analgesia with local anesthetics and opioids is widely used in pregnant and postpartum women who deliver both vaginally and by cesarean section. Even a low concentration of local anesthetics and/or fentanyl may cause somatosensory impairment in 7% to 66% of patients, resulting in stand and gait instability and fall.[1–3] No satisfactory method exists to evaluate gait instability at the bedside. Early mobilization after cesarean delivery, however, is encouraged to decrease thromboembolic events and shorten the length of hospital stay.[4] Although postoperative pain management with epidural analgesia can be used, it might impair the abilities to stand and walk.

Standing is a complex phenomenon requiring muscle strength and somatosensory integration. The modified Bromage score is not enough to measure standing stability because it assesses only muscle strength.[5] On the other hand, posturography is a feasible, objective, and quantitative measurement of standing stability.[6]

The objective of the current study was to compare standing stability measured by posturography in post-cesarean delivery women using two different concentrations of epidural fentanyl with continuous epidural analgesia in addition to local anesthetics.

Methods

This study was a prospective project to determine the safety and efficacy of different doses of epidural fentanyl in addition to local anesthetics at a single community hospital, using posturography to assess standing stability of participants who received postoperative epidural analgesia after their elective cesarean delivery. This project was approved by the local ethics committee of Kobari General Hospital on April 26, 2018 (34-2018), and written consents for study participation were obtained from all participants. The trial was registered at the ISRCTN registry retrospectively on March 29, 2020 [ISRCTN14517337] (https://doi.org/10.1186/ISRCTN14517337). This project adhered to the CONSORT (Consolidated Standards of Reporting Trials) Statement.[7]

The cohort included 16 at-term pregnant women with ASA (American Society of Anesthesiologists) physical status I or II who received an epidural catheter at T12/L1 following spinal anesthesia with hyperbaric bupivacaine 12 mg at L3/L4. All women underwent cesarean section after sensory block at T4 level had been achieved. Continuous epidural infusion of 0.2% ropivacaine containing either 2.5 mcg/mL (Group 1, n = 8) or 5 $mcg.mL^{-1}$ fentanyl (Group 2, n = 8) was randomly assigned to an individual by a table of random numbers.[8] The continuous epidural infusion started at the rate of 5 $mL.h^{-1}$ in the Postanesthesia Care Unit and continued for 48 hours after cesarean delivery in addition to standing acetaminophen and ibuprofen. Participants' pain status with the Visual Analogue Scale (VAS) was measured periodically up to postoperative day 7. Motor function of legs with the Bromage scale was measured on postoperative day 1.

Standing stability was the study's primary outcome, which was assessed based on analyses of posturography using a SYMPACK™ (Nihon Electric Company, Tokyo, Japan).[6,9,10,11] When a participant stands on the SYMPACK's foot plate, the transducer under the plate transmits movement-generated signals to a computer. The computer calculates and tracks both the force and movement of the participant's center of gravity. The actual assessment occurs while a participant stands barefoot with their legs together for one minute and their eyes open on a SYMPACK™ computerized force platform. Posturography was measured a day before cesarean delivery, and at days 1 and 7 after cesarean delivery. Posturography computed Sway area (Fig. 1) was measured, which is the simplest but most sensitive way to detect impairment of balance perception.[9]

Participants, the operator of the spinal anesthesia who also inserts the epidural catheter, and the operator of the posturography measurement were blinded to grouping. A nurse in the Postanesthesia Care Unit who started the continuous epidural infusion was not blinded, and a nurse in the general ward, who recorded pain status with the Visual Analogue Scale (VAS) and the Bromage scale, was blinded.

Descriptive statistics included counts and proportions for categorical variables and means and standard deviations for continuous variables. Normality was assessed with the Shapiro-Wilk test. The unpaired *t*-test was used to compare continuous variables between groups. To decrease type I errors from multiple comparisons in the study, the overall F test for differences in the means was conducted first. When F was significant, one-way Analysis of Variance (ANOVA) was further used to assess differences of sway area, VAS, and the Bromage scale measured repeatedly within groups, and $p < 0.05$ was considered statistically significant. Although equal group sizes in both groups 1 and 2 were used for ANOVA, the Leven's test was employed to make sure the assumption of homogeneity of variance. All analyses were conducted with StatView 5.0 software (Abacus Concepts, Berkeley, CA, USA).

Based on prior literature,[9] sample size was determined to detect mean difference of 1.5 cm^2 in Sway area (standard deviation = 0.8) with an alpha of 0.05 and power of 0.80 with three equally sized groups of measurements for One-Way ANOVA, which yielded a sample size minimum of 7 for each group to have medium effect size (G*Power 3.1 software package; Faul, Erdfelder, Lang, & Buchner, 2007).

Results

A total of 16 at term pregnant women were enrolled in the study (Fig. 2). Eight participants in each group completed the intended treatment. Participant demographics (age: 31.0 ± 2.4 years versus 34.0 ± 4.5 years, gestational weeks and days: 37 weeks 4 days ± 4 days versus 37 weeks 5 days ± 3 days, body weight: 64.9 ± 6.5 kg versus 63.9 ± 10.4 kg in Group 1 and 2, respectively) were not statistically significant between groups (Table 1). No participant showed hypotension during cesarean delivery or required vasopressors. No participant had significant blood loss during cesarean delivery which is defined as more than 1000 mL blood loss, including amniotic fluid. Pain status on postoperative day 1 (Visual Analogue Scale: 1[0-2] in Group 1 versus 1[0-2] in Group 2) was not statistically signif-

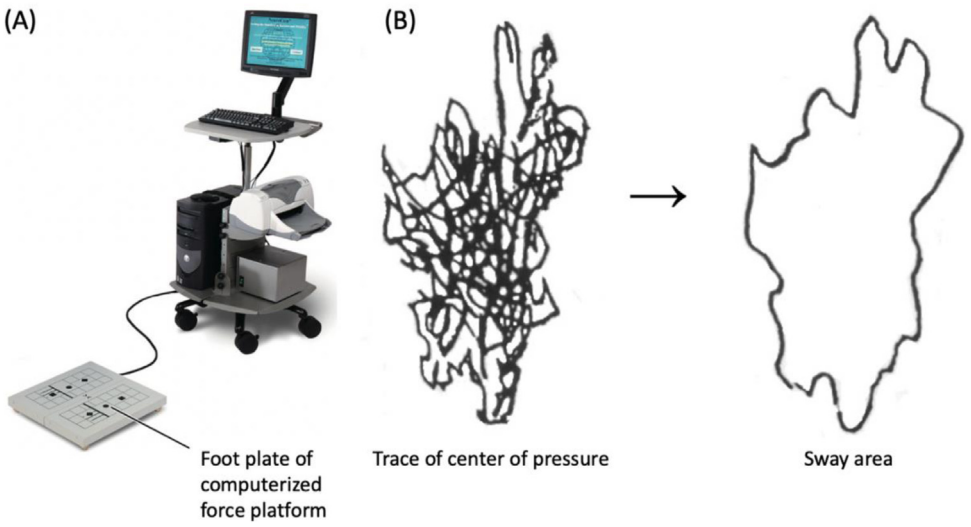

Figure 1 A, SYMPACK™ (Nihon Electric Company, Tokyo, Japan); B, Sway area: Area of sway from the outermost part of the locus of the center of foot pressure. The sway area presented herein was 2.92 cm^2.

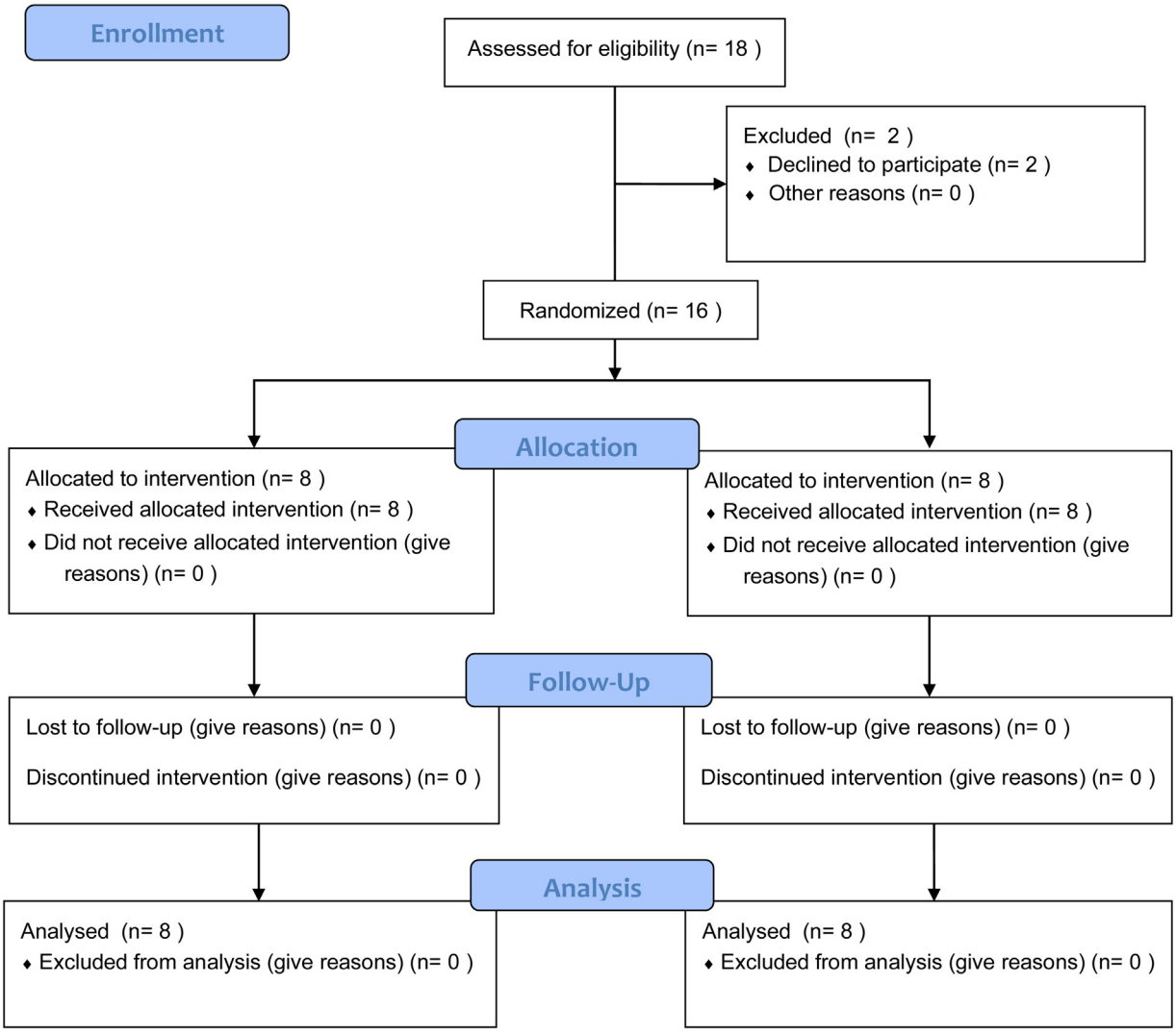

Figure 2 CONSORT diagram.

Table 1 Demographics of enrolled participants.

	Group 1	Group 2
Age (years)[a]	31.0 (2.4)	34.0 (4.5)
Height (cm)[a]	158.1 (7.3)	158.3 (7.1)
Weight (kg)[a]	64.9 (6.5)	63.9 (10.4)
Gestational weeks at birth[a]	37 weeks 4 days (4 days)	37 weeks 5 days (3 days)
Hypotension during cesarean delivery	0	0
Significant blood loss[b]	0	0

[a] No demographics were statistically different between two groups.
[b] Defined as more than a 1,000 mL blood loss including amniotic fluid.

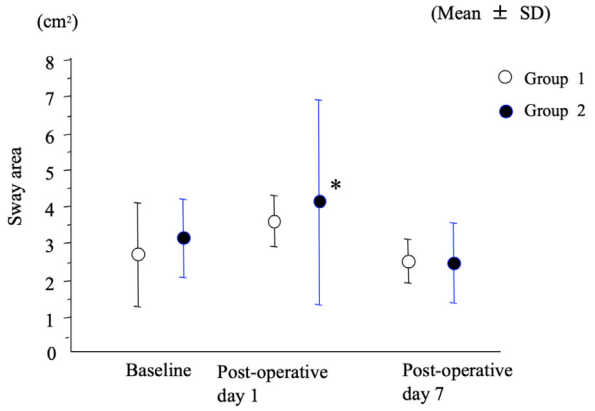

Figure 3 Differences of sway area measured a day before and 1 and 7 days after cesarean delivery within a group. In Group 2, sway area on postoperative day 1 was significantly higher than baseline and postoperative day 7 after cesarean delivery ($p < 0.05$). In Group 1, sway areas measured at each point were not statistically different.
* Statistically significant.

icant between groups. No participant required antiemetics throughout their hospital stay. All participants of both groups showed full flexion of knees without weakness (the Bromage scale = 1) on postoperative day 1. All participants were able to stand and ambulate for posturography on postoperative day 1 and on. No adverse events were reported during the study period.

Sway area in Group 1 was not different across 3 measurements (Fig. 3): 2.6 ± 1.4 cm^2 at the baseline; 3.5 ± 0.6 cm^2 on postoperative day 1; and 2.5 ± 0.6 cm^2 on postoperative day 7, respectively. However, sway area of Group 2 on postoperative day 1 was 4.1 ± 2.8 cm^2 during epidural analgesia, which was significantly higher than 3.1 ± 1.1 cm^2 at the baseline and 2.4 ± 1.1 cm^2 7 days after the cesarean delivery, respectively ($p < 0.05$) (Fig. 3).

Discussion

The main finding of the study was that both groups, receiving different concentrations of epidural fentanyl, saw participants able to ambulate and had the same pain effect after cesarean delivery. However, Group 2, which received a higher concentration of epidural fentanyl (5 $mcg.mL^{-1}$ at 5 $mL.h^{-1}$), showed potential impairment of standing ability on postoperative day 1. It was therefore determined that the lower concentration of continuous epidural fentanyl (2.5 $mcg.mL^{-1}$ at 5 $mL.h^{-1}$, received by Group 1) is preferred to avoid potential adverse events during ambulation for women post-cesarean delivery.

Adequate motor power, sensation, proprioception, vestibular function, and visual acuity all contribute to safe walking.[12] While a patient is on continuous epidural analgesia, standing stability involves multiple factors such as standing muscle strength, sensory blockade, and, most importantly, the integration of visual, somatosensory, and vestibular inputs to the brain stem and cerebellum. A prior study reported that the excellent muscle strength demonstrated by the modified Bromage score was not a sensitive indicator of standing stability.[13] Instead, Sway area is known to detect impairment of standing stability while a patient receives epidural analgesia.[9]

Before this study, there was only one study investigating the static postural stability of pregnant women. That study reported the Sway area of 2.8 ± 0.6 cm^2 in otherwise healthy pregnant women at 34–39 gestational weeks.[14] Although our findings appear to be consistent with this finding, there is no specific Sway area value that clearly indicates impairment of standing stability that could result in adverse events (i.e., fall) during ambulation. Another study by McCrory et al. explored dynamic postural stability instead of static stability in pregnant women with a history of falls during pregnancy.[15] They elucidated that dynamic balance was altered in pregnant women who fell during their pregnancy compared with pregnant women who did not fall during pregnancy. Because participants in a study of dynamic postural stability are explored on perturbations for their postural responses, dynamic postural stability is more challenging to assess in postoperative patients while on epidural analgesics than static postural stability. Future research is required to investigate postoperative safe walking and early hospital discharge in post-cesarean delivery women that uses an assessment of static postural stability.

The SYMPACK™ used to measure posturography in this study provides an easy and reliable measurement of standing stability however has a high cost ($20,000 USD) (Fig. 1). The cost covers a foot plate computerized force platform and a computer with corresponding software to quantify postural sway area.

In this study, there are a few possible reasons why the higher concentration of epidural fentanyl was associated with potential impairment of standing stability. First, it could be explained that epidural fentanyl was absorbed across the dura and then reached the brain cerebrospinal fluid and creating a spinal effect. Next, it is possible the epidural fentanyl was absorbed into the circulation and then reached the brain with blood flow and creating a systemic effect. With either potential explanation, the higher concentration of epidural fentanyl could influence balance perception. A previous study revealed that epidural fentanyl by continuous infusion had systemic effects rather than spinal effects.[16]

Strengths and weaknesses of the study

A limitation of the current study was that the presence of anemia was not measured, which can potentially have a confounding association with epidural fentanyl and with Sway area. However, we can deduce that hemodynamics of participants were stable given that no participants had significant blood loss during the cesarean deliveries. Another limitation was that the SYMPACK™ system assessed only static standing ability. Although the EquiTest™ (Neurocom International, Clackamas, OR) can detect functional balance with clinical situation inputs,[17] this instrument was not available at the study hospital. A strength of the study, however, is its original contribution to the literature given that a literature search in PubMed and Medline as of March 20, 2020, using posturography, epidural analgesia, and cesarean delivery as keywords, does not capture similar research.

Unanswered questions and future research

Future studies need to investigate how low the concentration of epidural fentanyl in addition to local anesthetics may be while ensuring standing stability and ensuring postoperative pain due to cesarean delivery is satisfactorily under control. Given that posturography is a useful tool to detect potentially impaired balance perception, this method should be used in future studies to explore postoperative ambulation.

Conclusions

Sway area computed from posturography deduced that patients taking a higher concentration of epidural fentanyl exhibited potential impairment of standing stability. This finding could result in adverse events during ambulation in these patients.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgement

As a recipient of Research Commendation, 2021-2023 Merit Awards Competition, Department of Anesthesiology & Pain Medicine, University of Toronto, KA acknowledges Department of Anesthesiology & Pain Medicine, University of Toronto, and Department of Anesthesia and Pain Medicine, Hospital for Sick Children, for their effort to secure academic time to conduct the current work.

References

1. Buggy D, Hughes N, Gardiner J. Posterior column sensory impairment during ambulatory extradural analgesia in labour. Br J Anaesth. 1994;73:540–2.
2. Parry MG, Fernando R, Bawa GP, et al. Dorsal column function after epidural and spinal blockade: implications for the safety of walking following low-dose regional analgesia for labour. Anaesthesia. 1998;53:382–7.
3. Breen TW, Shapiro T, Glass B, et al. Epidural anesthesia for labor in an ambulatory patient. Anesth Analg. 1993;77:919–24.
4. Hauk L. American Academy of Family Physicians. Planning for Labor and Vaginal Birth After Cesarean Delivery: Guidelines from the AAFP. Am Fam Physician. 2015;91:197–8.
5. Graham AC, McClure JH. Quantitative assessment of motor block in labouring women receiving epidural analgesia. Anaesthesia. 2001;56:470–6.
6. Song D, Chung F, Wong J, et al. The assessment of postural stability after ambulatory anesthesia: a comparison of desflurane with propofol. Anesth Analg. 2002;94:60–4, table of contents.
7. Moher D, Hopewell S, Schulz KF, et al. Consolidated Standards of Reporting Trials Group. CONSORT 2010 Explanation and Elaboration: Updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol. 2010;63:e1–37.
8. Kim J, Shin W. How to Do Random Allocation (Randomization). Clin Orthop Surg. 2014;6:103.
9. Akabane H, Shimada Y, Ogawa R. Usefulness of posturography after epidural block. J Nippon Med Sch. 2004;71:35–43.
10. Steward DJ, Volgyesi G. Stabilometry: a new tool for the measurement of recovery following general anaesthesia for outpatients. Can Anaesth Soc J. 1978;25:4–6.
11. Hiller A, Pyykkö I, Saarnivaara L. Evaluation of postural stability by computerised posturography following outpatient paediatric anaesthesia. Comparison of propofol/alfentanil/N2O anaesthesia with thiopentone/halothane/N2O anaesthesia. Acta Anaesthesiol Scand. 1993;37:556–61.
12. Elton CD, Ali P, Mushambi MC. ''Walking extradurals'' in labour: a step forward? Br J Anaesth. 1997;79:551–4.
13. Etches RC, Writer WD, Ansley D, et al. Continuous epidural ropivacaine 0.2% for analgesia after lower abdominal surgery. Anesth Analg. 1997;84:784–90.
14. Opala-Berdzik A, Błaszczyk JW, Bacik B, et al. Static Postural Stability in Women during and after Pregnancy: A Prospective Longitudinal Study. PLoS One. 2015;10:e0124207.
15. McCrory J, Chambers A, Daftary A, et al. Dynamic postural stability in pregnant fallers and non-fallers. BJOG An Int J Obstet Gynaecol. 2010;117:954–62.
16. Ginosar Y, Riley ET, Angst MS. The site of action of epidural fentanyl in humans: the difference between infusion and bolus administration. Anesth Analg. 2003;97:1428–38.
17. Pickering AE, Parry MG, Ousta B, et al. Effect of combined spinal-epidural ambulatory labor analgesia on balance. Anesthesiology. 1999;91:436–41.