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Anxiety About Surgery and Anticipated Intraoperative Pain Independently Predict Pain During Extension of Epidural Analgesia for Intrapartum Cesarean Delivery: A Prospective Cohort Study

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Abstract: Few studies have investigated the effects of preoperative psychological factors on pain during surgery. In this study, the association of preoperative psychological factors with the occurrence of intraoperative pain, the need for opioid supplementation, and the conversion to general anesthesia were examined during the extension of epidural analgesia for cesarean delivery. In parturients who received epidural labor analgesia, the visual analog scale (VAS; 0–100 mm) were used to evaluate trait anxiety, anxiety about surgery, and anticipated intraoperative pain before emergency cesarean delivery performed because of failure to progress. During surgery, the occurrence of intraoperative pain, need for opioid supplementation, and conversion to general anesthesia were observed. Spearman rank order correlation revealed a positive correlation between anxiety about surgery and the occurrence of intraoperative pain (correlation coefficient = 0.23, P = 0.008), between anticipated intraoperative pain and the occurrence of intraoperative pain (correlation coefficient = 0.31, P < 0.001), and between anticipated intraoperative pain and the need for opioid supplementation (correlation coefficient = 0.35, P = 0.012). Anxiety about surgery (odds ratio = 1.04 [1.02–1.07], P = 0.032) and anticipated intraoperative pain (odds ratio = 1.06 [1.02–1.11], P = 0.002) were independent predictors of the occurrence of intraoperative pain according to multiple logistic regression analysis, after controlling for maternal age and pain VAS score before cesarean delivery during labor pain. Anxiety about surgery and anticipated intraoperative pain are independent predictors of the occurrence of intraoperative pain during extension of epidural labor analgesia for intrapartum cesarean delivery performed because of failure to progress.

Keywords: Anxiety, Cesarean Delivery, Epidural Labor Analgesia

1. Introduction

An individual's pain perception after surgery can vary and alter the response to analgesics. The difference in a patient's response to pain can be explained by individual differences in pharmacologic, physiologic, and psychological factors [1]. Preoperative psychological factors including psychologic vulnerability, anxiety, and depression affect pain, analgesic requirements, hemodynamic changes, and neuroendocrine responses during the postoperative period [1]. Psychologic factors that influence interpersonal variability to pain in the postoperative period may affect pain sensitivity during an operation. However, little research has been conducted on the relationship between psychologic factors and intraoperative pain.

Regional anesthesia itself does not affect consciousness and, as such, if the anesthesia is incomplete, the patient experiences pain. Kinsella [2] reported that the rate of failure to perform a pain-free operation during cesarean delivery (CD) under epidural surgical anesthesia (ESA) following

epidural labor analgesia (ELA) was 24%. Because the patient's pain is directly reported by the patient while receiving ESA during CD, the correlation between preoperative psychologic factors and intraoperative pain can be identified.

The visual analog scale (VAS: 0–100 mm) has been proven to be a simple and useful way to measure preoperative anxiety [3]. Pan et al [4] reported that responses from a simple preoperative questionnaire (level of anxiety, anticipated pain, analgesic need from surgery) can predict pain intensity after CD with moderate accuracy. It was hypothesized that preoperative psychologic factors measured using a simple questionnaire and the VAS might predict intraoperative pain during CD under ESA.

To test this hypothesis and to further investigate the role of preoperative psychologic factors, the association of trait anxiety, anxiety about surgery, and anticipated intraoperative pain with the occurrence of intraoperative pain, the need for opioid supplementation, and conversion to general anesthesia were analyzed.

2. Methods

This prospective cohort study included participants who were scheduled for intrapartum CD because of a diagnosis of failure to progress with ELA. This study was approved by the Ethics and Research Committee of the Cheil General hospital.

2.1. Patient Characteristics

Written informed consent from all patients included in the study's prospective sample were obtained between November 11, 2015 and March 8, 2017. Patients had an American Society of Anesthesiologists physical status of I–II and a Royal College of Anaesthetists urgency classification category of 3 (needing early delivery but no maternal or fetal compromise) [5], based on a diagnosis of failure to progress and the administration of ELA by residents in their third or fourth year.

The patients had fasted for at least 8 h prior to surgery. The exclusion criteria were as follows: compromise of the parturient or fetus (urgency classification category of 1 or 2) other than failure to progress, malfunctioning epidural catheter or improper epidural placement, less than 2-h interval between ELA top-up and CD, complicated pregnancies (such as multiple gestation, placenta previa, and pregnancy-induced hypertension), antepartum hemorrhage, cardiac disease, and anxiety disorders. Severity of labor pain was evaluated with the VAS (0–100 mm). Patients with a malfunctioning epidural catheter, unsatisfactory analgesia (VAS > 30, additional epidural boluses), manipulation or replacement of an epidural catheter, unilateral blockade, catheter occlusion or migration, anxiety disorder, sensory (coldness) block height below T5 after ESA, duration of operation over 90 min, neonate birthweight of over 4,000 g, use of music, or sedative or meperidine administration during surgery were also excluded.

2.2. Variables

The predictors in this study were trait anxiety, anxiety about surgery, and anticipated intraoperative pain, and each of these was measured using the VAS. The outcome variables were the occurrence of intraoperative pain, the need for opioid supplementation, and conversion to general anesthesia.

2.3. Data Sources/Measurement

ELA was performed at the request of an obstetrician. With patients in the lateral decubitus position, lidocaine was infiltrated into the subcutaneous tissue in the L3–4 or L4–5 intervertebral space. An 18-gauge Tuohy needle (Portex® Epidural Minipack, SIMS Portex Ltd., UK) was inserted using the median or paramedian approach. The needle was advanced until the practitioner felt a loss of resistance using a syringe filled with air or saline. A 20-gauge multi-orifice epidural catheter (Portex® Epidural Minipack, SIMS Portex Ltd.) was inserted 4–5 cm into the epidural space. After aspiration, a 3-ml test dose of 2% lidocaine, followed by an 8-ml dose of 0.2% ropivacaine with 50 μg of fentanyl was administered via the epidural catheter. Continuous ELA was initiated at 10 ml/h using 0.1% ropivacaine with fentanyl at 1.5 μg/ml. Breakthrough pain, defined as labor pain with a VAS score > 30, was managed with epidural boluses of 10 ml ropivacaine (0.2%).

After the emergency CD was decided upon, the chart was used to determine whether the surgery was compatible with the inclusion criteria, who would perform ELA, and whether the rescue epidural bolus should be administered. An investigator in the waiting area in front of the operating room explained the study to the parturients and received written consent. Three preoperative psychologic factors (trait anxiety, anxiety about surgery, anticipated intraoperative pain) were measured using the VAS during periods without labor pain.

Trait anxiety was rated by asking how much anxiety was felt during normal times (on a scale of 0–100, with 0 being not anxious at all and 100 being extremely anxious). Anxiety about surgery was measured on a scale of 0–100, with 0 being not anxious at all and 100 being extremely anxious. Anticipated intraoperative pain was rated on a scale of 0–100, with 0 being no pain at all and 100 being pain as bad as you can imagine. If an investigator who is aware of preoperative psychologic factors performs intraoperative care or outcome assessment, this may affect the method for lowering anxiety such as music, encouraging words for parturients, observation of pain behavior, and administration of analgesics (performance bias and measurement bias); therefore, the investigator who measured psychologic factors did not participate in any activity related to the study after entering the operating room.

Another investigator who was blinded to the preoperative psychologic factors performed ESA using the catheter used for ELA, anesthetic management, and outcome measurements. Participants were monitored with electrocardiograms, automated blood pressure cuffs, and pulse oximetry after arriving at the operating room. A 24.1 ml mixed solution of lidocaine (20 ml of 2% lidocaine mixed

with 100 μg of fentanyl, 1:200,000 epinephrine/sodium bicarbonate at 2 mEq) was prepared immediately before injection. After negative aspiration from the epidural catheter was confirmed, 17 ml of the mixed solution of lidocaine was injected through the epidural catheter over 3 min. Five minutes after administration was completed, the block level was assessed every minute using an alcohol cotton swab to achieve a bilateral block along the mid-clavicular line up to T5. If this block was not achieved within 20 min from the injection, 5-ml boluses of the same solution were injected. If the sensory block for coldness was still absent at the T5 level 30 min after the first epidural injection (despite the supplement), the top-up was considered a failure. A skin incision was permitted when there was an adequate loss of sensation to cold block at T5 and patients experienced no pain from a skin pinch at the surgical site. ESA were converted to general anesthesia in both groups if the upper level of sensory block to coldness was below T5 or in the presence of a patchy block or pain reaction to forceps pinching at the surgical site. Patients who were switched to general anesthesia were excluded from the study.

An anesthesiologist and nurse in the operating room did not give any encouragement or hand grasp, instead giving only brief explanations about anesthesia and surgery, and answers to questions (if any). The parturients were told to speak whenever there was pain after the surgery was started. The pain score was assessed as a numeric rating scale (NRS: 0–10) when the patient reported the occurrence of pain or the pain was judged by facial expression. If the NRS score was greater than 3 or if the patient required analgesics, 100 μg of fentanyl was administered intravenously. If the pain persisted despite the injection of 100 μg of fentanyl, ESA was converted to general anesthesia. If the patient wanted to listen to music or be sedated, or if meperidine was administered for treatment of shivering during surgery, it was considered as follow-up loss and the patient was excluded from the study. The women whose duration of anesthesia was more than 90 min and whose neonate weighted over 4000 g were also excluded from the analysis because these factors are associated with the occurrence of pain during ESA for CD [2, 6].

2.4. Statistical Analysis

Because no previous data were available to calculate an effect size, no a priori sample size calculation was conducted. Data are presented as means ± standard deviation, medians (25% quartile, 75% quartile) or numbers (%). Two-tailed independent t-tests, the Mann–Whitney U test, or the chi-square test were used to analyze the demographic differences between the two groups (intraoperative pain or no intraoperative pain).

For primary comparisons, demographic, ELA data, and outcomes other than the occurrence of intraoperative pain between the groups with and without intraoperative pain were compared. The Spearman rank correlation test was chosen to examine the relationship between the predictors and outcome variables. To assess the independent associations between predictors and pain outcome variables, we performed multiple logistic regression analysis using outcomes as the dependent variables, and predictors as the independent variables, controlling for maternal age and VAS before CD during labor pain. Statistical analyses were performed with SigmaStat version 4.0 (USA). P values < 0.05 were considered significant.

3. Results

3.1. Study Flow

Of the 217 parturients diagnosed with failure to progress who underwent ESA following ELA performed for intrapartum CD, 39 were excluded (exclusion criteria met, n = 13; refusal to participate, n = 26). Consent was obtained from the remaining 178 participants and 58 parturients were lost to follow-up. The remaining 120 parturients were analyzed.

3.2. Comparison of Patients According to Occurrence of Intraoperative Pain

Table 1 shows a comparison of patient characteristics between the groups with and without intraoperative pain. No significant difference was observed between the two groups in maternal age, weight, height, gestational age, gravida, para, cervical dilation upon ELA, VAS before ELA, VAS 20 min after ELA, VAS before CD without labor pain, VAS before CD during labor pain, duration of ELA for labor, total volume of drugs administered for ELA, rate of conversion to general anesthesia, or trait anxiety. Significant differences were observed between the two groups with regard to administration of 100 μg of fentanyl (iv), anxiety about surgery, and anticipated intraoperative pain. Variables with a P value < 0.10 (maternal age and VAS before CD during labor pain) were regarded as potential confounders of the association between predictors and outcome variables [7].

Table 1. *Comparisons between Patients in the Groups with and without Intraoperative Pain.*

	Intraoperative pain (n = 20)	No intraoperative pain (n = 100)	P value	All (n = 120)
Maternal age (yr)	34.0 ± 2.6	35.6 ± 3.5	0.089	35.3 ± 3.4.
Maternal weight (kg)	68.9 ± 10.6	69.9 ± 9.7	0.679	69.7 ± 9.9
Maternal height (cm)	161.2 ± 7.9	161.9 ± 8.7	0.740	161.8 ± 8.6
Gestational age (wk)	40.3 (39.8–41.1)	40.1 (39.2–40.6)	0.126	40.1 (39.4–40.2)
Gravida	1 (1–2)	1 (1–2)	0.499	1 (1–2)
Para	0 (0–0)	0 (0–0)	0.244	0 (0–0)
Cervical dilation upon epidural analgesia (cm)	3 (2.5–3)	3 (3–3)	0.731	3 (2.5–3)
VAS before epidural analgesia	83 (72–92)	79 (64–88)	0.678	80 (68–89)

	Intraoperative pain (n = 20)	No intraoperative pain (n = 100)	P value	All (n = 120)
VAS 20 min after epidural analgesia	12 (10–18)	10 (9–21)	0.456	10 (9–20)
VAS before cesarean delivery without labor pain	19 (5–39)	17 (3–32)	0.642	17 (3–34)
VAS before cesarean delivery during labor pain	81(60–93)	68 (50–79)	0.092	70 (52–84)
Duration of epidural analgesia for labor (min)	365 (287–515)	342 (265–498)	0.774	348 (271–502)
Total volume of drugs given for epidural analgesia (ml)	71 (58–96)	67 (54–93)	0.775	686 (55–94)
Conversion to general anesthesia	1 (5%)	0	0.369	1 (0.8%)
Amount of fentanyl 100 μg (iv) administered	16 (80%)*	0	< 0.001	16 (13.3%)
Trait anxiety	58 (52–72)	56 (52–74)	0.196	56 (52–74)
Anxiety about surgery	82 (80–89)*	71 (31–78)	0.008	73 (35–79)
Anticipated intraoperative pain	72 (64–83)*	48 (27–66)	< 0.001	50(35–68)

Values represent means ± SD, medians (interquartile range), or number (%). Intraoperative pain: occurrence of pain during surgery. No intraoperative pain: no occurrence of pain during surgery. VAS: visual analog scale. *P < 0.05 vs. no intraoperative pain group.

3.3. Spearman Rank Order Correlation and Multiple Logistic Regression

Table 2 shows the Spearman rank order correlation between preoperative predictor factors and pain outcomes. Anxiety about surgery was associated with the occurrence of intraoperative pain (coefficient = 0.23, P = 0.008) and anticipated intraoperative pain was associated with the occurrence of intraoperative pain (coefficient = 0.31, P < 0.001) and the need for opioid supplementation (coefficient = 0.35, P = 0.012).

Table 2. *Spearman Rank Order Correlation between Predictors and Outcomes.*

	Intraoperative pain	Need for opioid supplementation	Conversion to general anesthesia
	Coefficient P value	Coefficient P value	Coefficient P value
Trait anxiety	0.11 0.196	0.02 0.778	0.14 0.107
Anxiety about surgery	0.23 0.008	0.08 0.363	0.11 0.199
Anticipated intraoperative pain	0.31 < 0.001	0.35 0.012	0.01 0.971

Maternal age and VAS before CD during labor pain (Table 1), for which P values were below 0.1, were considered potential confounding factors of the association between predictors and outcomes [7]. Multiple logistic regression was performed to identify variables associated with pain outcomes, controlling for maternal age and VAS before CD during labor pain. Anxiety about surgery and anticipated intraoperative pain were independent predictors of the occurrence of intraoperative pain (odds ratio = 1.04, P = 0.032, odds ratio = 1.06, P = 0.002, respectively).

Table 3. *Multiple Logistic Regression Analysis of the Association between Predictors and Outcomes.*

	Occurrence of intraoperative pain	Need for opioid supplementation
	Odds ratio (95% CI)* P value	Odds ratio (95% CI)* P value
Anxiety about surgery	1.04 (1.02–1.07) 0.032	1.00 (0.98–1.02) 0.929
Anticipated intraoperative pain	1.06 (1.02–1.11) 0.002	1.01 (0.98–1.05) 0.511

*Adjusted for maternal age, and visual analog scale before cesarean delivery during labor pain in a logistic regression mode

4. Discussion

The VAS results for trait anxiety, anxiety about surgery, and anticipated intraoperative pain of parturients diagnosed with failure to progress before intrapartum CD were 56 mm, 80 mm, and 71 mm, respectively. The multiple logistic regression analysis, controlling for maternal age, and VAS before CD during labor pain demonstrated that anxiety about surgery (P = 0.032) and anticipated intraoperative pain (P = 0.002) were significantly associated with the occurrence of intraoperative pain. To our knowledge, this is the first study on the relationship between preoperative psychologic factors and the occurrence of intraoperative pain with assessment based on direct reporting by patients.

Many studies have been conducted on the association between psychological variables and postoperative pain [1]. Psychologic vulnerability, anxiety (State Trait Anxiety Inventory), depression (Hospital Anxiety Depression Scale), fear, stress, expectation, and pain catastrophizing (Pain Catastrophizing Scale) have been found to be related to the severity of postoperative pain [1]. In a systematic review of 48 studies including 23,036 patients, age, anxiety, surgical procedure, and preexisting pain experiences were the most consistent predictive factors with large effect sizes [8]. In this study, the statistical significance (P value) of the difference in age between the groups with and without intraoperative pain was 0.089, and age was considered as a confounder in the analysis of multiple logistic regression. Anxiety has been reported to reduce the threshold of pain [1] and expectations regulate both subjective pain reporting and pain-induced brain activity [9].

A few reports have also been published on the relationship between psychological factors such as anxiety and the use of anesthetics during surgery. Maranets and Kain [10] found an association between anxiety (trait and state) and propofol requirement to maintain a bispectral index value during total

intravenous anesthesia. Kil et al. [11] found a correlation between psychologic factors (anxiety and pain sensitivity) and sevoflurane dose to maintain equal depths of anesthesia, as determined by bispectral index monitoring during general anesthesia. However, the bispectral index used to assess the level of anesthesia is not a marker of analgesia [12]. Therefore, those studies revealed no information about the effect of psychologic factors on intraoperative pain.

The following factors are known to affect the occurrence of pain and conversion to another anesthesia during intrapartum CD under ESA following ELA: administration of boluses during ELA, enhanced urgency of CD, care being provided by a non-obstetric anesthesiologist during ELA, duration of operation time over 90 min, and neonate birthweight over 4 kg [2,6,13,14]. To eliminate the confounding effects of these factors on pain outcomes, parturients who received additional boluses during ELA, those with an operation time of more than 90 min, and those with a neonate birthweight of over 4 kg were excluded. In addition, CD only when it was required based on a diagnosis of failure to progress was included, as well as parturients whose ELA was performed by residents in their third or fourth year.

A few limitations of this study warrant consideration. Of the eligible parturients, 12.7% (26/204) refused to participate in the research. These women may have refused to participate in the study because of high levels of anxiety or pain; differences in psychological states and emotional characteristics between those who did and did not participate in this study could have caused response bias [15]. In addition, 57 patients were lost to follow-up. This may have reduced external validity. Because ELA is associated with fever, 29 patients to whom meperidine was administered to treat shivering were excluded from the study [16]. This high rate of loss to follow-up may have reduced confounding effects, making attrition bias a concern because it is unlikely to occur randomly [17]. In this study, the occurrence of intraoperative pain was assessed according to the patients' voluntary reporting and responses to the investigators' questions. Depending on the investigator, the voluntary pain report of the patient and the ability to recognize pain in patients may have been different. It may have been difficult to distinguish between discomfort and pain, and patients with high anxiety might have reported pain more aggressively than did patients with low anxiety.

5. Conclusion

Anxiety about surgery and anticipated intraoperative pain are independent predictors of the occurrence of intraoperative pain during the extension of ELA for intrapartum CD performed because of failure to progress.

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