

Comparison of the Effect of Epidural Bolus and Continuous Infusion of Lidocaine %1 on Pain, the Progress of Vaginal Delivery and Motor Function in Labor Epidural Analgesia

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ABSTRACT

Background: The pain of childbirth is the most severe pain that a woman experiences. This study aimed to compare the effect of epidural bolus and epidural continuous infusion of lidocaine %1 on pain and progress of vaginal delivery and motor function in labor epidural analgesia.

Methods: This randomized clinical trial was conducted on 50 pregnant women aged between 18-45 years. They were randomly assigned into two groups of bolus injections of lidocaine 1% and continuous infusion using an epidural approach. The evaluated variables included systolic and diastolic blood pressures, mean arterial pressure, pain score, heart rate, satisfaction rate, nausea, vomiting, itching, the progress of delivery, and the level of motor and sensory block. The collected data were analyzed in SPSS software (Version 21). P-value less than 0.05 was considered statistically significant.

Results: Two groups were similar in age. There were no significant differences between two groups in terms of mean diastolic blood pressure, incidence of hypotension and C/S rate ($P > 0.005$). Mean arterial pressure, sedation score and neonatal Apgar scores in the first and fifth minutes in the continuous group were significantly lower than the bolus group.

Pain score (VAS) in the bolus group) 2.55 ± 1.04 (was significantly lower than infusion group (5.22 ± 2.50). The length of the first and second stages of labor in the bolus group (42.28 and 34.12) was less than continuous infusion (47.04 and 47.00) ($P < 0.005$).

Conclusion: In women undergoing epidural analgesia, epidural bolus injection of lidocaine 1% is associated with greater analgesia and satisfaction than continuous infusion.

Labor pain is a very unpleasant feeling that each woman may experience in her lifetime. Moreover, failure to control of labor pain can lead to severe maternal and fetal complications [1]. There are different methods for the relief of labor pain including pharmaceutical, and non-pharmaceutical methods.

Epidural analgesia is one of the most commonly used pain relief methods to relieve labor pain, which is noticeable due to quality, adaptability, safety, and pain relief [2-3]. If operative delivery is required, this approach can be developed into a surgical procedure [4-5]. According to the guidelines of American Society of

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Anesthesiologists (ASA) Task Force and Committee on Standards, analgesic techniques should be recommended based on the patients' medical status, the progress of labor, anesthetic and obstetric conditions, and health care facilities at the hospital [6]. Two main epidural methods include programmed intermittent epidural bolus (PIEB) and continuous epidural infusion (CEI) [7-8]. The PIEB is introduced as an alternative approach to CEI and in which boluses are injected at fixed planned intervals. This technique can be applied with or without opioids [2]. Moreover, it can be utilized as a background administration with PCEA technique [9-15]. Based on a meta-analysis, a decrease in local anesthetic administration and an increase in maternal satisfaction were observed among patients underwent PIEB, compared to those in the CEI group [16]. Lidocaine%1 and bupivacaine 0.25% and 0.125% are the most common local anesthetics, which are utilized in childbirth by epidural approaches. Lidocaine is suitable in pregnant women due to the faster onset of its effect as well as less cumulative and toxic effects [13]. Given the extensive use of epidural analgesia approaches by anesthesiologists and obstetricians, it is necessary to gain knowledge of their advantages and adverse effects [17]. There are very few studies conducted on the utilization of continuous injection through epidural. Therefore, this study aimed to compare the effect of epidural bolus and epidural continuous infusion of lidocaine%1 on the pain and progress of vaginal delivery and motor functioning epidural analgesia during labor.

Methods

This randomized clinical trial was approved by the Ethical Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1397.222) and Iranian Registry of Clinical Trials (IRCT20120915010841N9) and was conducted at Fatemeh Hospital of Hamadan in 2019. Data collection tools included a researcher-made questionnaire in accordance with the research goals and the research variables for recording pain scores, hemodynamic changes and level of patients satisfaction. The sample size of this study was estimated 50 patients in two groups (25 patients in each group).

The inclusion criteria were: nulliparous women, 18-45 years, American Society of Anesthesiologists physical status I or II, gestational age \geq 36 weeks with vertex presentation, candidates for vaginal delivery and request for epidural analgesia, with a cervical dilation more than 5 cm, pain score \geq 3 in visual analogue scale (VAS) before analgesia (using a 10 cm ruler) and lack of receiving sedation before entering the study. On the other hand, the cases with the contraindications of epidural anesthesia (i.e., coagulation problems, hypovolemia, increased intracranial pressure, skin infections on the back and anemia), maternal disease (i.e., severe asthma, liver, renal

and cardiac disease), lack of willingness to cooperate, Failed epidural technique and allergy to lidocaine were excluded from this study.

Patients were randomly allocated to one of the continuous infusion (C) or intermittent (I) boluses groups. In both groups, lidocaine 1% was utilized for epidural analgesia. Lidocaine 1% was injected via either continuous infusion or intermittent boluses.

Randomization was carried out by a block randomization with a block size of 4 for two groups. We chose a block at random and the first 4 treatments were allocated according to the permutations in that block. Then a new block was chosen at random and the next 4 treatments were allocated according to that block. We kept going until the required sample size was recruited. In all patients, systolic and diastolic blood pressure, heart rate, respiratory rate and SPO₂ were measured (by non-invasive blood pressure and ECG monitoring, Saadat, made in Iran) and recorded before epidural analgesia. Pain scores in visual analogue scale (VAS) before epidural analgesia were measured (using a 10 cm ruler) and recorded in questionnaire.

After receiving ringer lactate solution (500 ml), the patients were situated in a sitting position and then, the lumbar epidural space was determined with the loss-of-resistance technique in the L3-L4 or L4-L5 space using 18-gauge Tuohy needle. Then multi-orifice catheter was inserted into the epidural space. Patients who had aspirated blood or cerebrospinal fluid were excluded from this study. Subsequently, the both groups were received 10 ml lidocaine 1% plus 1 ml sufentanil through the catheter located into the epidural space and then infusion pump was inserted in continuous infusion patients.

In bolus group, patients were received 10 ml of lidocaine%1 every hour regularly until delivery through the catheter located into the epidural space. In the continuous infusion group, continuous infusion of 10 ml/h of lidocaine 1% was injected via a continuous infusion Epidural pump. Both groups were evaluated regarding pain scores and vital signs, including systolic and diastolic blood pressure, mean arterial pressure, oxygen saturation (SPO₂) and heart rate immediately after epidural injection, every 10 minutes until 60 minutes and the first and second stages of delivery (by non-invasive blood pressure and ECG monitoring, Saadat, Made in Iran). Moreover, a trained midwife assessed the total amount of consumed lidocaine, patient satisfaction, nausea, vomiting, itching, the progress of delivery process, and the level of motor and sensory block of the patient. The Apgar scores were recorded in the first and fifth minutes. The data were collected using a checklist, which was designed based on the aims of the study. If patients did not have enough pain relief (VAS \geq

6), additional doses were administered through epidural catheter and patients excluded from the study.

The pinprick test was applied to assess the sensory level. Furthermore, sedation and motor block were assessed using Ramsay and Bromage Scales, respectively. In cases of systolic blood pressure < 100 mmHg and heart rate < 60 beat/min, intravenous ephedrine (10 mg) and atropine (0.5mg) were injected respectively.

The pain intensity before and after induction of labor analgesia was also evaluated by the standard visual analog scale [(VAS) 0–10] method. VAS was measured by using a 10 cm ruler, the score is determined by measuring the distance on the 10-cm line between the zero and the patient's mark, providing a range of scores from 0–10, 0 being no pain, and 10 being the worst possible pain. Sedation was assessed by Ramsay sedation scale as follows:

Ramsay sedation scale

Score	Response
1	Anxious or restless or both
2	Cooperative, orientated and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

Ethical considerations

The study protocol was approved by the Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran (No. IR.UMSHA.REC 1397.222). This

trial was approved by the Iranian Registry of Clinical Trials (N0. IRCT20120915010841N9). Moreover, informed consent was obtained from all patients and they were all assured of the confidentiality of personal information. To observe the ethical considerations, the participants were informed of the confidentiality of the data, stages of the study, and research techniques. Moreover, they were all allowed to leave the project at any given time. No financial cost was imposed on the participants.

Statistical analysis

The data were analyzed in SPSS software (Version 21) through t-test, the Chi-square test, and ANOVA. Moreover, the frequency of all the variables was assessed in this study. P-value less than 0.05 was considered statistically significant.

Results

The mean age of subjects was 22.28 ± 4.04 and 23.08 ± 4.95 years in bullous injection and continuous intravenous lidocaine infusion group, respectively. According to the results, there was no significant difference between the two groups in terms of age ($P=0.53$). (Table 1) presents the comparison between two groups in terms of the length of the first and second stages of labor and drug dosage. According to the findings in the table 1, the mean length of the first and second stages of labor and the mean dose of lidocaine in the bolus injection group were significantly lower than the continuous infusion group.

Table 1- Comparison between the two groups regarding the length of the first and second stages of labor and drug dosage

Variables	Continuous		Bullous		P value
	Mean	SD	Mean	SD	
The length of the first stage of labor	47.04	17.43	42.28	26.24	0.03
The length of the second stage of labor	47	28.43	34.12	12.1	0.03
Dose of lidocaine	267.80	81.15	172	73.71	<0.001

(Table 2) represents the comparison between the two groups regarding systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). The mean systolic blood pressure at 20 and 30 minutes was significantly lower in continuous group than bullous group ($P<0.05$). Based on the results of the ANOVA test, there was a significant difference between the two groups in terms of systolic blood pressure at different times ($F=7.44$; $P=0.008$).

The mean of diastolic blood pressure (DBP) at 40 minutes in continuous group was significantly lower than bullous group ($P=0.02$). However, there was no significant difference between the two groups at different times regarding DBP ($F=0.02$; $P=3.02$). A significant difference was observed regarding mean arterial pressure

(MAP) up to 60 minutes ($P=0.002$). Moreover, there was a significant difference between the two groups in terms of MAP at different times ($F=7.4$; $P=0.01$).

The comparison of the two groups in terms of heart rate at different times showed no significant difference ($F=1.79$; $P=0.19$). Based on the ANOVA test, the comparison of the two groups showed a significant difference in terms of pain score ($F=18.13$; $P<0.001$). So that in 10 minutes and minutes after 30 minutes, the mean pain score of women in the bolus injection group was significantly lower than continuous infusion ($P<0.05$). According to the findings of the (Table 3), the mean sedation score was significantly lower in the continuous group than bolus group ($P<0.001$).

Table 2- Comparison systolic blood pressure, diastolic blood pressure and mean arterial pressure in the two groups

Variables	Systolic Blood Pressure			Diastolic Blood Pressure			Mean Arterial Pressure		
	Continuous	Bolus	P value	Continuous	Bolus	P value	Continuous	Bolus	P value
Baseline	121.42	122.54	0.74	73.25	74.75	0.602	90.08	91.39	0.64
After injection	116.24	122.19	0.053	68.60	74.28	0.08	83.76	93.15	0.005
10m	112.80	120.28	0.050	68.32	71.56	0.83	83.16	90.56	0.01
20m	111.44	119.52	0.02	69.20	74.08	0.09	82.72	90.08	0.01
30m	111.76	120.44	0.01	69.76	75.56	0.057	83.12	89.32	0.055
40m	114.37	121.63	0.06	67.72	74.18	0.02	83.68	91.52	0.01
60m	115.80	121.29	0.18	70.28	74.58	0.15	85.48	90.52	0.002
End of first stage	117.20	123.36	0.96	72.24	75.16	0.24	88.36	92.44	0.08
End of second stage	118.080	119.56	0.62	73.80	71.52	0.49	88.80	89.58	0.16

Table 3- Comparison heart rate, pain score, and sedation in the two groups

Variables	Heart rate			Pain Score			Sedation		
	Continuous	Bolus	P value	Continuous	Bolus	P value	Continuous	Bolus	P value
Baseline	98.64	105.68	0.16	9.44	9.52	0.14	1	1.08	0.42
After injection	93.28	101.47	0.09	6.80	5.80	0.25	1.28	1.78	0.005
10m	86.44	91.68	0.18	3.48	2.16	0.01	1.68	2.2	0.007
20m	84.24	96.72	0.01	3.36	1.24	0.001	1.72	2.28	0.002
30m	87.40	97.08	0.04	3.00	1.16	0.001	1.68	2.28	0.003
40m	88.76	93.27	0.24	4.16	2.04	0.001	1.4	2.09	0.001
60m	86/84	97.76	0.101	6.12	3.00	0.003	1.32	2	0.004
End of first stage	89.86	98.20	0.08	7.44	2.16	0.001	1.24	1.81	<0.001
End of second stage	92.52	99.62	0.14	7.44	2.89	0.001	1.2	1.76	<0.001

No participants were reported with hypotension in continuous intravenous lidocaine infusion group, whereas in bullous injection group, one case with hypotension was observed in after 10th minute after injection. Regarding the rate of hypotension, there was no significant difference between the two groups ($P > 0.001$).

However, a significant difference was reported between the two groups in terms of tachycardia at 10, 20, and 60 minutes ($P < 0.001$). The comparison between the two groups in terms of hypotension and tachycardia at different times is shown in (Table 4).

Table 4- Comparison between the two groups at different times regarding hypotension and tachycardia

Variables	Hypotension					Tachycardia				
	Continuous		Bolus		P value	Continuous		Bolus		P value
No	%	No	%	No		%	No	%		
Baseline	0	0	0	0	0	11	44	14	56	0.39
After injection	0	0	0	0	0	8	32	12	58	0.08
10m	1	4	0	0	1	0	0	5	20	0.006
20m	1	4	0	0	1	2	8	10	40	0.008
30m	1	4	0	0	1	4	16	9	36	0.107
40m	1	4	0	0	1	3	12	6	24	0.27
60m	1	4	0	0	1	5	20	9	36	0.026
End of first stage	1	4	0	0	1	8	32	8	32	1
End of second stage	1	4	0	0	1	7	24	8	32	0.68

About 4% (n=1) and 36% (n=9) of patients suffered from nausea in bullous and in CEI groups, respectively. There was a significant difference between the two groups regarding nausea ($P=0.005$). The symptoms, such as vomiting, itching, and tingling lips were not reported

in any groups. In addition, there were no vacuum delivery, forceps delivery, dystocia, respiratory distress, and motor block in the groups. In addition, the cesarean section was reported in two cases in the CEI (n=1 or 4%)

and bullous (n=1 or 4%) groups. The both cases were due to fetal distress.

The mean values of Apgar score at the first minute after delivery were 8.96 ± 0.2 and 8.71 ± 0.55 in bullous injection and continuous intravenous lidocaine infusion groups, respectively. There was a significant difference between the two groups in terms of Apgar score at the first minute after delivery ($P=0.03$). Moreover, the mean values of Apgar score at fifth minute after delivery were

9.96 ± 0.2 and 9.66 ± 0.7 , in bullous injection and continuous intravenous lidocaine infusion group, respectively. There was a significant difference between the two groups in terms of Apgar score at fifth minute after delivery ($P=0.03$). The comparison of satisfaction with analgesia in two groups is shown in Table 5. There was a significant difference between the two groups regarding the satisfaction with analgesia. ($P<0.001$).

Table 5- Comparison of satisfaction with analgesia in two groups

Variables	Continuous		Bolus		P value
	NO	%	NO	%	
Low	6	24	0	0	<0.001
Moderate	8	32	3	12	
High	9	36	3	12	
Very high	2	8	19	76	

Discussion

Based on the obtained results of this study, the mean of systolic blood pressure, MAP, the frequency of tachycardia, Apgar score in the first and fifth minutes, and satisfaction were significantly higher in women underwent epidural bolus group, compared to CEI group. Moreover, mean values of pain score, first and second delivery duration, nausea and lidocaine consumption were lower among women underwent epidural bolus, compared to those in the CEI group.

The effectiveness of epidural analgesia has been proved regarding the management of pain during labor of term pregnancies [18-19]. In a study conducted by Feng et al., a similar incidence in maternal fever and better analgesia in the regular intermittent bolus was compared with continuous infusion during epidural labor analgesia. They attributed the epidural-related rise in maternal temperature to the IL-6 level elevation [20].

In this study, the adverse effects of epidural bolus technique were assessed and compared with CEI. Based on one study performed by Mazouni et al., labor duration or incidence of adverse events did not increase due to epidural analgesia in women underwent mid and late termination of pregnancy [21]. Consistent with our findings, Lim et al. showed lower pain scores and higher satisfaction with analgesia in women underwent regular intermittent epidural boluses, compared to those in the continuous epidural infusion group and contrary to our study, they showed a higher rate of nausea in regular intermittent epidural boluses; however, it was not significant. Moreover, no significant difference was observed between the two groups in terms of motor block, vomiting, and hypotension [22]. The obtained results were similar to our finding. In another study by Wong et al., more patients' satisfaction and less need for drug injection were observed in basal intermittent boluses group, compared to PCEA [15].

According to another study by Lin et al., CEI was compared with the PIEB technique in women underwent

spontaneous delivery. They showed a lower visual analog scale (VAS) in the PIEB group than those in the CEI group. In the same line, pain score was lower in those underwent epidural bolus, compared to those in the CEI group in this study. Moreover, the patients in the two groups showed no difference in terms of duration of different stages of labor, delivery methods, sensory block, fetal Apgar scores, and the maternal outcomes [23]. However, in this study, there was a difference between the two groups regarding the length of the first and second stages of labor and fetal Apgar scores. This may be related to different characteristics of the selected sample. Moreover, this may be attributed to the effect of various modes of anesthetic infusion (i.e., IEB or CEI) due to different dosing regimens of these approaches utilized by various obstetric practices and anesthesia providers.

In both studies, the subjects received lidocaine 1%. However, this study utilized 10 ml of 1% lidocaine plus 1 ml sufentanil, while the patients in a study conducted by Lin et al. were subjected to 4 ml test dose of lidocaine plus 0.15% ropivacaine 10 ml five minutes later.

Maggiore et al. investigated the role of epidural analgesia (i.e., CEI vs. PIEB) in the management of pain in the second trimester termination of pregnancy. Similar to this study, they showed a lower pain score in PIEB, compared to CEI technique. Moreover, there was no difference between the two groups in terms of hypotension and vomiting. Furthermore, they showed a lower incidence of motor block, greater patient satisfaction, and less nausea in the second trimester of pregnancy in the PIEB group, compared to CEI technique [24].

Similar to the study conducted by Maggiore et al., higher levels of satisfaction with analgesia and lower nausea were reported in women underwent in epidural bolus group, compared to CEI in this study [24]. Higher consumption of opioids in the CEI Group may lead to a greater incidence of nausea. However, no difference was

observed between the two groups in terms of the incidence of motor block.

Another study by Capogna et al. was performed to compare the CEI and PIEB techniques for labor analgesia among term parturients. Based on the results of the study performed Capogna et al., the rate of motor block was lower in CEI and PIEB groups, compared to the findings of this study. Other adverse events were not compared between the two groups in the mentioned study [9]. It is believed that the observed difference is associated with various distribution and concentration of local anesthetic and different agents (Lidocaine 1% vs. bupivacaine and fentanyl) used in the compared studies.

Intervertebral foramen leads to the more uniform distribution of solution in the epidural space and there is an association between intermittent boluses of local anesthetics and uniform spread; however, it is not the same regarding continuous infusion [25]. Clinical advantages of epidural boluses in comparison to the infusion are supported by clinical observations, which showed a reduction in drug consumption, higher sensory block, and patient satisfaction among patients underwent epidural boluses [15, 23-24, 26].

However, there was no difference between two groups regarding the motor block which may be due to the concentration of local anesthetic and different used drug in the compared studies.

Conclusion

In women undergoing epidural analgesia, epidural bolus injection of lidocaine 1% is associated with greater analgesia and satisfaction than continuous infusion. Moreover, pain score, first and second delivery duration, and lidocaine consumption were lower in women underwent bolus injection, compared to those in continuous infusion group.

References

- [1] Junge C, von Soest T, Weidner K, Seidler A, Eberhard-Gran M, Garthus-Niegel S. Labor pain in women with and without severe fear of childbirth: A population-based, longitudinal study. 2018; 45(4):469-77.
- [2] McKenzie C, Cobb B, Riley E, Carvalho B. Programmed intermittent epidural boluses for maintenance of labor analgesia: an impact study. *Int J Obstet Anesth.* 2016; 26:32-8.
- [3] Manouchehrian N, Rabiei S, Moradi A, Lakpur Z. Comparison of Intrathecal Injection of Fentanyl and Sufentanil on the Onset, Duration, and Quality of Analgesia in Labor: A Randomized, Double-Blind Clinical Trial. *Anesth Pain Med.* 2020; 10(3): e99843.
- [4] Powell MF, Jarzombek KW, Venhuizen KJ, Tubinis MD, Morgan CJ, Frölich MA. Comparing Bupivacaine, Lidocaine, and a Combination of Bupivacaine and Lidocaine for Labor Epidural Activation: A Prospective, Randomized, Double-Blind Study. *Asian J Anesthesiol.* 2019; 57(2): 55-60.
- [5] Afolabi BB, Lesi FE. Regional versus general anaesthesia for caesarean section. *Cochrane Database Syst Rev.* 2012; 10:Cd004350.
- [6] Practice Guidelines for Obstetric Anesthesia: An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *Anesthesiology.* 2016; 124(2):270-300.
- [7] Van der Vyver M, Halpern S, Joseph G. Patient-controlled epidural analgesia versus continuous infusion for labour analgesia: a meta-analysis. *Br J Anaesth.* 2002; 89(3):459-65.
- [8] Halpern SH, Carvalho B. Patient-controlled epidural analgesia for labor. *Anesth Analg.* 2009; 108(3):921-8.
- [9] Capogna G, Camorcia M, Stirparo S, Farcomeni A. Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: the effects on maternal motor function and labor outcome. A randomized double-blind study in nulliparous women. *Anesth Analg.* 2011; 113(4):826-31.
- [10] Chua SM, Sia AT. Automated intermittent epidural boluses improve analgesia induced by intrathecal fentanyl during labour. *Can J Anaesth.* 2004; 51(6):581-5.
- [11] Fettes P, Moore C, Whiteside J, McLeod G, Wildsmith J. Intermittent vs continuous administration of epidural ropivacaine with fentanyl for analgesia during labour. *Br J Anaesth.* 2006; 97(3):359-64.
- [12] Leo S, Ocampo C, Lim Y, Sia A. A randomized comparison of automated intermittent mandatory boluses with a basal infusion in combination with patient-controlled epidural analgesia for labor and delivery. *Int J Obstet Anesth.* 2010; 19(4):357-64.
- [13] Lim Y, Chakravarty S, Ocampo CE, Sia AT. Comparison of automated intermittent low volume bolus with continuous infusion for labour epidural analgesia. *Anaesth Intensive Care.* 2010; 38(5):894-9.
- [14] Sia AT, Lim Y, Ocampo C. A comparison of a basal infusion with automated mandatory boluses in parturient-controlled epidural analgesia during labor. *Anesth Analg.* 2007 Mar;104(3):673-8.
- [15] 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.
- [16] 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.
- [17] Onuoha OC. Epidural Analgesia for Labor: Continuous Infusion Versus Programmed Intermittent Bolus. *Anesthesiol Clin*. 2017; 35(1):1-14.
- [18] Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. *Cochrane Database Syst Rev*. 2011(12):Cd000331.
- [19] Jones L, Othman M, Dowswell T, Alfirevic Z, Gates S, Newburn M, et al. Pain management for women in labour: an overview of systematic reviews. *Cochrane Database Syst Rev*. 2012(3): Cd009234.
- [20] Feng SW, Xu SQ, Ma L, Li CJ, Wang X, Yuan HM, et al. Regular intermittent bolus provides similar incidence of maternal fever compared with continuous infusion during epidural labor analgesia. *Saudi Med J*. 2014; 35(10):1237-42.
- [21] Mazouni C, Guidicelli B, Gamberre M, Voiret C, Pellegrin V. Influence of epidural analgesia on labor in mid and late termination of pregnancy: an observational study. *Int J Obstet Anesth*. 2007;16(4):383-4.
- [22] Lim Y, Sia AT, Ocampo C. Automated regular boluses for epidural analgesia: a comparison with continuous infusion. *Int J Obstet Anesth*. 2005;14(4):305-9.
- [23] Lin Y, Li Q, Liu J, Yang R, Liu J. Comparison of continuous epidural infusion and programmed intermittent epidural bolus in labor analgesia. *Therapeutics and clinical risk management*. 2016; 12:1107-12.
- [24] Leone Roberti Maggiore U, Silanos R, Carlevaro S, Gratarola A, Venturini PL, Ferrero S, et al. Programmed intermittent epidural bolus versus continuous epidural infusion for pain relief during termination of pregnancy: a prospective, double-blind, randomized trial. *Int J Obstet Anesth*. 2016; 25:37-44.
- [25] Hogan Q. Distribution of solution in the epidural space: examination by cryomicrotome section. *Reg Anesth Pain Med*. 2002; 27(2):150-6.
- [26] Ueda K, Ueda W, Manabe M. A comparative study of sequential epidural bolus technique and continuous epidural infusion. *Anesthesiology*. 2005; 103(1):126-9.