Original Article

Gestational diabetes and intraoperative tubal sterilization are risk factors for high incidence of pain after cesarean delivery: a prospective observational study

Patchareya Nivatpumin[1]^, Pawinee Pangthipampai[1], Sukanya Dej-Arkom[1], Somkiat Aroonpruksakul[1], Tripop Lertbunnaphong[2], Tanyanun Ngam-ek-eu[1]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; [2]Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Contributions: (I) Conception and design: P Nivatpumin, T Lertbunnaphong; (II) Administrative support: P Nivatpumin, P Pangthipampai, S Dej-Arkom; (III) Provision of study materials or patients: P Nivatpumin, S Aroonpruksakul; (IV) Collection and assembly of data: P Nivatpumin, T Ngam-ek-eu; (V) Data analysis and interpretation: P Nivatpumin, T Lertbunnaphong, T Ngam-ek-eu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Patchareya Nivatpumin. Associate Professor, Division of Obstetric Anesthesia, Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkok 10700, Thailand. Email: patchareya.niv@mahidol.ac.th.

Background: Postcesarean delivery pain leads to several adverse maternal outcomes. The primary objective of this study was to determine the incidence of moderate-to-severe pain after the use of spinal morphine for cesarean delivery. The secondary aim was to identify factors influencing moderate-to-severe pain.

Methods: This was a prospective observational study. The inclusion criteria were a patient age of ≥18 years, and undergoing elective cesarean delivery under spinal anesthesia with intrathecal morphine (200 mcg). Moderate-to-severe pain was defined as a numerical rating scale score of more than 3. Preoperative and intraoperative data were collected including parity, history of cesarean delivery, pregnancy-associated problem, anesthesia blockade level, level of surgeon experience, incision type, tubal sterilization or appendectomy, and peritoneum suture. Chi-squared or Fisher's exact tests were used to examine risk factors. Multiple logistic regression was used to analyze independent factors associated with moderate to severe pain.

Results: In all, 660 patients were enrolled. As 16 were subsequently removed because they met the study withdrawal criteria, data relating to 644 patients were analyzed. The incidence of moderate-to-severe pain during the first postoperative day was 451/644 patients [70.03%; 95% confidence interval (CI): 66.38–73.44%]. The median pain score [interquartile range (IQR)] was 5 (3–6), with 176/644 (27.33%) patients needing rescue analgesics. A multivariate analysis revealed that two factors were associated with moderate-to-severe pain on the first postoperative day: gestational diabetes [adjusted OR (AOR), 1.849; 95% CI: 1.068–3.203; P=0.028] and intraoperative tubal sterilization (AOR, 1.533; 95% CI: 1.060–2.218; P=0.023). A significantly higher number of patients experienced moderate-to-severe pain on postoperative Day 1 [451/644 (70.03%)] than on Day 2 [349/644 (54.19%); P<0.001]. The median pain score [IQR] on postoperative Day 2 was 4 [3–5], which was less than on Day 1 (P<0.001).

Conclusions: A high incidence of moderate-to-severe postoperative pain was found after a single dose of spinal morphine for cesarean delivery. Adequate pain control is required in women at risk of postcesarean delivery pain. More studies are needed on the analgesic requirements of diabetic patients or patients who receive intraoperative tubal sterilization.

Keywords: Cesarean delivery; gestational diabetes; postoperative pain; tubal sterilization

^ ORCID: 0000-0003-1386-4855.

Submitted Aug 06, 2021. Accepted for publication Nov 12, 2021.
doi: 10.21037/apm-21-2139
View this article at: https://dx.doi.org/10.21037/apm-21-2139

Introduction

Cesarean delivery is a common procedure, and its rate has increased continually to unprecedented levels worldwide (1). Postcesarean delivery pain leads to an unpleasant maternal experience, delays functional recovery, interferes with breastfeeding, and increases the rate of postpartum depression (2-4). Moreover, severe postcesarean delivery pain contributes to persistent postsurgical pain (3,5,6). The provision of optimum postcesarean delivery pain control is therefore essential. Even though intrathecal morphine produces bothersome side effects (for example, pruritus, nausea, and vomiting), it is generally used as a postcesarean delivery analgesic due to its good efficacy and long analgesic duration (7,8). A systematic review reported that prolonged postcesarean delivery pain relief was obtained with a variety of intrathecal morphine doses, with a median of 27 hours (range, 11–29 hours) before the first analgesic requirement (9). However, some patients suffer from a high intensity of pain during the first postoperative day. Borges *et al.* found that a substantial proportion of patients (78.4%) experienced moderate-to-severe pain (numerical pain scale ≥5) after spinal anesthesia with intrathecal morphine for cesarean delivery, and the associated factor was preoperative anxiety (10). Another study revealed that patients' responses to suprathreshold thermal stimuli as well as their degree of preoperative anxiety were predictors for postcesarean section pain (11).

Moreover, surgical factors can affect postoperative pain levels. Kurek Eken *et al.* revealed that closure of both the parietal and visceral peritonea increased postoperative pain after cesarean delivery (12). A qualitative systematic review found that the degree of postoperative pain and analgesic consumption were affected by the presence of preoperative pain; patient anxiety; patient age; and surgery type (such as open abdominal, thoracic, or orthopedic) (13).

The available evidence shows that the aforementioned items affect pain after surgery. However, not all factors associated with pain after cesarean delivery have been identified. Our research focus was on identifying the items that are specifically associated with postcesarean pain. To this end, we considered factors that had not previously been investigated. We postulated that surgical factors—such as the type of skin incision, or a cesarean section with tubal sterilization or appendectomy—may influence postoperative pain. Additionally, other items that may be associated with postoperative pain were examined: patient education level, the presence of gestational diabetes or hypertension, and anesthetic features (such as intraoperative pain and an inadequate intraoperative block).

This study set out to determine the incidence of moderate-to-severe postoperative pain after the administration of spinal morphine for cesarean delivery, as well as the predictive factors related to that pain. If any of these factors were modifiable, analgesic management during the perioperative period could be improved, allowing postoperative pain levels to be reduced. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-2139/rc).

Methods

Study design and subjects

This prospective observational study was conducted at a single university hospital. The research was carried out in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand [protocol number, 164/2560 (EC2); approval number, Si 248/2017]. The protocol was registered with www.clinicaltrials.gov; registration number NCT03205813, date of registration 02 July 2017. Informed consent was obtained from all patients. Data collection was conducted from July 2017 to August 2019. The inclusion criteria were a patient age of ≥18 years; an American Society of Anesthesiologists physical status I or II; term pregnancy; elective cesarean delivery under spinal anesthesia with intrathecal morphine; and a proper understanding of the numerical rating scale of pain. Patients were not enrolled if they did not understand Thai; they had a complicated pregnancy for which general anesthesia may be required during the cesarean delivery; or the use of spinal anesthesia with intrathecal morphine was contraindicated. Patients were also excluded if they received either general anesthesia or a peripheral nerve blockade after the spinal anesthesia.

Procedures

Patients were evaluated the day before surgery by an anesthesiologist. The following preoperative data were recorded: demographic characteristics; education level; history of previous normal labor or cesarean delivery; and comorbidities (including gestational diabetes and hypertension). On the morning of the surgery, they were premedicated with oral ranitidine (150 mg) and metoclopramide (10 mg), as per standard practice. In the operating theatre, the patients received intravenous fluid and were monitored in the standard manner. The spinal anesthesia was administered in the lateral position at L2–3 or L3–4 with a 26- or 27-gauge Quincke spinal needle (Becton Dickinson, Franklin Lakes, NJ, USA) or a 25-gauge Whitacre spinal needle (Becton Dickinson), depending on the decision of the anesthesiologist. The intrathecal medication given to all patients was 0.5% heavy bupivacaine (10–12 mg) with morphine (200 mcg). Details were collected of the intraoperative data (anesthesia level testing by cold sensation at 15 min after spinal anesthesia, and the number of uterotonic agents used) and intraoperative pain. Intraoperative pain was defined as the usage of an intravenous opioid analgesic medication or ketamine while the patients were undergoing surgery. Records were also made of the surgical data: skin-incision type (midline or Pfannenstiel incision); the surgeon (trainees, such as residents; or graduated obstetricians, like obstetric fellows or consultants); peritoneal closure or non-closure; and concurrent operations (for instance, tubal sterilization or appendectomy). All patients were taken to the recovery room and observed for 1 to 2 hours. They were then transferred to the maternity ward.

Measures and outcomes

One of 4 research assistants and research nurses who had been trained in data collection and outcome assessment visited the patients in the maternity ward at 24 and 48 hours postoperatively. The staff member assessed the level of pain, nausea or vomiting symptoms, the need for pain medication, and satisfaction. Patients rated their pain using an 11-point numerical rating scale, with 0 signifying "no pain", and 10 representing "the worst possible pain". Those patients scoring 4–6 were considered to have moderate pain, whereas those with scores of 7 to 10 were deemed to be experiencing severe pain (14). If required, the rescue analgesic employed was either intravenous pethidine (20 mg) or tramadol (25 mg). Other analgesic medications—such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs)—were administered at the discretion of each obstetrician. Nausea and vomiting were graded with the following 4-point system: 0, no symptoms; 1, nausea; 2, vomiting 1–2 times; and 3, vomiting >2 times. The patients were requested to rate their satisfaction with their perioperative pain management 24 hours postoperatively, using a scale of 0 to 100 (with 100 denoting "totally satisfied"). The intraoperative and postoperative data were also retrieved from the anesthetic records, operative notes, and admission charts.

Statistical analysis

The determination of the sample size was based on the results of a survey that had been performed previously at our institute. That work found that the incidence of moderate to severe degrees of post-operative pain that was experienced by women during the first 24 hours following a cesarean delivery was 55% (unpublished data). Our sample-size calculation used the formula $n=Z_{(1-\alpha)}^{2}\ p(1-p)/d^{2}$; we employed a confidence level (1-α) of 95% and a maximum allowable error of 0.05. The result was that 381 women would be needed for the investigation. As to the secondary study aim, 20 factors related to the women and the cesarean procedure were anticipated to be linked with levels of pain ranging from moderate to severe. The factors relating to the women were age, BMI, educational level, gestational diabetes, gestational hypertension, primigravida, multiple pregnancy, and a history of vaginal or cesarean delivery. The surgical factors were incision type; type of surgeon performing the operation (trainee or graduated obstetrician); closure of both the parietal and visceral peritonea; concurrent fallopian tubal sterilization or appendectomy; use of more than one type of uterotonic agent; intra-operative pain requiring a rescue analgesic; anesthetic level lower than the 4th thoracic dermatomal level (T4); neonatal birthweight (with twin pregnancies, the summation of the two neonatal birthweights was used for analytical purposes); and post-operative use of paracetamol or NSAIDs.

Our estimation of the size of the sample needed was driven by a statistician recommendation relating to multiple logistic regression analyses. Specifically, the number of women who should be recruited for our research should be at least 10 times the number of possible risk factors (15). In view of that, there would be a need to have around 400 women who experienced moderate to severe levels of pain. However, to accomplish both

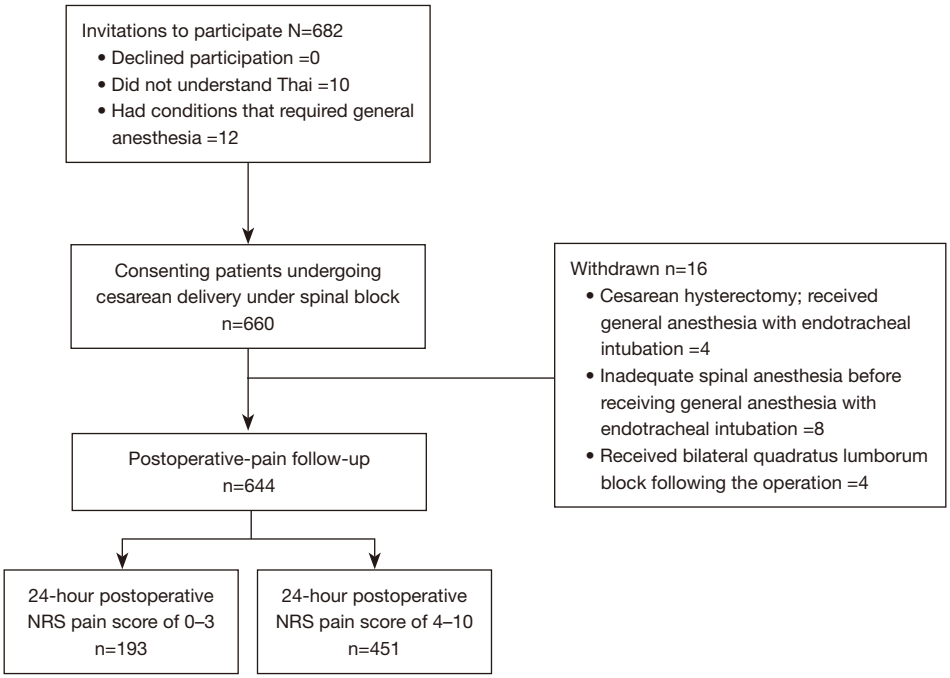

Figure 1 Enrollment of participants. NRS, numerical rating scale.

the primary and secondary aims of our research, a study cohort of 600 women was deemed to be sufficient. To compensate for inevitable losses during the investigation, a final enrolment figure of 660 women was employed.

All analyses were performed using PASW Statistics for Windows (version 18.0; SPSS Inc., Chicago, Ill., USA). Categorical data are presented as number and proportion, expressed as a percentage. The decreasing of number of patients experiencing pain from postoperative Day 1 to Day 2 was identified using McNemar's Test. Chi-squared tests were used to analyze categorical data. Continuous data are reported as mean ± standard deviation, or as median with interquartile range. For the univariate analysis, chi-squared tests or Fisher's exact tests were used to examine the risk factors. Risk factors with a P value of <0.20 from the univariate analysis were entered into the multivariate analysis of moderate-to-severe postoperative pain using forward stepwise logistic regression. Crude and adjusted odds ratio (OR) and 95% confidence interval (CI) are used to present the data. P values <0.05 (two-sided) were considered statistically significant.

Results

A total of 660 patients were enrolled. Twelve were subsequently withdrawn because they received general anesthesia (four underwent a hysterectomy after the cesarean delivery, while the remaining eight failed to achieve an adequate level of spinal block). A further 4 patients were excluded as they received a quadratus lumborum block upon completion of the operation. Therefore, 644 patients entered the complete analysis (*Figure 1*); their demographic and obstetric data are listed in *Table 1*. One patient had a history of chronic pain and received pain relieving medication preoperatively. The number of patients reporting a pain score of ≥4 on postoperative Day 1 and Day 2 were 451/644 and 349/644 patients, representing 70.03% (95% CI: 66.38–73.44%) and 54.19% (95% CI: 50.33–58.0%), respectively. Although there was a high proportion of patients with a pain score of ≥4 on the first postoperative day, the number requiring rescue pain medication was only 176/644 (27.33%). The percentage of patients experiencing moderate-to-severe pain decreased significantly from Day 1 to Day 2 (P<0.001). There was a corresponding fall in the average pain score, with a statistically significant decline from 4.9±2.3 (mean ± standard deviation) for the first postoperative day to 3.8±1.8 for the second day (P<0.001; *Table 2*). The factors that had been assumed to be associated with postcesarean delivery pain are described and analyzed in *Table 3*. The authors used the cut point of a

Table 1 Clinical and demographic characteristics (n=644)

Parameter	Mean ± SD or number (%)
Age (yrs)	33.6±5.5
Weight (kg)	72.4±13.0
Height (cm)	159.3±5.7
BMI (kg/m^2)	32.0±3.2
ASA classification	
I	532 (82.6)
II[†]	112 (17.4)
Gestational age (wks)	38.3±0.9
Parity	
0	288 (44.7)
≥1	356 (55.3)
Gestation	
Singleton	626 (97.2)
Twin	18 (2.8)
Indication for cesarean delivery	
Previous cesarean delivery	337 (52.3)
Cephalopelvic disproportion	17 (2.6)
Elective cesarean delivery	276 (42.9)
Other[‡]	14 (2.2)
Pregnancy-associated problem:	
Gestational HT	19 (2.9)
Gestational diabetes	89 (13.8)
Preeclampsia	3 (0.5)
Other[§]	4 (0.6)

[†], ASA classification II: asthma, thalassemia, obesity, and thyroid disease; [‡], other indications for cesarean delivery: oligohydramnios and breech presentation; [§], other pregnancy problem: low-lying posterior placenta previa. BMI, body mass index; ASA, American Society of Anesthesiologists; HT, hypertension; SD, standard deviation.

neonatal birthweight of >4,000 gm as the definition of fetal macrosomia (16). The univariate analysis revealed that two factors were related: gestational diabetes and intraoperative tubal sterilization. The multiple logistic regression was then performed using the associated factors from the univariate analysis with a P value of <0.2, namely, maternal age ≥35, gestational diabetes, patients with a history of normal labor, patients with a history of previous cesarean delivery, patients with an intraoperative anesthetic level below the 4th thoracic dermatome, residents as the surgeon performing operation, and intraoperative tubal ligation. The multivariate analysis revealed two factors were independently related to postcesarean delivery pain: gestational diabetes (adjusted OR, 1.849; 95% CI: 1.068–3.203; P=0.028) and intraoperative tubal ligation (adjusted OR, 1.533; 95% CI: 1.060–2.218; P=0.023). The mean satisfaction score of postoperative pain management (ranging from 0–100) was 93±8.8. On the first postoperative day, 584 patients (90.7%) had no symptoms of either nausea or vomiting. Of the other 60 patients, 30 (4.7%) experienced nausea but not vomiting; 16 (2.5%) vomited but did not need treatment; and the remaining 14 (2.2%) vomited >2 times and required treatment.

Discussion

A considerable proportion of the patients—approximately 70%—experienced moderate-to-severe pain on the first postoperative day following cesarean delivery involving a single shot of spinal anesthesia with morphine (200 mcg). Likewise, Borges *et al.* revealed a sizable percentage of patients experienced moderate-to-severe pain after spinal anesthesia with intrathecal morphine for cesarean delivery (78.4%) (10). Our study defined moderate-to-severe pain as a numerical rating scale pain score of 3 or more. This was different from that used by Borges and colleagues: their cut point for moderate pain was more than 4 (10). A dissimilarity in the intrathecal morphine quantity explains the higher incidence of pain in the work by Borges *et al.* Our study used a higher dose of 200 mcg for every patient, which was the usual amount at our institute, Borges and colleagues used a lower average spinal morphine dose of 86.5±12.2 mcg (10). A meta-analysis found that the mean time to the first analgesic requirement with a high dose of spinal morphine was 4.49 hours longer than that for a low dose. The range for the high dose (>100 mcg) was 13.8 to 39.5 hours, compared with 9.7–26.6 hours for the low dose (50–100 mcg) (8). However, the meta-analysis also found that the means of the pain score and the supplemental morphine consumption of the high- and low-dose groups were not different (8). It is interesting to note that our study also revealed that—despite the high incidence of moderate-to-severe postoperative pain on Day 1—only a relatively small percentage of patients (27.3%) required the rescue analgesic.

A systematic review identified that a younger patient

Table 2 Description of pain on postoperative Day 1 and Day 2 (n=644)

Patient characteristics	Day 1	Day 2	P value
Mild pain, n (%)	193 (30.0)	295 (45.8)	<0.001*†
Moderate to severe pain, n (%)	451 (70.0)	349 (54.2)	<0.001*†
Severe pain, n (%)	151 (23.4)	58 (9.0)	<0.001*†
Number of patients requiring rescue pain medication, n (%)	176 (27.3)	11 (1.7)	<0.001*†
Pain score (NRS 0–10)			
Mean ± SD	4.9±2.3	3.8±1.8	<0.001*‡
Median [IQR]	5 [3–6]	4 [3–5]	<0.001*§

*, statistically significant; †, McNemar's test; ‡, Paired *t*-test; §, Wilcoxon signed-rank test. NRS, numerical rating scale; SD, standard deviation; IQR, interquartile range.

Table 3 Factors involved with moderate-to-severe pain on postoperative Day 1—univariate analysis and multivariate analysis (n=644)

Variables	Pain score ≥4 (n=451)	Pain score <4 (n=193)	Univariate analysis		Multivariate analysis	
			P value	Odds ratio (95% CI)	P value	Odds ratio (95% CI)
Age ≥35 yrs	208 (46.1)	78 (40.4)	0.182	1.262 (0.897–1.777)		
BMI ≥35 kg/m^2	17 (8.8)	40 (8.9)	0.980	1.008 (0.556–1.825)		
Primigravida	196 (43.4)	92 (47.7)	0.325	0.844 (0.602–1.184)		
Twin (n=18)	13 (2.9)	5 (2.6)	0.837	1.116 (0.392–3.175)		
Level of education ≥ high school	409 (63.5)	178 (27.6)	0.528	0.821 (0.444–1.518)		
Gestational HT	13 (2.8)	6 (3.1)	0.876	0.925 (0.346–2.471)		
Gestational DM	71 (15.7)	18 (9.3)	0.031*	1.817 (1.051–3.140)	0.028*	1.849 (1.068–3.203)
History of vaginal delivery	28 (6.2)	18 (9.3)	0.159	0.643(0.347–1.194)		
History of cesarean delivery	245 (54.3)	92 (47.6)	0.121	1.306 (0.931–1.830)		
Resident as the surgeon	303 (67.2)	144 (74.6)	0.061	1.435 (0.983–2.097)		
Midline incision used	42 (9.3)	18 (9.3)	0.996	1.002 (0.561–1.789)		
Intraoperative pain	12 (2.7)	4 (2.1)	0.787	1.292 (0.411–4.056)		
Block-level lower than T4	81 (18.0)	23 (11.9)	0.056	1.618 (0.984–2.661)		
Tubal sterilization (n=221)	167 (37.0)	54 (28.0)	0.027*	1.514 (1.048–2.187)	0.023*	1.533 (1.060–2.218)
Appendectomy (n=17)	12 (2.7)	5 (2.6)	0.959	1.028 (0.357–2.958)		
Parietal & visceral peritoneum suture	426 (94.4)	181 (93.8)	0.736	1.130 (0.555–2.298)		
Neonatal birthweight ≥4,000 grams	24 (5.3)	8 (4.1)	0.529	1.300 (0.555–2.298)		
Two or more uterotonic agents used	59 (13.1)	20 (10.4)	0.335	1.302 (0.760–2.229)		
Postoperative paracetamol used	446 (98.9)	190 (98.4)	0.702	1.408 (0.333–5.953)		
Postoperative NSAIDs used	327 (72.5)	135 (69.9)	0.509	1.133 (0.782–1.641)		

Data presented as number (percent). *, statistically significant. 95% CI, 95% confidence interval; BMI, body mass index; kg/m^2, kilogram/meter^2; HT, hypertension; DM, diabetes mellitus; T4, the fourth thoracic dermatomal level; NSAIDs, nonsteroidal anti-inflammatory drugs.

age was a factor associated with postoperative pain (13). However, that review also found that there were some conflicting reports about the correlation between patient age and postoperative pain. Moreover, some of the studies examined by the review had used sample sizes which were too small to detect any correlation. In the case of our study, patient age demonstrated no significant relationship with pain. However, this finding is explained by the narrow age range of our study cohort (mean, 33.6 ± 5 years). In addition, whereas numerous studies have shown that preoperative pain was a factor related to postoperative pain (2,10,13), our study revealed an extremely low incidence. As there was only one patient who had a history of chronic pain before the cesarean section, the preoperative pain factor was not included in our analysis.

Gestational diabetes was one of the two independent factors that our study found to be associated with pain after cesarean delivery. Karci *et al.* found that diabetic patients undergoing a total abdominal hysterectomy had higher pain scores and required larger amounts of additional morphine postoperatively than nondiabetic patients (17). In addition, Kim *et al.* reported a significant correlation between preoperative HbA1c (plasma glycosylated hemoglobin) levels and opioid consumption in the first 48 hours following elective open nephrectomy (18). Moreover, another recent study found that gestational diabetic patients required a higher dosage and frequency of an opioid analgesic six hours after a cesarean section than patients without diabetes (19). Those gestational diabetic patients also reported a higher mean visual analog pain score for the 24-hour period after their cesarean delivery. The reason for the heightened perception of pain and consequential elevated usage of opioids by those gestational diabetic patients is assumed to be changes in the pharmacokinetics and pharmacodynamics of opioids when administered to diabetics. A study on animals demonstrated that a hyperglycemic state decreased the analgesic effect of morphine (20). Several studies have reported that diabetic patients have higher pain scores and tend to have a higher opioid consumption. The studies suggested that these patients have different pain perception due to the decrease in the analgesic effect of opioids resulting from a direct antagonistic effect on opioid receptors (17-19). Consistent with that, the present work identified that almost 80% (71/89) of the gestational diabetic patients experienced moderate-to-severe pain after their operation. Gestational diabetic mothers have an elevated risk of developing fetal macrosomia (16). We assumed that a neonatal birthweight equal or more than 4,000 grams might affect pain levels after cesarean delivery because of the surrounding tissue trauma experienced during the operation. Nevertheless, our study did not discover any differences in the maternal pain scores for this factor (OR 1.300; 95% CI: 0.555–2.298; P=0.529).

There are two components of postcesarean delivery pain. The first relates to the somatic pain derived from the skin incision together with the visceral pain arising from the peritoneum; the second component involves the cramping that arises from uterine involution after delivery (2,12,21,22). We assumed the surgical incision type or the skill level of the surgeon performing the cesarean delivery (for instance, a trainee versus a graduated obstetrician) would influence the degree of skin and soft tissue trauma and hence the postoperative pain level. However, no difference was found for the parameters of skin incision or surgeon type.

Other surgical factors related to postcesarean delivery were studied. Kurek Eken *et al.* revealed that patients receiving closure of both the parietal and visceral peritonea reported higher visual analog pain scores than those only receiving a parietal peritoneal closure (12). Tissue trauma and ischemia from suturing may explain the higher postoperative pain (12). However, our study showed a small number of patients (37/644; 5.7%) only received a parietal peritoneal closure, and no difference was found in the pain scores for this factor. On the other hand, we identified that tubal sterilization after cesarean delivery was associated with postoperative pain. Three quarters of the patients receiving tubal sterilization (167/221; 75.6%) reported having moderate-to-severe postoperative pain. Pain from tubal sterilization is believed to be derived from the prostaglandins released from the traumatized fallopian tubes (23). As well, pain arises from ischemia or necrosis of the ligation site of the tubes (24). These reasons explain why the tubal sterilization had a high likelihood of generating postoperative pain.

We assumed that anesthetic factors would affect postcesarean delivery pain. Even though the level of sensory blockade below T4 tended to be related with pain after the operation, there was no statistical significance (OR 1.618; 95% CI: 0.984–2.661; P=0.056). We could not find a correlation between patients experiencing intraoperative pain and postoperative pain as only a small number of patients (16 patients) required intravenous opioid medications in the operating theatre.

Although many studies have concluded that uterine involution causes pain after delivery (21,22), we did not find

that the usage of more than one uterotonic agent promoting additional uterine contraction affected pain. A systematic review showed that the NSAIDs used were better than a placebo and paracetamol for the relief of pain arising from uterine cramping (21). Furthermore, NSAIDs have been reported to have an opioid-sparing effect after cesarean delivery (22). Nevertheless, our study failed to demonstrate the effects of NSAIDs on postcesarean section pain.

The early identification of the predictors in patients at risk of experiencing postoperative pain will allow more effective interventions and better management. Carvalho *et al.* suggested the personalized management of pain (25). That is, patients would be able to make individual choices for their pain protocol by selecting one of three doses of spinal morphine: low (50 mcg), medium (100 mcg), and high (200 mcg) (25). However, higher doses of intrathecal morphine, as well as of several other analgesic medications, have more possible side effects, like nausea and vomiting, itchiness, and the risk of sedation. Therefore, the plausible complications should be advised to patients.

The main limitation of this study was that data were not collected on the blood sugar levels that may affect pain after surgery. Therefore, we were not able to find a direct correlation between hyperglycemia and the pain score ratings of the patients. Additionally, the side effects of the use of the high-dose spinal opioid (such as sedation and pruritus) were not recorded. It is acknowledged that the usage of 200 mcg of spinal morphine causes a higher incidence of pruritus than a lower dose (<100 mcg). Future research should be conducted on postoperative cesarean section pain medication requirements for diabetic patients. Also, other factors that may associate with postcesarean delivery pain were not investigated. They include preoperative anxiety and postoperative uterine contraction from breastfeeding.

Conclusions

At 70%, the incidence of moderate-to-severe pain after cesarean delivery was high. The independent factors were gestational diabetes and intraoperative tubal sterilization. We therefore suggest that it is essential to identify the risk of developing a higher pain intensity after surgery and to provide adequate postoperative pain control.

Acknowledgments

The authors gratefully thank the consultants, residents, and nursing staff of the Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, for their assistance during the study. We also thank Miss Chusana Rungjindamai for her help with paperwork. Mr. Suthipol Udompunturak deserves special thanks for his significant help with the statistical analyses. Finally, we are indebted to Mr. David Park for his professional editing of this manuscript.

Funding: This study was supported by a grant from the Siriraj Research Development Fund (managed by Routine-to-Research [R2R], Faculty of Medicine Siriraj Hospital, Mahidol University) (Grant No. (IO) R016135005).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-2139/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-21-2139/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-2139/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The research was carried out in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Siriraj Institutional Review Board, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand (protocol number, 164/2560 [EC2]; approval number, Si 248/2017). Informed consent was obtained from all patients.

References

1. Betrán AP, Ye J, Moller AB, et al. The Increasing Trend in

Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. PLoS One 2016;11:e0148343.
2. Carvalho B, Butwick AJ. Postcesarean delivery analgesia. Best Pract Res Clin Anaesthesiol 2017;31:69-79.
3. Eisenach JC, Pan PH, Smiley R, et al. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. Pain 2008;140:87-94.
4. Hirose M, Hara Y, Hosokawa T, et al. The effect of postoperative analgesia with continuous epidural bupivacaine after cesarean section on the amount of breast feeding and infant weight gain. Anesth Analg 1996;82:1166-9.
5. Sng BL, Sia AT, Quek K, et al. Incidence and risk factors for chronic pain after caesarean section under spinal anaesthesia. Anaesth Intensive Care 2009;37:748-52.
6. de Brito Cançado TO, Omais M, Ashmawi HA, et al. Chronic pain after cesarean section. Influence of anesthetic/surgical technique and postoperative analgesia. Rev Bras Anestesiol 2012;62:762-74.
7. Rex S, Devroe S. Anesthesia for pregnant women with pulmonary hypertension. Curr Opin Anaesthesiol 2016;29:273-81.
8. Sultan P, Halpern SH, Pushpanathan E, et al. The Effect of Intrathecal Morphine Dose on Outcomes After Elective Cesarean Delivery: A Meta-Analysis. Anesth Analg 2016;123:154-64.
9. Dahl JB, Jeppesen IS, Jorgensen H, et al. Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials. Anesthesiology 1999;91:1919-27.
10. Borges NC, Pereira LV, de Moura LA, et al. Predictors for Moderate to Severe Acute Postoperative Pain after Cesarean Section. Pain Res Manag 2016;2016:5783817.
11. Pan PH, Coghill R, Houle TT, et al. Multifactorial preoperative predictors for postcesarean section pain and analgesic requirement. Anesthesiology 2006;104:417-25.
12. Kurek Eken M, Ozkaya E, Tarhan T, et al. Effects of closure versus non-closure of the visceral and parietal peritoneum at cesarean section: does it have any effect on postoperative vital signs? A prospective randomized study. J Matern Fetal Neonatal Med 2017;30:922-6.
13. Ip HY, Abrishami A, Peng PW, et al. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. Anesthesiology 2009;111:657-77.
14. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain 1997;72:95-7.
15. White S. Basic & Clinical Biostatistics: Fifth Edition. McGraw-Hill Education; 2019.
16. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. Ann Nutr Metab 2015;66 Suppl 2:14-20.
17. Karci A, Tasdogen A, Erkin Y, et al. The analgesic effect of morphine on postoperative pain in diabetic patients. Acta Anaesthesiol Scand 2004;48:619-24.
18. Kim SH, Hwang JH. Preoperative glycosylated haemoglobin as a predictor of postoperative analgesic requirements in diabetic patients: A prospective observational study. Eur J Anaesthesiol 2015;32:705-11.
19. Yang C, Geng WL, Hu J, et al. The effect of gestational diabetes mellitus on sufentanil consumption after cesarean section: a prospective cohort study. BMC Anesthesiol 2020;20:14.
20. Raz I, Hasdai D, Seltzer Z, et al. Effect of hyperglycemia on pain perception and on efficacy of morphine analgesia in rats. Diabetes 1988;37:1253-9.
21. Deussen AR, Ashwood P, Martis R. Analgesia for relief of pain due to uterine cramping/involution after birth. Cochrane Database Syst Rev 2011;(5):CD004908.
22. Zeng AM, Nami NF, Wu CL, et al. The Analgesic Efficacy of Nonsteroidal Anti-inflammatory Agents (NSAIDs) in Patients Undergoing Cesarean Deliveries: A Meta-Analysis. Reg Anesth Pain Med 2016;41:763-72.
23. Brodie BL, Casper RF. Prostaglandins mediate postoperative pain in Falope ring sterilization. Am J Obstet Gynecol 1985;151:175-7.
24. Harrison MS, DiNapoli MN, Westhoff CL. Reducing postoperative pain after tubal ligation with rings or clips: a systematic review and meta-analysis. Obstet Gynecol 2014;124:68-75.
25. Carvalho B, Habib AS. Personalized analgesic management for cesarean delivery. Int J Obstet Anesth 2019;40:91-100.

Cite this article as: Nivatpumin P, Pangthipampai P, Dej-Arkom S, Aroonpruksakul S, Lertbunnaphong T, Ngam-ek-eu T. Gestational diabetes and intraoperative tubal sterilization are risk factors for high incidence of pain after cesarean delivery: a prospective observational study. Ann Palliat Med 2022;11(4):1170-1178. doi: 10.21037/apm-21-2139

