Original Article

Comparison of computer-integrated patient-controlled epidural analgesia with no initial basal infusion versus moderate basal infusion for labor and delivery: A randomized controlled trial

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Abstract

Background and Aims: Computer-integrated patient-controlled epidural analgesia (CIPCEA) is a novel epidural drug delivery system. It automatically adjusts the basal infusion based on the individual's need for analgesia as labor progresses.

Materials and Methods: This study compared the time-weighted local anesthetic (LA) consumption by comparing parturients using CIPCEA with no initial basal infusion (CIPCEA0) with CIPCEA with initial moderate basal infusion of 5 ml/H (CIPCEA5). We recruited 76 subjects after ethics approval. The computer integration of CIPCEA titrate the basal infusion to 5, 10, 15, or 20 ml/H if the parturient required respectively, one, two, three, or four patient demands in the previous hour. The basal infusion reduced by 5 ml/H if there was no demand in the previous hour. The sample size was calculated to show equivalence in LA consumption.

Results: The time-weighted LA consumption between both groups were similar with CIPCEA0 group (mean [standard deviation (SD)] 8.9 [3.5] mg/H) compared to the CIPCEA5 group (mean [SD] 9.9 [3.5] mg/H), $P = 0.080$. Both groups had a similar incidence of breakthrough pain, duration of the second stage, mode of delivery, and patient satisfaction. However, more subjects in the CIPCEA0 group required patient self-bolus. There were no differences in fetal outcomes.

Discussion: Both CIPCEA regimens had similar time-weighted LA consumption and initial moderate basal infusion with CIPCEA may not be required.

Key words: Anesthesia, epidural, obstetrical

Introduction

Patient-controlled epidural analgesia (PCEA) is an established method of safe and effective technique to maintain labor epidural analgesia since its introduction in 1988 by Gambling.[1,2] PCEA has been shown to reduce anesthetist top-ups, less motor blockade while reducing local anesthetic (LA) consumption compared to continuous epidural infusion.[3]

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The current debate hovers regarding the optimal PCEA regimen to achieve the best pain relief and high maternal satisfaction. Initial studies have suggested that basal infusion with PCEA led to greater consumption of LAs without improving comfort, patient satisfaction, or decreasing breakthrough pain.[4-6] More recently, basal infusion with PCEA has been advocated to reduce anesthetist workload and LA consumption when compared with demand only PCEA.[7]

Computer-integrated patient-controlled epidural analgesia (CIPCEA) is a novel epidural delivery system programmed to analyze the LA use across the last hour and adjusts the background infusion rate according to an algorithm [Figure 1]. The majority of subjects who developed breakthrough pain had rapid progress in labor despite the increased background infusion rate.[8] Hence, an initial moderate basal infusion may be required to allow a faster upward titration of LAs. However, this may lead to higher LA consumption.

We have modified the algorithm to start the maintenance infusion to an initial no basal infusion or initial moderate basal

infusion rate of 5 ml/H in this randomized double-blinded controlled trial [Figures 1 and 2]. Our primary outcome was the time-weighted, hourly consumption of LA for the duration of labor epidural analgesia in this equivalence study. We also assessed the incidence of breakthrough pain, duration of labor analgesia, side-effects, and maternal satisfaction.

Materials and Methods

The Centralized Institutional Review Board Ethics Committee approved this study and informed consent was obtained from each subject in this study. We recruited 152 American Society of Anesthesiologists 1 nulliparous parturients at 36 weeks gestation or more, who had requested for epidural analgesia into this randomized, double-blind controlled trial at our tertiary care hospital between October 2010 and June 2011. We included parturients in established labor with cervical dilation ≤5 cm and with baseline pain score >5 (on 0-10 numerical rating scale (NRS): 0 being no pain, 10 being worst pain imaginable), who had a singleton fetus with vertex presentation at term and no pregnancy related complications. We excluded parturients who received parenteral opioids within 2 h.

Each subject received a preload of intravenous (IV) Ringer Lactate solution 500 ml. Baseline pain scores were obtained. Systolic blood pressure was measured in the right brachial artery using a noninvasive blood pressure monitor (Dinamap, Critikon, FL, USA) with the parturient supine with left uterine displacement. The use of cervical prostaglandin E2, IV oxytocin and the cervical dilation prior to combined spinal-epidural (CSE) were recorded.

The CSE technique was performed with the parturient in the sitting position. After the epidural space was located with 18 Gauge Espocan needle using loss of resistance using <2 ml of saline, dural puncture was performed using a 27 gauge pencil point spinal needle (Espocan, B Braun, Melsungen, Germany) through the epidural needle. Ropivacaine 2 mg and fentanyl 15 μg diluted with normal saline to a total volume of 2 ml was injected intrathecally over 15 s, with the orifice of the spinal needle facing in a cephalad direction. A multi-orifice epidural catheter was inserted 3-4 cm into the epidural space and tested with 3 ml of 1.5% lignocaine to exclude the intrathecal placement. In the event of significant motor block (inability to flex the knees) or a reduction of >20% in systolic blood pressure, the subject was to be withdrawn from the study due to suspected intrathecal catheter placement. Subjects who had blood or cerebrospinal fluid aspirated from the catheter were also withdrawn from the study.

We randomly allocated subjects using sealed opaque envelopes into two groups using computer generated random number tables. Group CIPCEA0 (CIPCEA with no initial basal infusion) received CIPCEA regimen with no initial basal infusion of epidural anesthetic (0.1% ropivacaine and fentanyl 2 mcg/ml). The starting basal infusion was 0 ml/H, but the computer integration allowed the infusion to increase by 5 ml/H if the subject required one demand bolus in the previous hour. If the subject required two demand boluses in the previous hour, the infusion rate increased to 10 ml/H. If the subject required three demand boluses in the previous hour, the infusion rate increased to 15 ml/H. The maximum infusion rate was limited to 20 ml/H, and further demand boluses would activate an alarm to alert the attending anesthetist to

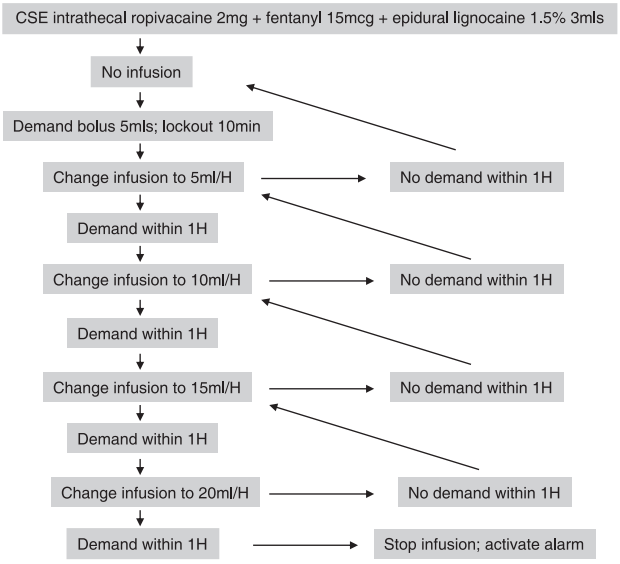

Figure 1: Computer-integrated patient controlled epidural analgesia with no initial basal infusion (CIPCEA0)

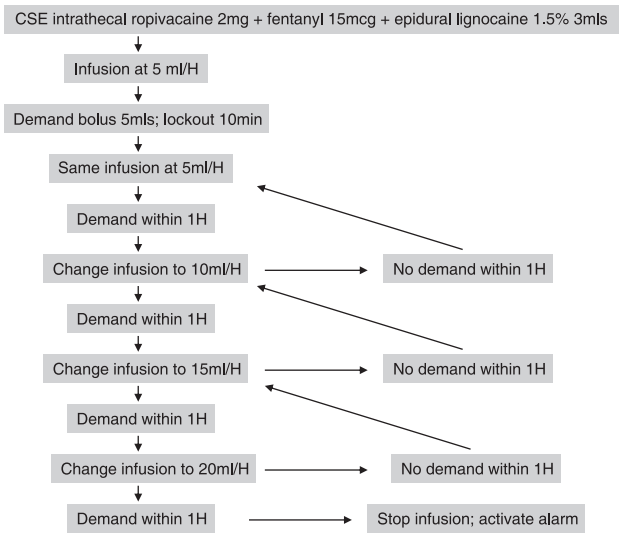

Figure 2: Computer-integrated patient controlled epidural analgesia with initial moderate basal infusion 5 ml/H (CIPCEA5)

review the patient. On the other hand, if there was no demand in the previous hour, the infusion decreased by 5 ml/H.

Group CIPCEA5 (CIPCEA with 5 ml/H initial basal infusion) received a similar regimen except that a minimum 5 ml/H moderate basal infusion is maintained and is the starting infusion rate and the regimen maintains a minimum 5 ml/H basal infusion at all times.

The patients were blinded to their group allocation and were not told of their epidural regimen they were assigned to. Both groups received a hand-held device and instructed to self-administer epidural bolus by pressing a button. They were instructed to activate an epidural bolus when they experienced mild to moderate pain, before the pain intensity became severe. Subjects who did not obtain satisfactory pain relief (NRS <3) 15 min after the CSE were deemed to have a failed block. In this event, rescue epidural supplementation through the epidural catheter would be delivered, and the subject removed from the study.

An anesthetist who was not involved in performing the block collected the following data at 0, 15, and 30 min after CSE technique and at 2, 4, 6, 8, 10, and 12 h for subjects who had not delivered: Systolic blood pressure, maternal and fetal heart rate, pain scores using NRS, sensory level testing using loss of cold sensation and degree of lower limb motor block using the modified Bromage score (0 = no motor block, 1 = inability to raise extended leg, able to flex knee, 2 = inability to flex the knee, able to move the foot only, 3 = inability to move foot or knee). The side-effects reported included: Pruritus, shivering, hypotension, nausea, vomiting, and fetal bradycardia.

Breakthrough pain was defined as failure of the regimen to provide adequate pain relief and necessitating unscheduled epidural supplementation by the anesthetist prior to delivery. The attending anesthetist assessed the reason for breakthrough pain; Pain score using NRS and administered 5 ml 0.2% ropivacaine. If the pain score remained above 3 despite administering a total of up to 15 ml of 0.2% ropivacaine (in aliquots of 5 ml over 30 min), the epidural catheter would be labeled as ineffective, and the subject excluded from the analysis. After breakthrough pain was relieved, the subject continued on their assigned regimen. The duration of effective analgesia was defined as the duration from initiation of epidural analgesia until breakthrough pain or delivery of the fetus whichever occurred first.

The fetal heart rate (from continuous cardiotocography) was assessed by the attending obstetrician who was blinded to the drugs and regimen being administered. The time of delivery, mode of delivery, neonatal APGAR scores, and overall satisfaction with the epidural analgesia were assessed and recorded within 2 h of delivery using a 0-100 scale (0 = very dissatisfied, 100 = very satisfied).

The null hypothesis in this equivalence trial stated that the hourly consumption of LAs during CIPCEA with no initial basal infusion was less than CIPCEA with initial moderate basal infusion. The CIPCEA regimen uses variable background infusion titrated to parturient's demands, and we propose that an initial moderate basal infusion may not increase LA consumption. The standard deviation (SD) of time-weighted LA consumption is 3 mg/H with mean of 9 mg/H using CIPCEA.[8] We assumed the equivalent limit of within 1.5 mg/H being the cut-off between the two regimens. A sample size of 68 per group was needed to reject the null hypothesis (of nonequivalence) with a power of 80% and significance level of 5% if the alternative hypothesis (of equivalence) was true. $P < 0.05$ is considered as statistically significant. We would recruit 76 per group after accounting for 10% withdrawal rate. Analysis of dichotomous data was performed using the Chi-square test. The Student's *t*-test and Mann-Whitney U-test were employed for parametric and nonparametric data, respectively. Statistical analyses were performed using the SAS statistical package.

Results

There were 152 parturients who completed this study, and there was no drop out. 164 subjects were screened. Seven subjects refused consent for the study; 3 subjects had cervical dilation more than 5 cm, 1 subject received intramuscular pethidine within 2 h and 1 subject had pain score <5. There were no differences in the demographic and baseline obstetric data between the two groups [Table 1]. All parturients had pain scores <3 within 15 min after CSE initiation. There were no failed blocks or ineffective catheters.

The time-weighted consumption of epidural LA from the time of induction of the CSE to the time of delivery, were similar in both groups with CIPCEA0 group (mean [SD] 8.9 [3.5] mg/H) compared to the CIPCEA5 group (mean [SD] 9.9 [3.5] mg/H), $P = 0.080$. There were no significant differences in the total amount of LA used and maximum basal rate [Table 2].

Both groups showed a similar cumulative incidence to breakthrough pain from the initiation of epidural analgesia [Figure 3]. All subjects in the CIPCEA0 group required bolus demands, while 92.1% of subjects in the CIPCEA5 group. Six subjects did not require any self-bolus demands in the CIPCEA5 group. However, the CIPCEA0 and CIPCEA5 groups did not differ significantly in the incidence

Table 1: Baseline demographic and obstetric data

Study group	CIPCEA0 no initial basal infusion (*n* = 76)	CIPCEA5 initial moderate basal infusion (*n* = 76)	*P* value
Age (year)	29.5 (21-40, 26-32)	30.0 (21-42, 26-33)	0.407
Weight (kg)	71.6 (9.5)	69.1 (6.7)	0.053
Height (cm)	158.7 (5.4)	158.1 (5.0)	0.465
Body mass index	28.4 (3.4)	27.7 (2.8)	0.133
Systolic blood pressure (mmHg)	113.4 (12.3)	116.7 (11.4)	0.086
Maternal heart rate (/min)	80.6 (11.0)	79.0 (11.7)	0.391
Fetal heart rate (/min)	139.8 (11.7)	138.9 (11.4)	0.638
Preblock cervical dilatation (cm)	3.0 (1.0-5.0, 3.0-3.0)	3.0 (1.0-5.0, 3.0-3.0)	0.693
Preblock pain score (NRS)	7.0 (5.0-10.0, 6.0-9.0)	8.0 (5.0-10.0, 7.0-9.0)	0.080
Use of oxytocin before induction of epidural analgesia (%)	31 (40.8)	27 (35.5)	0.617
Use of prostaglandin E2 for induction of labor (%)	33 (43.4)	25 (32.9)	0.182
Spontaneous labor (%)	30 (39.5)	37 (48.7)	0.327

Values are mean (SD), n (%), median (range), CIPCEA = Computer-integrated patient controlled epidural analgesia, NRS = Numerical rating scale, SD = Standard deviation

Table 2: Characteristics of labor analgesia and obstetric outcome

Study group	CIPCEA0 no initial basal infusion (*n* = 76)	CIPCEA5 initial moderate basal infusion (*n* = 76)	*P* value
Maximal dermatomal block to cold	T8 (T5-T10, T6-T8)	T7 (T5-T10, T6-T8)	0.605
Mode of delivery (%)			
Normal vaginal delivery	49 (64.5)	48 (63.2)	0.969
Instrumental delivery	9 (11.8)	10 (13.2)	
Cesarean delivery	18 (23.7)	18 (23.7)	
Gestational age (week)	38 (36-41, 37-39)	38 (36-40, 37-39)	0.391
Duration of 2nd stage (min)	68 (10-190, 32-113) (*n*=58)	71 (5-192, 31-95) (*n*=58)	0.773
Duration of labor (min)	410 (115-923, 292-554)	389 (77-1018, 256-565)	0.509
Duration of effective analgesia (min)	395 (115-923, 276-544)	374 (77-1018, 228-565)	0.502
Use of bolus demand (%)	76 (100)	70 (92.1)	0.028
Time to first bolus demand (min)	93.5 (26-217, 70-128)	97.5 (19-300, 70-161)	0.242
LA infusion rate at delivery (mg/H)	9.1 (3.7)	10.1 (3.7)	0.073
Total LA (mg)	62.2 (30.2)	68.8 (36.3)	0.226
Time-weighted LA (mg/H)	8.9 (3.5)	9.9 (3.5)	0.080
Maximum basal rate (ml/H)	14.9 (4.3)	13.8 (6.0)	0.187
Fetal birth weight (g)	3190 (366)	3073 (456)	0.083
Apgar score at 5 min	9 (8-9, 9-9)	9 (9-9, 9-9)	0.325
Maternal satisfaction score (%)	90 (65-100, 80-93)	85 (75-100, 80-90)	0.198

Values are mean (SD), n (%), median (range, IQR), CIPCEA = Computer-integrated patient controlled epidural analgesia, SD = Standard deviation, IQR = Interquartile range, LA = Local anesthetic

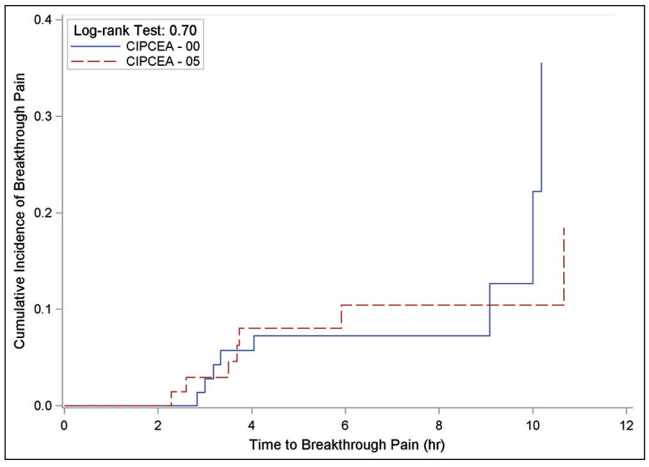

Figure 3: Cumulative incidence of breakthrough pain from initiation of epidural analgesia

of breakthrough pain prior to delivery [Table 3]. There was no significant difference in maternal satisfaction scores between the groups (mean [SD] 87.7% [8.3%] vs. 86.1% [7.1%], $P = 0.182$). The LA infusion rate at delivery was also similar (mean [SD] 9.1 [3.7] mg/H vs. 10.1 [3.7] mg/H, $P = 0.073$) [Table 2]. Mode of delivery, fetal weight, Apgar scores [Table 2] and side-effect profiles did not differ significantly [Table 4]. All subjects had Bromage score of 0.

Discussion

This study showed that there was no difference in the time-weighted LA consumption between the CIPCEA regimens with no initial basal infusion versus an initial moderate basal

Table 3: Profile at time of breakthrough pain

Study group	CIPCEA0 no initial basal infusion (n = 76)	CIPCEA5 initial moderate basal infusion (n = 76)	P value
Breakthrough pain (%)	8 (10.5)	7 (9.2)	1.000
Pain score at breakthrough (NRS)	6.5 (6.0-8.0, 6.0-8.0)	7.0 (5.0-10.0, 7.0-10.0)	0.287
Use of oxytocin infusion at breakthrough (%)	8 (100)	7 (100)	1.000
Rate of epidural infusion at breakthrough (ml/H)	17.5 (10-20)	15.0 (10-15)	0.180
Cervical dilation at breakthrough (cm)	7.0 (5-9, 5-8)	7.0 (5-9, 5-8)	1.000

Values are n (%), mean (SD), median (range), CIPCEA = Computer-integrated patient controlled epidural analgesia, NRS = Numerical rating scale, SD = Standard deviation

Table 4: Side effects

Study group	CIPCEA0 no initial basal infusion (n = 76) (%)	CIPCEA5 initial moderate basal infusion (n = 76) (%)	P value
Pruritus	36 (47.4)	37 (48.7)	1.000
Nausea	4 (5.3)	5 (6.6)	1.000
Vomiting	9 (11.8)	7 (9.2)	0.792
Shivering	24 (31.6)	26 (34.2)	0.863
Hypotension (<90 mmHg)	1 (1.3)	1 (1.3)	1.000
Fetal bradycardia	0 (0.0)	0 (0.0)	1.000
Maternal fever (>38.5°C)	6 (7.9)	3 (3.9)	0.494

Values are n (%), CIPCEA = Computer-integrated patient controlled epidural analgesia

infusion of 5 ml/H. All subjects in CIPCEA0 group required self-bolus, whilst 92.1% (70) required self-bolus demands in CIPCEA5 group. There were no differences in obstetric, anesthetic, or fetal outcomes.

The role of basal infusion in PCEA regimens has been the subject of debate. Early studies reported that PCEA with basal infusion resulted in greater consumption of LA without improving comfort or maternal satisfaction.[4-6] More recent studies, however, suggested that a background infusion may improve maternal analgesia and reduce clinician interventions,[9,10] leading to more recommendation to use PCEA with a basal infusion in recent years.[11,12] There is no consensus on the optimal regimen of the basal infusion; the benefit seems to be stronger in studies utilizing higher rate of infusion, although that is associated with greater LA consumption. Our approach to determine the optimal rate of basal infusion based on PCEA demand led to the development of our CIPCEA. In our previous study, we demonstrated that the CIPCEA system may increase maternal satisfaction without increasing breakthrough pain or LA consumption.[8]

In this study, we changed the CIPCEA algorithm by starting the epidural analgesia with a moderate basal infusion (5 ml/H), in an attempt to maintain LA solution in the epidural space, with the aim of reducing the incidence of early labor breakthrough pain. The lack of a basal infusion in demand only PCEA has been associated with an increased incidence of breakthrough pain.[9,13] We observed that this modified algorithm results in a similar time-weighted hourly consumption of LA when compared with CIPCEA with no initial basal infusion. There were no significant differences in the incidence of breakthrough pain suggesting that initial moderate basal infusion may not be essential. The total amount of LA used also appeared to be comparable. All 76 subjects in the CIPCEA0 group required patient self-bolus, while 6 subjects in the CIPCEA5 group delivered without patient demands. However, the clinical significance needs to be defined as there were no differences in patient satisfaction.

Eight subjects from the CIPCEA0 group and 7 subjects from the CIPCEA5 group experienced breakthrough pain. All events of breakthrough pain in both groups occurred during the advanced phase of the first stage of labor with median cervical dilatation at 7 cm, and all patients who experienced breakthrough pain in both groups were receiving IV oxytocin infusion. This may support earlier observation that induced labor may require a higher effective dose of epidural anesthetic than spontaneous labor.[14] The incidence of breakthrough pain using the CIPCEA regimen is between 6.7% and 15% that compares favorably to conventional PCEA regimens.[8,15,16] The cumulative incidence of breakthrough pain over time suggest that breakthrough pain occurs after 2 h of initiation of CSE analgesia, probably related to the duration of action of the spinal component.

Conclusion

The CIPCEA regimen with no initial basal infusion compared to initial moderate basal infusion resulted in similar LA consumption. There were no differences in incidence of breakthrough pain, duration of the second stage of labor, mode of delivery and patient satisfaction. However, more subjects in the CIPCEA0 group required patient self-bolus. The initial moderate basal infusion in the CIPCEA regimen may not be required.

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