Original Article

Continuous preperitoneal infusion of ropivacaine for postoperative analgesia in patients undergoing major abdominal or pelvic surgeries. A prospective controlled randomized study

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Abstract

Background and Aims: This study was conducted to compare continuous preperitoneal infusion (CPI) with continuous epidural infusion (CEI) of ropivacaine for pain relief and effect on pulmonary functions after major abdominal and pelvic surgeries.
Material and Methods: One hundred patients were randomized into two equal groups. Patients in CPI group ($n = 50$) received analgesia by continuous infusion of 0.2% ropivacaine, whereas those in the CEI group ($n = 50$) received continuous epidural infusion of 0.2% ropivacaine. The primary outcome was the first request of analgesia. The secondary outcome was the influence on the pulmonary functions.
Results: The time for the first request of analgesia was longer in the CPI group compared with that in the CEI group (7.3 ± 1.6 vs. 4.1 ± 1.1 h with P value = 0.001). The daily dose of morphine was lesser in CPI versus CEI group (11.3 ± 1 against 17.4 ± 0.9 mg). The pulmonary function tests were comparable except peak expiratory flow rate, which was better in CPI (170 ± 5.4) than CEI group (148.1 ± 5.8; with P value = 0.001).
Conclusion: Continuous preperitoneal infusion provides a superior analgesic effect than the continuous epidural infusion as regards delayed first request of analgesia, better pain scores, lesser usage of additional analgesics with better respiratory function.

Keywords: Abdominal tumors, epidural infusion, pelvic tumors and ropivacaine, preperitoneal infusion

Introduction

Pain from major abdominal or pelvic surgeries is severe and increases in intensity during mobilization.[1]This pain increases perioperative complications, healthcare costs, and even mortality. Consequently, adequate management of postoperative pain is mandatory.[2]

Continuous epidural infusion (CEI) is still the gold standard analgesic technique in abdominal surgeries. It offers a superior analgesic effect than systemic administration of opioid.[3] However, CEI is associated with 5-25% risk of failure[4] and may be associated with complications such as respiratory depression, hypotension, urinary retention, epidural hematoma, or inadequate analgesic distribution.[5,6]

Continuous preperitoneal infusion (CPI) with local anesthetics is characterized by effectiveness, simplicity, and safety[7] It is superior to systemic opioids.[8] In addition, CPI has a very low rate of technical failure (~1%) and zero toxicity.[9]

Existing literature comparing CPI and CEI shows varying results, from superiority of CEI[10,11] to superiority of CPI.[12-14]

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Therefore, this prospective study was planned to compare CEI and CPI with regard to the postoperative pain relief measured by the postoperative opioid requirements and the time of the first analgesic request. We also recorded the changes in respiratory function and haemodynamics with both techniques.

Material and Methods

This prospective randomized study was conducted between June 2015 and July 2018 after receiving the approval from local institutional review board with the coded number (R/15.05.03). Patients of both sexes aged 18–80 years and ASA physical status I or II who were to undergo elective open resection of abdominal tumors through a periumbilical midline incision were invited to participate in this study.

Patients who refused to participate, those with pregnancy, or any contraindication for the epidural catheter, those with a known history of sensitivity to any of the local anesthetics used, moderate to severe respiratory dysfunction, active drug addiction or ongoing treatment with opiates, and those with inability to communicate or mental disorders or disturbed consciousness were excluded from the study. Lastly, patients in whom separate closure of the peritoneum was not possible due to previous surgery and those scheduled for laparoscopic surgery were also excluded.

In the preoperative visit, the study protocol and the linear Visual Analogue Scale (VAS) were explained to every patient using a graded ruler from 0 to 10. A written informed consent was signed by every patient. All patients received 0.02 mg/kg midazolam as premedication the night before the operation.

In the operation theater, basic monitors were applied and basal vital parameters were monitored and recorded. Oxygen was provided via face mask (6 L/min) for 5 min before induction of anesthesia. Infusion of Ringer's Lactate solution at a rate of 5 mL/kg via 18-gauge cannula was done.

Randomization was done by a computer-generated randomization sequence. The staff member who performed the randomization sequence had no clinical knowledge of the study and was not involved with patient recruitment or data collection. Allocation concealment was achieved by the usage of opaque and sealed envelopes. Participants were randomly allocated into two equal groups, 50 patients in every group.

The first group received the analgesia via CPI ($n = 50$): The epidural catheter was inserted between the parietal peritoneum and the transversalis fascia during the closing of the wound with 10 mL of ropivacaine 0.2% followed by a continuous infusion of ropivacaine 0.2% at the rate of 5 mL/h through a syringe pump for the next 48 h. In the second group, the patients received analgesia via CEI ($n = 50$): The epidural catheter was inserted between T8 and T10 before induction of anesthesia and the patient received 10 mL of 2% ropivacaine as a test dose. Afterward a continuous infusion of ropivacaine 0.2% at the rate of 5 mL/h through a syringe pump for 48 h.

Induction of anesthesia was accomplished with 2–3 μg/kg of fentanyl followed by intravenous propofol slowly (2 mg/kg) until loss of verbal contact. Tracheal intubation was facilitated with 0.5 mg/kg atracurium; one fifth of this dose was used for maintenance of muscle relaxation. The initial setting of mechanical ventilation was adjusted with tidal volume 8 mL/kg, respiratory rate 12 breath/min, positive end-expiratory pressure 5 cmH_2O, and I/E ratio 1:2 aiming to maintain end tidal $CO_2 \sim 35$ mmHg. Anesthesia was maintained with sevoflurane in O_2/air mixture. Once the surgery ended, the neuromuscular residual blockade was reversed, with a mixture of neostigmine 0.04 mL/kg and atropine 0.02 mL/kg. Tracheal extubation was performed when the patient was conscious and breathing comfortably.

During the wound closure, the single participating surgeon inserted a 16-gauge epidural catheter after creation of multiple perforations by 22 G needle, 1 cm apart until a length suitable for the wound. The catheter was inserted 3 cm away from the lower end of midline incision. A bacterial filter was fixed to the catheter. The catheter was positioned between the closed parietal peritoneum and the undersurface of the transversalis fascia, along the full length of the wound. Thereafter, the surgeon closed the wound in layers. The catheter was secured with a Steri-Strip and covered with a sterile transparent dressing independent of the wound. The anesthetic nurse injected the assigned bolus dose of the assigned solution through the catheter and connected with the syringe pump while the pump was set at a rate of 5 mL/h. The catheter was removed after 48 hours, after injection of the last dose and being sure of complete catheter extraction.

The assessment of pain was done by the recorded visual analogue score (VAS) of pain at 1 h following transfer the patient to PACU then at 2,4,8,12, and 16 h. The pain assessment during rest and on coughing was recorded at 24 and 48 h postoperatively. If the recorded VAS was ≥3, a bolus dose of 5 mL of ropivacaine was given. Reassessment of VAS was done within 30 min and if VAS was still ≥3, one mg morphine was given intravenously as an analgesic rescue. The time of the first request of analgesia was recorded. Also, the dose of morphine used in the first and second postoperative day were recorded.

The evaluation of respiratory functions was done by recording the respiratory rate preoperatively, and during the same time intervals of recorded VAS. Pulmonary function tests were done preoperatively, 24 and 48 h after the surgery by measuring forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) using a spirometer (SP10, CONTEC™). The ratio FEV1/FVC was calculated. The peak expiratory flow rate (PEFR) was recorded using a peak flow meter.

The postoperative hemodynamic variables, which included the heart rate and mean arterial blood pressure were recorded at 1, 2,4, 8, 12, 16, 24, and 48 h. C-reactive protein (CRP) was recorded 72-h postoperatively. Any other side effects were recorded such as nausea or vomiting, which necessitated treatment with intravenous 10 mg of metoclopramide.

Sample size calculation

The results of a pilot study showed 20% decrease of VAS at the fourth hour postoperative. The calculated effect size was 0.8, α error = 0.05, and the power of the study was 0.90. The calculated sample size was 88 cases, but there may be a 20% drop out rate. Therefore, we needed a total number of 100 cases (50 cases per group).

Statistical analysis

The data were analysed using SPSS version 20. The normality of the distribution of data was tested by Kolmogorov–Smirnov test. Mean ± standard deviation was used to describe the continuous or quantitative data, whereas the number and percentage were used to describe the categorical (qualitative) data. Association between these data was tested using Chi-square (χ^2) or Fisher's exact test. Normally distributed data were tested using Student's *t*-test (unpaired), whereas Mann–Whitney *U*-test was used to test data with non-normal distribution. The *P* value was set at statistical significance of <0.05.

Results

During the period of the study, 150 patients were assessed for eligibility; 40 patients had one or more exclusion criteria. 10 patients refused to participate in this study.

The demographics and surgical characteristics were comparable between the two groups [Table 1]. The table also shows the time to first analgesia, and the total morphine consumption

Table 1: Demographic and surgical characteristics. Data were presented in mean±SD or number and percentage of the patients

	Group CPI (*n*=50)	Group CEI (*n*=50)	*P*
Demographics			
Age (years)	46.8±7.0	45.6±6.9	0.4
Gender (M/F)	14/33	11/37	0.4
BMI (kg/m²)	29.6±3.8	30.2+3.5	0.7
ASA I	31 (65.1%)	32 (66.7%)	0.9
ASA II	16 (34.0%)	16 (33.3%)	0.9
Operative time (min)	162±28.2	156.52+33.4	0.3
Length of the wound (cm)	15.8±4.6	16.2±4.8	0.7
Type of tumor			
Uterine carcinoma	13 (27.7%)	15 (31.3%)	
Cancer colon	13 (27.7%)	11 (22.9%)	0.9
Ovarian cancer	10 (21.3%)	15 (31.3%)	
Urinary tumor	11 (23.4%)	7 (14.6%)	
Tumor pathology			
Malignant	35	37	0.7
Nonmalignant	12	11	
First request of analgesia (h)	7.3±1.6	4.07±1.1*	0.001
The dose of morphine on the first postoperative day	11.3±1	17.39±0.9*	0.001
The dose of morphine on the second postoperative day	7.06±0.9	13.25±0.9*	0.001

*SD: Standard deviation; CPI: Continuous preperitoneal infusion; CEI: Continuous epidural infusion; BMI: Body mass index; ASA: American Society of Anesthesiologists. *P-value≤0.05: Statistically significant*

Table 2: The postoperative assessment of pain within the studied groups measured by the visual analogue score (VAS). Data presented as median (IQR)

	Group CPI (*n*=50)		Group CEI (*n*=50)		*P*
	Median	IQR	Median	IQR	
1 h	3	(2-4)	3	(2-4)	0.6
2 h	3	(2-4)	3	(2-4)	0.7
4 h	2	(0-4)	3	(3-4)*	0.001
8 h	3	(2-4)	4	(3-5)*	0.001
12 h	3	(1-3)	4	(3-5)*	0.001
16 h	2	(1-3)	3	(2-4)*	0.001
24 h at rest	3	(2-4)	4	(2-5)*	0.001
24 h at cough	3	(4-5)	4	(4-5)*	0.001
48 h at rest	1	(0-3)	2	(2-3)*	0.001
48 h at cough	2	(2-4)	3	(3-4)*	0.01

*CPI: Continuous preperitoneal infusion; CEI: Continuous epidural infusion; CI: Confidence interval. *P-value ≤ 0.05: Statistically significant* on the first and second postoperative days. The CEI group had shorter analgesia and consumed more morphine on both postoperative days.

Table 2 shows the VAS scores in the two groups along with intergroup comparisons at different times. The CEI group had higher pain scores throughout the period of the study starting at 2 hours postoperative than CPI group.

CEI group had a lower respiratory, heart rate, and blood pressure starting at 2 hours postoperativethan CPE group [Figures 1 and 2].

Table 3 shows the respiratory functions and CRP values. The CEI group had a lower PEFR and CRP values than the CPI group.

Tables 3: Preoperative and postoperative pulmonary function tests (FVC, FVE1), the ratio between them, PEFR, and CRP during the first 48 h. Data were expressed in mean±SD

	Group CPI (*n*=50)		Group CEI (*n*=50)		*P*
	Mean	SD	Mean	SD	
FVC (%)					
Basal	86.1±2.9		87.0±2.8		0.8
24 h	87.3±2.9		87.5±3.0		0.7
48 h	87.8±2.8		87.4±2.9		0.5
FEV1 (%)					
Basal	97.8±1.3		97.9±1.6		0.7
24 h	97.1±3.6		97.6±3.5		0.5
48 h	97.5±3.5		97.6±3.3		0.9
PEFR					
Basal	282.0±6.4		274.9±6.0*		0.001
24 h	170.5±5.4		148.1±5.8*		0.001
48 h	191.8±6.7		164.5±5.4*		0.001
FEV1/					
FVC	1.1±0.1		1.1±0.1		0.9
Basal	1.1±0.1		1.1±0.1		0.8
24 h	1.1±0.1		1.1±0.1		0.6
48 h					
CRP	35.3±3.8		39.9±5.9*		0.001

*FVC1: Forced vital capacity, FEV1: Forced expired volume, PEFR: Peak expiratory flow rate, CRP: C-reactive protein; CPI: Continuous preperitoneal infusion; CEI: Continuous epidural infusion. *P-value≤0.05: Statistically significant*

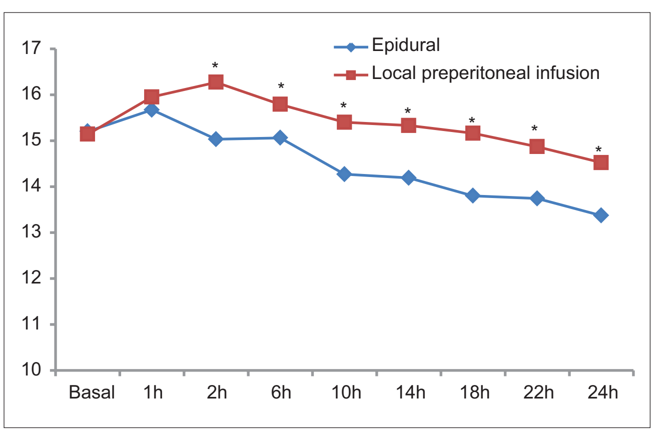

Figure 1: The recorded changes in the respiratory rate in the studied groups

The incidence of nausea was comparable among the studied groups.: Seven patients (14%) in the CPI group with five vomiting compared to nine patients (18%) with nausea and five with vomiting in the CEI group.

Discussion

This prospective randomized study found that continuous peritoneal infusion (CPI) had a significant prolongation of the first analgesic request, more reduction of VAS of pain, and a reduction of analgesic consumption of morphine in comparison with CEI. Moreover, it resulted in better respiratory rates and respiratory functions with better stabilization of hemodynamics.

Similar results exist in the literature. Bertoglio *et al.*[13] found a reduction of VAS in the CPI group without any difference in morphine consumption. Neil *et al.*[12] had similar results in full-term pregnant patients with continuous wound infiltration (CWI) being superior to CEI. Dhanapal *et al.*[14] also found CPI superior in terms of VAS scores and postoperative morphine consumption.

On the other hand Jouve *et al.*[11] had recorded the reduction of median postoperative dynamic pain score in the CEI group than in CWI group [10 (0.6–20) vs. 37 (30–49) with *P* value <0.001]. However, this study was conducted on a

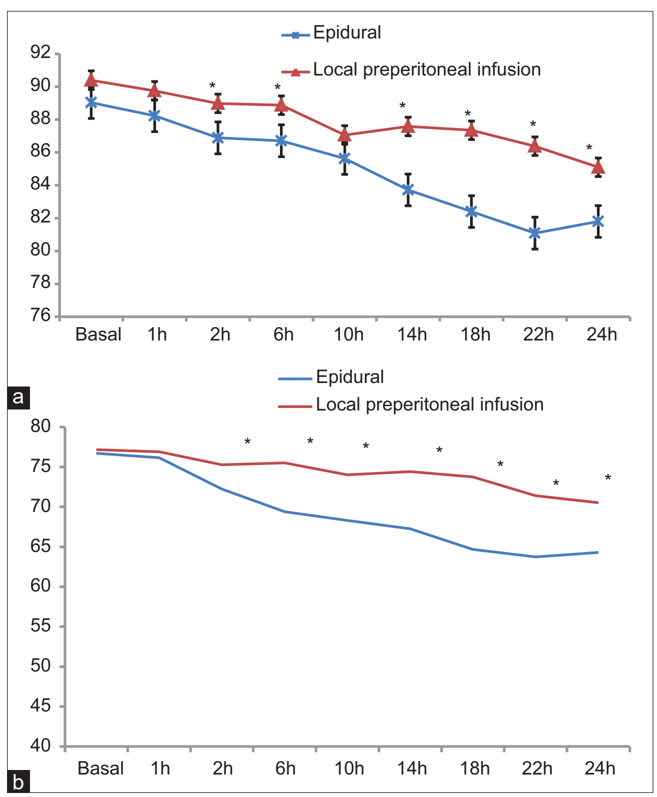

Figure 2: (a) The recorded changes of postoperative mean arterial blood pressure (mmHg) in the studied groups. (b) The recorded changes of postoperative heart rate (beat/min) in the studied groups

small sample size of only 50 patients. Mouawad *et al.*[10] also demonstrated that the recorded pain scores were significantly higher in continuous preperitoneal wound catheter group when compared with continuous epidural group in the PACU and on the day of surgery, with similar secondary outcomes viz., postoperative complications, return of bowel function and length of hospital stay.

Peritoneum plays an important role in pain perception after injury through a complex array of neuro-immuno-humoral cascades via secretion of various mediators responsible for systemic and local inflammatory response.[15] The neural pathway involves both vagal and spinal afferents. The release of pro-inflammatory cytokines sensitizes the peritoneum and results normal nonpainful stimuli being perceived as painful and in exaggeration of perception of painful stimuli. In addition, injury to the peritoneum causes changes in the central nervous system leading to an increase in spontaneous firing of wide dynamic neurons in the rat spinal dorsal horn.[16] We chose ropivacaine in this study due to its suppression of bradykinin and substance P-mediated signaling.[17]

The anti-inflammatory effect of local anesthetic infusion was evident by the significant drop of CRP in the preperitoneal group. This is an additional benefit of CPI over CEI and may contribute to better analgesia. Sammour *et al*.[15] also concluded that the inflammatory response of peritonium to injury is the main central component of surgical stress.

Various investigators have placed the catheter subcutaneously,[18] above the fascia,[19] below the fascia,[20] or in the preperitoneal space. Encouraging analgesic results have been seen when the catheter is placed deep to the fascia or in the preperitoneal space in patients undergoing midline laparotomy or open nephrectomy and renal transplant surgery.[21,22]

The better respiratory rate with CPI in our study may be due to the better analgesic effect of CPI, which influences better movement of the chest. However, Ozturk *et al.*[23] found no difference in FEV1 and FEV1/FVC between preperitoneal admnistration of levobupivacaine and isotonic saline. Sistla *et al.*[24] also concluded that there were no benefits in pulmonary function with intermittent wound perfusion with bupivacaine.

Results of some studies were in contrast to our findings. Ozturk *et al.*[23] compared 10 mL of 0.25% levobupivacaine and 0.9% saline through preperitoneal wound catheter twice daily for 24 h postoperatively. They observed that the forced expiratory volumes in the first second (FEV1) and the ratio of FEV1/FVC were decreased from the preoperative values in both groups but were not different in the two groups ($P = 0.4$). Sistla *et al.*[24] also observed no beneficial effect of intermittent wound perfusion of bupivacaine on the pulmonary function.

No hemodynamic complications were observed during the period of study. However, HR and MAP were significantly decreased in the CEI group but were still within normal limits.

Conclusion

In conclusion, continuous preperitoneal infusion of ropivacaine had a significant analgesic effect with decreased consumption of opioid and delayed request for additive analgesia with better respiratory function and better stability of hemodynamics compared to continuous epidural infusion.

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Conflicts of interest
This research received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors. The authors have no financial or other conflict of interest to declare and no financial or other relationships leading to conflict of interest associated with publication of this manuscript.

Manuscript had been read and approved by all authors, that the requirement for authorship. Each author believes that the manuscript represent honest work.

References

1. Liu S. Anesthesia and analgesia for colon surgery. Res Anesth Pain Med 2004;29:52-7.
2. Kehlet H, Jensen TS, Wolf CJ. Persistent postsurgical pain risk factors and prevention. Lancet 2006;367:1618-25.
3. Wu CL, Cohen SR, Richman JM, Rowlingson AJ, Courpas GE, Cheung K, *et al*. Efficacy of postoperative patient- controlled and continuous infusion epidural analgesia versus intravenous patient-controlled analgesia with opioids: A meta-analysis. Anesthesiology 2005;103:1079-88.
4. Marret E, Remy C, Bonnet F. Meta-analysis of epidural analgesia versus parenteral opioid analgesia after colorectal surgery. Br J Surg 2007;94:665-73.
5. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: A meta-analysis. JAMA 2003;290:2455-63.
6. Christie IW, Mc Cabe S. Major complications of epidural analgesia after surgery: Results of a six-year survey. Anaesthesia 2007;62:335-41.
7. Liu SS, Richman JM, Thirlby RC, Wu CL. Efficacy of continuous wound catheters delivering local anesthetic for postoperative analgesia: A quantitative qualitative review of randomized controlled trials. J Am Coll Surg 2006;203:914-32.
8. Cheong WK, Seow-Choen F, Eu KW, Tang CL, Heah SM. Randomized clinical trial of local bupivacaine perfusion versus parenteral

morphine infusion for pain relief after laparotomy. Br J Surg 2001;88:357-9.
9. Beaussier M, El'Ayoubi H, Schiffer E, Rollin M, Parc Y, Mazoit JX, *et al*. Continuous preperitoneal infusion of ropivacaine provides effective analgesia and accelerates recovery after colorectal surgery a randomized, double -blind, placebo-controlled study. Anesthesiology 2007;107:461-8.
10. Mouawad NJ, Leichtle SW, Kaoutzanis C, Welch K, Winter S, Lampman R, *et al*. Pain control with continuous infusion preperitoneal wound catheters versus continuous epidural analgesia in colon and rectal surgery: A randomized controlled trial. Am J Surg 2018;215:570-6.
11. Jouve P, Bazin JE, Petit A, Minville V, Gerard A, Buc E, *et al*. Epidural versus continuous preperitoneal analgesia during fast-track open colorectal surgery: A randomized controlled trial. Anesthesiology 2013;118:622-30.
12. O'Neill P, Duarte F, Ribeiro I, Centeno MJ, Moreira J. Ropivacaine continuous wound infusion vs epidural morphine for postoperative analgesia after cesarean delivery. A randomized controlled trial. Anesth Analg 2012;114:179-85.
13. Bertoglio S, Fabiani F, Negri PD, Corcione A, Merlo DF, Cafiero F, *et al*. The postoperative analgesic efficacy of preperitoneal continuous wound infusion compared to epidural continuous infusion with local anesthetics after colorectal cancer surgery: A randomized controlled multicenter study. Anesth Analg 2012;115:1442-50.
14. Dhanapal B, Sistla SC, Badhe AS, Ali SM, Ravichandran NT, Galidevara I. Effectiveness of continuous wound infusion of local anesthetics after abdominal surgeries. J Surg Res 2017;212:94-100.
15. Sammour T, Kahokehr A, Mattias S, Hill A. Peritoneal damage: The inflammatory response and clinical implications of the neuro-immuno-humoral axis. World J Surg 2010;34:704-20.
16. Sugiyama D, Furue H, Imoto K, Kawatama M. Contribution of peritoneum incision to generation of spontaneous activity in rat spinal cord dorsal horn neurons. Neurosci Res 2009;65:S142.
17. Dias MP, Newton DJ, McLeod GA, Khan F, Belch JJF. The inhibitory effects of local anaesthetics on the vascular flare responses to bradykinin and substance P in human skin. Anaesthesia 2008;63:151-5.
18. Baig MK, Zmora O, Derdemezi J, Weiss EG, Nogueras JJ, Wexner SD. Use of the on-Q pain management system is associated with decreased postoperative analgesic requirement: Double-blind randomised placebo pilot study. J Am Coll Surg 2006;202:297-305.
19. Fredman B, Zohar E, Tarabykin A, Shapiro A, Mayo A, Klein E, *et al.* Bupivacaine wound installation via an electronic patient-controlled analgesia device and double-catheter system does not decrease postoperative pain or opioid requirements after major abdominal surgery. Anesth Analg 2001;92:189-93.
20. Wang LW, Wong SW, Crowe PJ, Khor KE, Jastrzab G, Parasyn AD, *et al.* Wound infusion with local anaesthetic after laparotomy: A randomized controlled trial. ANZ J Surg 2010;80:794-801.
21. Biglarnia AR, Tufveson G, Lorant T, Lennmyr F, Wadström J. Efficacy and safety of continuous local infusion of ropivacaine after retroperitoneoscopic live donor nephrectomy. Am J Transplantation 2011;11:93-100.
22. Forastiere E, Sofra M, Giannarelli D, Fabrizi L, Simone G. Effectiveness of continuous wound infusion of 0.5% ropivacaine by On-Q pain relief system for postoperative pain management after open nephrectomy. Br J Anaesth 2008;101:841-7.
23. Ozturk E, Yilmazlar A, Coskum F, Isik O, Yilmazlar T. The beneficial effects of preperitoneal catheter analgesia following colon and rectal resections: A prospective, randomized, double-blind, placebo-controlled study. Tech Coloproctol 2011;15:331-6.
24. Sistla SC, Sibal AK, Ravishankar M. Intermittent wound perfusion for postoperative pain relief following upper abdominal surgery: A surgeons perspective. Pain Pract 2009;9:65-70.