Original Article

Predicting postoperative pain by using preoperative pain threshold in response to electrical stimulus in women undergoing gynaecological cancer surgery - Single-arm, prospective, observational study

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ABSTRACT

Background and Aims: Individual variability leading to different pain experiences makes pain prediction challenging. This study aimed to evaluate whether preoperative electrical pain threshold testing is predictive of postoperative pain. **Methods:** Following ethics committee approval and registration of the trial, 40 consenting patients undergoing open laparotomy (interval debulking surgery) for ovarian cancer were included in the study. Electrical stimulus (maximum of 256 μA) was used preoperatively to determine the current perception threshold (CPT) and pain equivalent current (PEC). A numerical rating scale (NRS; 0–10, with 0 indicating no pain and 10 indicating severe pain) was used to assess pain. All patients received intravenous paracetamol in accordance to body weight, diclofenac (1 mg/kg, maximum 50 mg), and tramadol (1 mg/kg, maximum 50 mg) eight hourly for 24 hours. The preoperative PEC was compared with worst pain score (PS) at movement at the end of 24 hours. PEC was also compared with average PS at rest, at movement, and with opioid requirement (24 hours). **Results:** The median values of CPT and PEC were 12.51 (45 [10.1–14.6]) μA and 94.75 (174 [48.8–94.7]) μA, respectively. A moderate correlation was observed between PEC and worst PS ($P = 0.01$, $r = -0.402$), with patients having PEC less than 60 μA being associated with moderate-to-severe PS. There was no correlation between PEC and average PS at rest ($P = 0.16$, $r = 0.225$), at movement ($P = 0.46$, $r = 0.119$), and the postoperative opioid consumption in the first 24 hours ($P = 0.50$, $r = -0.110$). **Conclusion:** There is a moderate association between preoperative pain threshold in response to electrical stimulus and worst PS in the postoperative period following interval debulking surgery for ovarian cancer.

Key words: Analgesia, opioid, cytoreductive surgeries, laparotomy, ovarian cancer, pain, electrical stimulus

INTRODUCTION

Management of postoperative pain is an integral part of the enhanced recovery after surgery (ERAS) programme. Poorly managed pain can lead to inadequate patient mobilisation with its negative consequences on postoperative recovery and rehabilitation.[1] Appropriate pain relief leads to shortened hospital stay, reduced costs, and increased patient satisfaction.[2] Treatment of postoperative pain is an increasingly monitored measure for the quality of care offered to patients.[3]

In addition to physiological, emotional, and behavioural components, pain is influenced by genetic

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factors.[4,5] Individual variability leads to varied pain experiences and affects responses to pain treatment. Identifying the patients at risk of experiencing significant postoperative pain will allow for more individualised and effective pain management.[6]

Though different stimuli have been described for pain prediction, the utility and optimal modality for pain prediction remain unclear.[6] In this single-arm, prospective, observational study, we proposed to induce preoperative experimental pain through small electrical stimuli, that is, the pain equivalent current (PEC), and correlate the same with postoperative surgical pain following open laparotomy for ovarian cancer. The primary aim of the study was to evaluate the correlation between preoperative PEC and postoperative pain intensity noted as the worst pain score (PS) at movement in the first 24 hours. The secondary aim was to study the correlation of PEC with the average PS at rest, average PS at movement, 24-hour postoperative analgesic requirement. We also planned to study the association of pain with other independent variables like (age, body weight, duration, nature of surgery, and current perception threshold [CPT]).

METHODS

The current study was approved by the Institutional review board (vide approval number 3298 dated 18th June 2020) and registered with the Clinical Trials Registry – India [vide registration number: CTRI/2019/06/019812-https://ctri.nic.in/]. The study was conducted in tertiary care hospital following the ethical principles laid down for medical research by the Declaration of Helsinki, 2013. After explaining the study protocol, written informed consent was obtained from all the patients for participation in the study and using the patient data for research and publication. Patients who were up to 70 years of age, had American Society of Anesthesiologists (ASA) physical status I and II, diagnosed with ovarian cancer, and were scheduled for open laparotomy (interval debulking surgery [IDS]) under general anaesthesia were enrolled. Patients who had a history of alcohol or drug abuse, had a psychiatric disease, were on pain medications or in preoperative pain, had any medical condition that prevented the use of paracetamol, diclofenac, or opioids in the postoperative period were excluded. Patients who had chemotherapy-induced peripheral neuropathy (CIPN) grade 2 or above were also excluded. Patients in whom epidural analgesia was planned and those in whom surgical incision was extended, intraoperatively, beyond the normal periumbilical incision needing regional catheters were excluded.

On the day prior to the surgery, the patients were explained about the Numeric Rating Scale (NRS, in which 0 indicated no pain and 10 indicated severe pain) and its categorisation (mild [1–3], moderate [4–6], and severe/intolerable [7–10] pain).[7,8] Patients were then assessed for their pain thresholds by using an electrical stimulator called the Pain Vision (PS-2100, Nipro Co., Japan). This device is composed of an electrical stimulation system and a power-driven control system. It is used to objectively measure pain and is occasionally used for the diagnosis of neuropathy.[9,10]

The bipolar stimulating electrodes of the device were applied on the medial aspect of the left cubital fossa of the patients. The patients were given a stop switch and were asked to press the switch when endpoints were met. A 200 V current with a 50-Hz frequency and a pulse duration of 0.3 millisecond was used. Current strength was increased at 5 μA increments with a maximum of 256 μA to detect the CPT, which is the least current strength at which an individual would perceive the electrical stimulus. The electrical current was gradually increased till the patient perceived the stimulus as intolerable (more than 7 on the NRS). This was recorded as PEC. An average of three readings was noted for each patient.

Induction of general anaesthesia was standardised and included premedication with intravenous fentanyl (1–2 μg/kg) followed by propofol (1.5–2 mg/kg) and vecuronium (0.1 mg/kg) or atracurium (0.6 mg/kg). A suitably sized endotracheal tube was inserted into the trachea. Anaesthesia was maintained using oxygen, nitrous oxide in the ratio of 40:60, and sevoflurane (minimum alveolar concentration [MAC] of 0.8–1.2]. Non-invasive blood pressure, electrocardiogram, oxygen saturation, and capnogram were recorded. Intraoperative analgesic usage was restricted to intravenous morphine (0.1 mg/kg adjusted to lean body mass), given 30–45 minutes after induction. Intravenous fentanyl could be repeated as and when clinically indicated (intraoperative heart rate and blood pressure measuring higher than 15% of baseline). All patients received intravenous paracetamol as per body weight (<50 kg- 15 mg/kg; >50 kg received 1 gm) at the end of the surgery.

The postoperative pain regime was standardised for all patients. In the post-anaesthesia care unit (PACU), intravenous, fentanyl boluses were administered to treat moderate-to-severe pain, as per the patients' self-rated PS assessed using the NRS. All patients received intravenous tramadol (1 mg/kg, maximum 50 mg) 15 minutes after arrival to recovery or after the last dose of fentanyl, whichever was later. Intravenous diclofenac (1 mg/kg, maximum 50 mg) was given eight-hourly, timed two hours after injection of tramadol. Intravenous paracetamol was continued eight-hourly, timed to the last dose given in the operation theatre. In case of persistent pain above NRS 4/10 (on more than three occasions), fentanyl-filled patient-controlled analgesia (PCA) pump was to be started intravenously by the team members of the Acute Pain Service (APS) as per existing APS protocols. The PS was assessed six times in 24 hours: on arrival to PACU, two hours after surgery, on shifting out of the PACU, on the night of the surgery, the next morning, and at the end of 24 hours. The arithmetic mean of all PSs rounded to the nearest digit was noted as the average PS. All rescue opioid boluses inclusive of intraoperative doses were converted into morphine equivalents. At the end of 24 hours, the patients were interviewed by a member of the investigating team, who was blinded to analgesic requirements. Patients were to rate their worst pain experience in 24 hours on the NRS.

Due to a paucity of literature on the use of this technique in the prediction of postoperative pain, our sample size calculation was based on a previous study that used pressure for predicting post-operative pain.[11] In the same study, pressure pain assessment was done on 40 women, and it was seen that preoperative pressure pain tolerance significantly correlated with the Visual Analogue Scale (VAS) pain scores within 24 hours postoperatively ($P < 0.001$, $r = -0.52$). Hence, for our study, a sample size of 40 patients was calculated, which was powered to elicit a correlation of at least 0.45.

The relation between preoperative PEC and the postoperative NRS was done using the Spearman rho test. The Spearman rho test was used to compare PEC with analgesic consumption. A multiple regression analysis was used to determine the independent variables that were predictive of worst PS at the end of 24 hours. $P < 0.05$ was considered to be statistically significant. The IBM SPSS Statistics version 25.0 (IBM, NY, USA) was used to perform statistical analysis. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies were followed.

RESULTS

A total of 60 patients scheduled for IDS were screened from June 2019 to November 2019. Forty-six patients met the inclusion criteria and 40 patients who consented were included in the study [Figure 1]. Protocol deviation was found in three patients. In one patient, injection etomidate was used as an induction agent. In the second patient, intravenous midazolam 1 mg was administered for anxiolysis before induction. In the third patient, the study protocol of administering tramadol eight-hourly was changed by the surgeon. This led to the patient skipping the planned dose of opioids. As the patient experienced no exacerbation of pain, the planned opioid dose was not administered. All deviations in the trial were notified to the hospital's ethics board. As the implication on the study results were considered minimal, the data from the above three patients was included in the final analysis. No adverse events were encountered. Preoperative factors are elaborated in Table 1. The PEC ranged from 25.1 to 198.6 μA. Intraoperative parameters including perioperative opioid consumption are enumerated in Table 2.

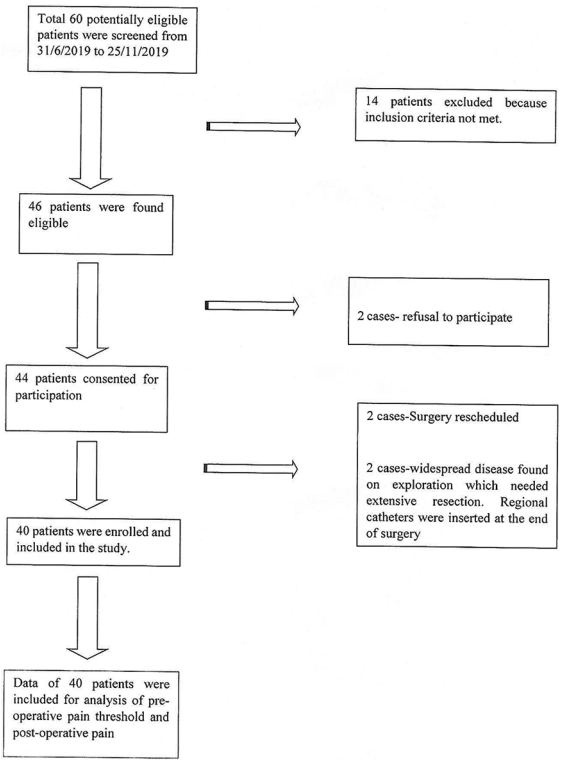

Figure 1: Flow diagram for recruitment of patients in the trial

Most of the patients (*n*-37) had moderate pain experiences, with three patients reporting severe pain in the first 24 hours [Figure 2]. A significant correlation was found between the worst PS and PEC ($P = 0.01$, $r = -0.402$) [Figure 3]. The association between PEC and worst PS suggests that patients with PEC less than 60 μA are more likely to have moderate-to-severe pain scores in the postoperative period.

There was no correlation between PEC and average PS at rest ($P = 0.16$, $r = -0.225$) or average pain score at movement and PEC ($P = 0.46$, $r = 0.119$). The median opioid requirement in the first 24 hours was 21 (25 [19–27.8]) mg. There was no correlation between PEC and postoperative opioid consumption at the end of 24 hours ($P = 0.50$, $r = -0.110$). We did not find any correlation between age, weight, average current perception threshold, duration of surgery with the worst PS at movement in 24 hours. A multiple regression analysis did not show any correlation of worst PS with age ($P = 0.42$), weight ($P = 0.69$), average CPT ($P = 0.76$) and duration of surgery ($P = 0.31$).

Table 1: Preoperative patient factors

Variable		Result
Age (years)	Mean±SD	47.7±10
Body weight (kg)	Mean±SD	54.9±13
Height (cm)	Mean±SD	153.6±7
BMI (kg/m^2)	Mean±SD	23.3±5
ASA physical status (Number of patients)	I	26
	II	14
Chemotherapy-induced peripheral neuropathy (number of patients) grade	0	20
	1	20
CPT (μA)	Median (IQR)	12.51 (10.1–14.6)
PEC (μA)	Median (IQR)	94.75 (48.8–94.7)

SD – Standard deviation; BMI – Body mass index; ASA – American society of anesthesiologists; CPT – Current perception threshold; PEC – Pain equivalent current; IQR – Interquartile range

Table 2: Intraoperative parameters and perioperative opioid requirement

Variable		Result
Blood loss (ml)	Mean±SD	501±314
Duration of surgery (hours)	Mean±SD	3.9±0.6
Intraoperative opioid consumption morphine equivalent	Median (IQR)	20 (18.25–25.75)
Total opioid consumption morphine equivalent	Median (IQR)	21 (19–27.87)

SD – Standard deviation; IQR – Interquartile range

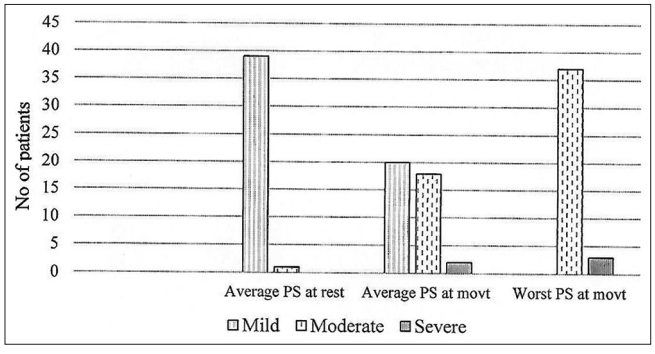

Figure 2: Severity of pain at the end of 24 hours. PS = Pain score. No= Number, Movt = Movement

DISCUSSION

In this study, a significant correlation was observed between PEC and worst PS in the first 24 hours following surgery ($P = 0.01$, $r = -0.402$). Patients with PEC less than 60 μA were more likely to have moderate-to-severe PS in the postoperative period. No correlation was found between PEC and opioid requirements in the perioperative period ($P = 0.503$, $r = -0.181$). Results of a multiple regression analysis suggested that age, body weight, duration of surgery, and CPT were not independent variables that predicted postoperative pain.

Prediction of pain promises more individualised pain management and thus the prevention of unpleasant experiences.[6] Though one cannot mimic the clinical circumstance of extensive tissue damage and overlay of emotional aspects, pain models are useful in generating painful stimuli under controlled and standardised situations.[11] Previous studies have looked into pain prediction.[12–14] One such study concluded that reduced tolerance to heat and cold pain stimulus preoperatively was associated with increased postoperative analgesic requirements.[14] A study involving female patients undergoing lower abdominal gynaecological surgery suggested that the

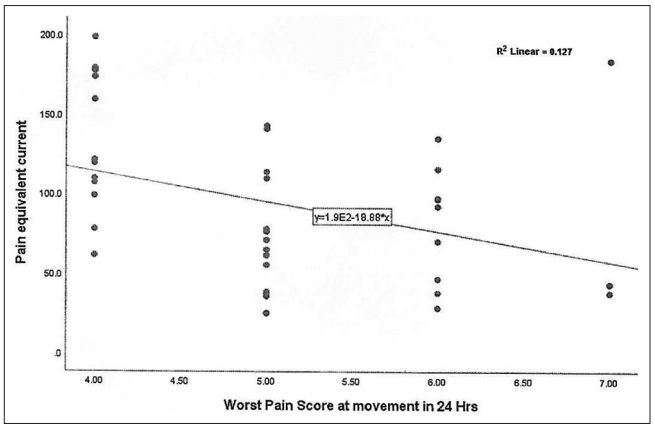

Figure 3: Graph showing the correlation between preoperative pain equivalent current (PEC) and worst pain scores (PSs) at the end of 24 hours. Hrs = Hours. Current in μA. PS as noted on the Numerical Rating Scale (NRS; 0–10, with 0 indicating no pain and 10 indicating severe pain)

level of postoperative pain significantly correlated with preoperative pressure pain tolerance.[11] There is varied literature on the usage of physical parameters, with some studies suggesting that electrical pain threshold has more predictive power, whereas a few conclude that suprathreshold heat pain most consistently correlates with postoperative pain.[7,15] A study conducted on an obstetric population planned for elective section compared pain assessment by electrical stimulation with pressure algometer testing.[16] The electrical pain threshold proved promising for predicting intravenous (IV)-PCA morphine requirements.[16] We used electrical stimulation in our study. Also, familiarity with electric stimuli–based devices like peripheral nerve stimulators and neuromuscular junction monitoring makes it easier to use these devices.

Oncology patients potentially have a variety of pain sources, including acute pain secondary to the underlying malignancy or surgical procedures, in addition to chronic pain related to the malignancy and the sequelae of treatments rendered.[17] Exploratory laparotomy for cancer surgery is traditionally considered a 'High risk surgery' with recommendation for epidural analgesia for pain management.[18] Our own experience in oncology surgeries in gynaecology has challenged this myth, and we have moved towards regional analgesia in cases with extensive dissection and skin incisions extending mainly to the supra-umbilical region.[19] In the current study, we selected cases in which extensive dissection was not planned and the skin incision was limited to around the umbilicus. To standardise perioperative pain management, regional analgesia was not incorporated for any of the patients enrolled in the trial. The association between PEC and worst PS suggests that patients with PEC less than 60 μA are more likely to have moderate-to-severe PS in the postoperative period. This group can be counselled and pain management including epidural analgesia or regional blocks should be aggressively pursued.

We did not find any correlation between fentanyl requirement and PEC. This is contrary to other studies that have shown a correlation between preoperative prediction and postoperative opioid requirement.[16] In our case, patients were on round-the-clock analgesics like tramadol (weak opioid) for the first 24 hours with the provision of fentanyl boluses in the PACU and connection of PCA, if required. Barring the severe pain in the PACU, none of the patients continued to have severe pain in the ward. In the third case, with protocol deviation and on changing the order of the opioid to as per need before 24 hours, there was no clinical requirement of the planned opioid dose. Hence, the possibility that the analgesic regime was adequate and may be in excess for a few patients cannot be ruled out. This could also explain the failure to establish any association between PEC and opioid consumption.

Literature suggests that age, gender, anxiety, preoperative pain, and type of surgery influence the level of postoperative pain and act as predictors of the same.[20–22] To minimise the influence of confounders, we selected female patients and restricted the sample to include women undergoing IDS for ovarian cancer. All patients in our trial had received similar chemotherapy regimens prior to surgery, and we ensured that we excluded patients with severe CIPN. Also, patients with preoperative pain and known psychiatric diseases were excluded. Patients sensitive to opioids, i.e. morbidly obese individuals were not included. Also, as we restricted our inclusion to ovarian cancer most of the patients were middle-aged women. Though age has been found to be an independent predictor of postoperative pain in previous studies, we did not find age, body weight, duration of surgery, and CPT as independent variables to predict postoperative pain.[21]

The main limitation of our study is that we used only experimental pain for pain prediction. Though preoperative pain assessment using a simple electrical device is more feasible than conducting a complex sensory test and using time-consuming psychometric screening tools, one must understand their limitations.[16] Though we found a significant association between PEC and worst PS, the association was moderate.[23] This suggests that experimental pain cannot be a stand-alone assessment tool. However, studies that have incorporated psychological and psychophysical measures have still failed to deliver a strong prediction.[24]

Despite all advancements and understanding of pain mechanism and pain management, a number of patients continue to experience severe pain in the postoperative period.[25] One must consider other factors that influence the pain experience, including sensitivity to analgesics which varies markedly among individuals.[26] Additionally, preoperative patient understanding for postoperative pain management may increase the quality of postoperative pain management and promote recovery.[27] Hence, there

remains a need for a comprehensive 'pain predicting score' which should be inclusive of experimental pain, extent of tissue damage expected, anxiety scales, response to pain education, and environmental factors. Further research in this direction is essential.

CONCLUSION

Preoperative pain threshold in response to an electrical stimulus can predict postoperative pain. However, though significant, the association is moderate, and patients with PEC less than 60 μA are more likely to have moderate-to-severe pain scores in the postoperative period.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and prevention. Lancet 2006;367:1618-25.
2. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg 2013;26:191-6.
3. Meissner W, Huygen F, Neugebauer E, Osterbrink J, Benhamou D, Betteridge N, *et al*. Management of acute pain in the postoperative setting: The importance of quality indicators. Curr Med Res Opin 2018;34:187-6.
4. Sia AT, Lim Y, Lim EC, Goh RW, Law HY, Landau R, *et al*. A118G single nucleotide polymorphism of human mu-opioid receptor gene influences pain perception and patient-controlled intravenous morphine consumption after intrathecal morphine for postcesarean analgesia. Anesthesiology 2008;109:520-6.
5. Hayashida M, Nagashima M, Satoh Y, Katoh R, Tagami M, Ide S, *et al*. Analgesic requirements after major abdominal surgery are associated with OPRM1 gene polymorphism genotype and haplotype. Pharmacogenomics 2008;9:1605-16.
6. Abrishami A, Chan J, Chung F, Wong J. Preoperative pain sensitivity and its correlation with postoperative pain and analgesic consumption: A qualitative systematic review. Anesthesiology 2011;114:445–57.
7. Krebs EE, Carey TS, Weinberger M. Accuracy of the pain numeric rating scale as a screening test in primary care. J Gen Intern Med 2007;22:1453-8.
8. Dihle A, Helseth S, Paul SM, Miaskowski C. The exploration of the establishment of cutpoints to categorize the severity of acute postoperative pain. Clin J Pain 2006;22:617-24.
9. Mifune Y, Inui A, Nagura I, Sakata R, Muto T, Harada Y, *et al*. Application of pain quantitative analysis device for assessment of postoperative pain after arthroscopic rotator cuff repair. Open Orthop J 2015:9:89-93.
10. Gu Y, Zhao Y, Dai M, Ma J, Feng B, Li X, *et al*. PainVision™: A simple, rapid, and objective method with potential for screening diabetic peripheral neuropathy. Int J Clin Exp Med 2017;10:1043-50.
11. Hsu YW, Somma J, Hung YC, Tsai PS, Yang CH, Chen CC. Predicting postoperative pain by preoperative pressure pain assessment. Anesthesiology 2005;103:613-8.
12. Abdullayev R, Uludag O, Celik B. Índice de Analgesia/Nocicepção: Avaliação da dor aguda pós-operatória [Analgesia Nociception Index: Assessment of acute postoperative pain]. Braz J Anesthesiol 2019;69:396-402.
13. MacLachlan C, Shipton EA, Wells JE. The cold pressor test as a predictor of prolonged postoperative pain, a prospective cohort study. Pain Ther 2016;5:203-13.
14. Ahmad S, De Oliveira GS Jr, Bialek JM, McCarthy RJ. Thermal quantitative sensory testing to predict postoperative pain outcomes following gynecologic surgery. Pain Med 2014;15:857-64.
15. Werner MU, Mjöbo HN, Nielsen PR, Rudin A. Prediction of postoperative pain: A systematic review of predictive experimental pain studies. Anesthesiology 2010;112:1494-502.
16. Buhagiar LM, Cassar OA, Brincat MP, Buttigieg GG, Inglott AS, Adami MZ, *et al*. Pre-operative pain sensitivity: A prediction of post-operative outcome in the obstetric population. J Anaesthesiol Clin Pharmacol 2013;29:465-71.
17. Hacker KE, Reynolds RK, Uppal S. Ongoing strategies and updates on pain management in gynecologic oncology patients. Gynecol Oncol 2018;14:410-19.
18. Abdominal Hysterectomy. PROSPECT Recommendations. Available from: www.postoppain.org. [Last accessed on 2022 Jun 30].
19. Bakshi SG, Mapari A, Shylasree TS. REctus Sheath block for postoperative analgesia in gynecological ONcology Surgery (RESONS): A randomized-controlled trial. Bloc de la gaine des grands droits pour une analgésie postopératoire en chirurgie gynéco-oncologique: RESONS, une étude randomisée contrôlée. Can J Anaesth 2016;63:1335-44.
20. Yang MMH, Hartley RL, Leung AA, Ronksley PE, Jetté N, Casha S, *et al*. Preoperative predictors of poor acute postoperative pain control: A systematic review and meta-analysis. BMJ Open 2019;9:e025091.
21. Kalkman JC, Visser K, Moen J, Bonsel JG, Grobbee ED, Moons MKG. Preoperative prediction of severe postoperative pain. Pain 2003;105:415-23.
22. Gatti AP. Review of predictors of postoperative pain. World J Surg Surgical Res 2018;1:1048.
23. Schober P, Boer C, Schwarte LA. Correlation coefficients: Appropriate use and interpretation. Anesth Analg 2018;126:1763-8.
24. Strulov L, Zimmer EZ, Granot M, Tamir A, Jakobi P, Lowenstein L. Pain catastrophizing, response to experimental heat stimuli, and post-cesarean section pain. J Pain 2007;8:273-9.
25. Rao M. Acute postoperative pain. Indian J Anaesth 2006;50:340-4.
26. Pasternak GW. Opiate pharmacology and relief of pain. J Clin Oncol 2014;32:1655-61.
27. Sjöling M, Nordahl G, Olofsson N, Asplund K. The impact of preoperative information on state anxiety, postoperative pain and satisfaction with pain management. Patient Educ Couns 2003;51:169-76.