Dexamethasone and Lidocaine Effects in 24 hours Post Cesarean Pain Reduction under Spinal Anesthesia: A Randomized Controlled Trial

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ABSTRACT

Objective: This study aimed to compare the efficacy of additional local infiltration of dexamethasone and lidocaine among post-cesarean parturient underwent spinal anesthesia compared to the control group.

Materials and Methods: This randomized controlled trial was conducted at Thammasat University Hospital, Thailand, between June and November 2022. Singleton pregnant women who underwent cesarean delivery were randomized into 3 groups: dexamethasone (D), lidocaine (L), and control groups (C). Before skin closure, D, L and C group received infiltration of 16 mg of dexamethasone, 2% lidocaine with adrenaline and none, respectively. A visual analog scale (VAS, 0-10) was used for the evaluation of post-cesarean pain at two, four, six, eight, twelve, and twenty-four hours. VAS, demographic, and obstetric data were collected for analysis. Additional opioid was recorded for secondary outcome.

Results: A total of 279 participants were recruited and divided into 3 groups. Half of the participants (151/279) were nulliparity. Other demographics were similar. Subjects in the D group had lower moderate to severe pain after 6 hours onwards and less additional opioid requirement compared to the C and L groups significantly. Subjects in the L group had lower moderate to severe pain than the C group at 4 hours after surgery. Postoperative complications were comparable among the groups.

Conclusion: Local dexamethasone infiltration could reduce and prolong post-cesarean pain relief within 24 hours after cesarean delivery.

Keywords: Cesarean delivery; pain; dexamethasone; lidocaine (Siriraj Med J 2024; 76: 567-572)

INTRODUCTION

The incidence of cesarean delivery is increasing widely, reaching 32 percent of births in 2021.[1] In Thailand, the rate increased from 25 percent over the past 15 years, with a further increase to 50 percent by 2023.[2-4]

According to a Cochrane review in 2020, half to three-quarters of cases who underwent cesarean delivery experienced moderate to intense pain after surgery.[5] Spinal nerve blocks with hyperbaric bupivacaine and opioids are routinely utilized during cesarean delivery.[6,7] However, postoperative pain is often reduced by various drugs, including opioids, lidocaine, and steroid derivatives.

Among postoperative pain reducers, opioids are often administered and cause many adverse reactions, such as

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nausea, vomiting, and sedation.[8] To minimize these side effects, multimodal analgesia is recommended. Additive and synergistic medications such as dexamethasone and lidocaine can reduce the required additional opioid doses. Even a minimal dosage of local dexamethasone infiltration could prolong the anesthetic effect of the local anesthetic infiltration at the surgical wound.[9,10] Dexamethasone has a 5-hour elimination half-life and acts to reduce tissue edema and inflammatory mediators.[11] Despite some studies reporting adverse effects of dexamethasone, such as an increased risk of infection in certain participant groups, a systematic review conducted by Maged revealed that the majority of studies supported its safety.[11]

Meanwhile, lidocaine, an amide-type local anesthetic used in wound infiltration, acts by blocking nerve-ending voltage-gated sodium channels with 2 hours of half-life.[12] This half-life extends to 5 hours with the addition of adrenaline.[13] Even though adding adrenaline affected tissue perfusion, there was no evidence of adverse effects on abdominal skin.[13]

Therefore, this study aimed to investigate the additional benefits of local infiltration of dexamethasone or lidocaine compared to the control group for pain reduction, additional meperidine requirement, and opioid side effects compared to the control group in parturients undergoing cesarean delivery via spinal anesthesia.

MATERIALS AND METHODS

This double-blind, randomized control trial was conducted at Thammasat University Hospital, Thailand, between June and November 2022. The study was approved by the Human Ethics Committee of Thammasat University (MTU-EC-OB-2-015/64) and the Thai Clinical Trial Registry (TCTR20220524002). We enrolled term singleton gravidas aged at least 20 years old. Participants who had indication for cesarean delivery during the study period were recruited. Exclusion criteria were allergy to lidocaine or bupivacaine, insulin-dependent diabetes mellitus, pre-existing chronic illnesses, and refusal to participate.

The sample size was calculated using 1.4 as the mean difference between the two groups as placebo versus dexamethasone[14] and 1.2 as the standard deviation from the previous studies.[15] With a 1% alpha-type error rate and a statistical power of 80%, the formula of $n_2 = \{(Z_{1-\alpha} + Z_{1-\beta/2})^2 \delta^2 (1+1/k)\} / (\delta - |\varepsilon|)^2$ was used with $\varepsilon = \mu_2 - \mu_1$, $k = n_1/n_2$ and $n_1 = kn_2$. The final sample size was at least 87 cases per group with ten percent was added to account for data loss, the total sample size was 300 cases. A total of 300 cases were recruited for this study and 18 cases declined attendance due to concerns about drug side effects, worries regarding post-operative pain control, and insufficient time to complete the survey.

After thoroughly explaining the protocol to the participants, either at the antenatal care clinic or in the labor room, they were then asked to sign the written consent form. Participants were randomized into three groups equally using a computer number generator after signing the consent form. Subjects received either 16 mg of dexamethasone (D; dexamethasone group), or 20 ml of 1:200,000 2% lidocaine with adrenaline (L; lidocaine with adrenaline group), or neither (C; control group) locally in addition to routine spinal nerve block.

Spinal anesthesia was administered using a combination of 2 ml of 0.5% hyperbaric bupivacaine with 0.2 mg morphine, delivered via the intraspinal route. Participants received general anesthesia if they were unable to undergo spinal anesthesia, then dropped out from this research. Before the closure of the subcutaneous fat, operating surgeons would locally infiltrate the medication, either dexamethasone, lidocaine with adrenaline, or none, according to the assigned group of D, L, or C group, respectively. The scrub nurse would allocate the participants in a queue and note the prescribed medication inside a sealed envelope, which would match the patient's identification and later be given to the researcher along with the result.

In the first 24 hours after surgery, participants were interviewed by registered nurses about their pain scores using the visual analog scale (VAS) ranging from 0 to 10 (0 = no pain, 10 = worst imaginable pain), at 2, 4, 6, 12, 18, and 24-hour post-operation. Pain scores were categorized into no pain (VAS 0), mild pain (VAS 1-3), moderate pain (VAS 4-6), and severe pain (VAS 7-10).[16] Participants with moderate-to-severe pain scores will be offered meperidine for pain control. After 24 hours, participants with persistent post-cesarean delivery pain and desiring adjunctive anesthesia, regardless of pain score, will be offered non-steroidal anti-inflammatory drugs. Thus, both the patient and the investigator who recorded the VAS were blinded.

The primary outcome of this study was the pain score within the first 24 hours. The secondary outcomes included meperidine requirement and prevalence of nausea, itching, abdominal distension, and demand for alternative medication after 24 hours post-surgery. After gathering the required information, data analysis was performed using the Statistical Package for the Social Sciences version 23 (SPSS Inc., Chicago, IL, USA). Continuous data were analyzed using one-way ANOVA, while categorized data were evaluated with the chi-square test.

RESULTS

Three hundred participants were enrolled. After consideration of the inclusion and exclusion criteria, 279 gravidas were randomized into three groups. Two cases in the dexamethasone group and one case in the lidocaine group dropped out during the time of operation because the patients were undergoing general anesthesia. None dropped out from the control group (Fig 1).

Most pregnant women were in their thirties. Half of the parturient (151/279) were nulliparous. One-third (103/279) of participants have a history of cesarean delivery. All groups show no significant differences in characteristics, as shown in Table 1.

Most cases underwent cesarean delivery with an operative time of less than one hour. There were two and four postpartum hemorrhage cases in D and C groups, respectively. One-quarter (72/279) of subjects underwent tubal resection procedures without differences among the three groups.

At 2 and 4 hours after surgery, all three groups had comparable pain scores. Postoperative after 6 hours onwards, the D group had a lower pain score than the C group with statistical significance. There was no difference in pain scores between the L and the C group. The number of cases with moderate to severe pain in the D group was lower than the C group significantly from 4 hours onwards after the operation. In contrast, the L group had fewer cases of moderate to severe pain at only 4 hours post-operation compared to the C group (Table 2).

Within 24 hours after cesarean delivery, meperidine required for pain control was used in only 38.5 percent (35/91) of participants in the D group. Meperidine requirements among L and C group were comparable at nearly 60 percent (54/92 and 53/93, respectively). There were no complications associated with the local infiltration of dexamethasone nor lidocaine. Moreover, there were also no differences in postoperative complications, and participants who required additional oral pain relievers were no different between groups after 24 hours post-operation (Table 2).

DISCUSSION

According to the pain scores in this study, the average pain score following postoperative cesarean delivery was 3.5 at 6 hours and 3.6 at 24 hours, respectively, which aligns with the results of the previous study.[17] Roughly half of the participants experienced moderate to severe pain in the initial 24 hours, which has the same result as Cochrane review.[5]

In the first 2 hours of the current study, the pain scores and the number of participants experiencing moderate to severe pain showed no difference among all participants. This result can be explained by the spinal nerve blocks with hyperbaric bupivacaine and opioids, which provide excellent pain control lasting up to 142 minutes, depending on the dose administration.[6,7] At 4 hours post-operation, although the pain scores show similar results among the three groups, the number of participants experiencing moderate to severe pain in both intervention groups was significantly less than in the control group. After 4 hours, there was no difference observed in any outcome between the L group and the C group, including pain score, number of moderate to severe pain incidence, meperidine usage, or additional pain relief. This can be explained by the duration of lidocaine with adrenaline, which lasts approximately 5 hours.[13]

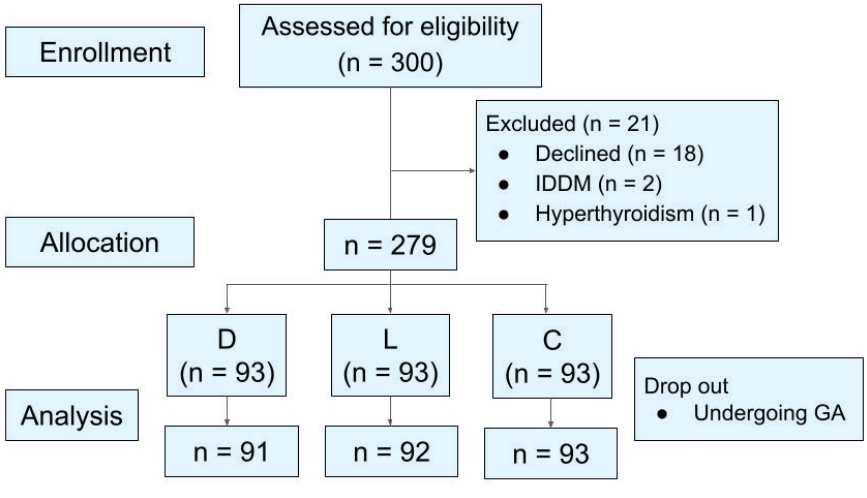

Fig 1. CONSORT flow diagram

Abbreviations: IDDM: Diabetes controlled with insulin, D: Dexamethasone group, L: Lidocaine with adrenaline group, C: Control group, GA: general anesthesia

TABLE 1. Baseline characteristics and operative data (93 cases per group for baseline data and 91,92, and 93 for D, L, and C group, respectively for operative data)

	D	L	C	*p*-value
Age (years) *	32.0 ± 4.8	31.7 ± 5.3	32.4 ± 4.8	0.634
GA (weeks) *	38.2 ± 0.8	38.1 ± 0.8	38.2 ± 0.7	0.557
Nulliparity **	46 (49.5)	47 (50.5)	58 (62.4)	0.147
BMI (kg/m^2) *	22.8 ± 3.8	23.9 ± 4.6	23.6 ± 4.1	0.211
Obesity (BMI kg/m^2) **				0.688
Underweight (<18.5)	9 (9.7)	8 (8.6)	8 (8.6)	
Normal (18.5-22.9)	44 (47.3)	42 (45.2)	40 (43.0)	
Overweight (23-24.9)	19 (20.4)	12 (12.9)	16 (17.2)	
Obese (≥25)	21 (22.6)	31 (33.3)	29 (31.2)	
Weight gain (kg) *	14.0 ± 5.2	14.2 ± 5.3	13.2 ± 4.8	0.337
AMA **	31 (33.3)	33 (35.5)	30 (32.3)	0.894
History of cesarean delivery **	38 (40.9)	36 (31.8.7)	29 (31.2)	0.357
Occupation **				0.101
Government	25 (26.9)	15 (16.1)	14 (15.1)	
Employee	30 (32.3)	30 (32.3)	36 (38.7)	
Self-employed	23 (24.7)	30 (32.3)	36 (38.7)	
Housewife	15 (16.2)	18 (19.4)	7 (7.6)	
Income (USD/month) **				0.089
<800	8 (8.6)	5 (5.4)	8 (8.6)	
800-1,400	64 (68.8)	80 (86.0)	73 (78.5)	
>1,400	21 (22.6)	8 (8.6)	12 (12.9)	
Operative data				
Time within 1 hour **	79 (86.8)	86 (93.5)	88 (94.6)	0.118
Board-certified **	71 (78.0)	80 (87.0)	75 (80.6)	0.272
EBL (ml) *	381.9 ± 173.4	381.5 ± 139.4	400 ± 230.0	0.363
PPH **	2 (2.2)	0 (0)	4 (4.3)	0.134
Tubal resection **	27 (29.7)	25 (27.2)	20 (21.5)	0.433

*: mean ± standard deviation, **: n (%)

Abbreviations: D: dexamethasone group, L: lidocaine with adrenaline group, C: control group, GA: gestational age, BMI: body mass index, AMA: advanced maternal age, USD: United States Dollar, Board-certified: board-certified obstetrician and gynecologist as the operator, EBL: Estimated blood loss, PPH: Postpartum hemorrhage

Despite its 5-hour elimination half-life, the effect of decreasing tissue edema and inflammatory mediators could explain how dexamethasone lowers the pain score.[18-21] While the VAS indicated a decrease in pain for the D group compared to the control group from 6 hours onwards, this reduction was not clinically significant. However, in D group, the number of participants experiencing moderate to severe pain was significantly lower than in the C group, ranging from 4 to 24 hours, consistent with previous research.[11] Furthermore, the use of opioids also showed a decrease compared to the C group, which correlates with previous studies.[22] This can be explained by the results of all groups experienced similarly low percentages of side effects which resulting in no difference in opioid use. Additionally, the incidence of post-operative complications was similarly low across both groups, indicating no significant difference.

A randomized controlled trial was chosen to select the sample group, along with double-blinded controls, which can be used to minimize bias in the outcomes.

TABLE 2. Outcome and complications.

	D (n= 91)	L (n=92)	C (n=93)	*p*-value		
				All	*D&C*	*L&C*
Pain score (hour)*						
2	3.1 ± 1.2	3.4 ± 1.4	3.1 ± 0.9	0.111	0.787	0.074
4	3.2 ± 1.0	3.2 ± 0.9	3.4 ± 1.1	0.261	0.278	0.121
6	3.0 ± 0.8	3.3 ± 1.0	3.5 ± 1.2	0.019	0.002	0.126
12	3.4 ± 1.3	3.8 ± 1.5	3.9 ± 1.2	0.003	0.006	0.778
18	3.5 ± 1.3	3.7 ± 1.1	3.9 ± 1.2	0.021	0.015	0.548
24	3.1 ± 1.0	3.7 ± 1.3	3.6 ± 1.1	<0.001	0.004	0.454
Moderate-to-severe pain (hour) **						
2	13 (14.3)	19 (20.7)	17 (18.3)	0.523	0.463	0.684
4	15 (16.5)	14 (15.2)	27 (29.0)	0.036	0.043	0.024
6	11 (12.1)	15 (16.3)	22 (23.7)	0.111	0.041	0.211
12	20 (22.0)	34 (37.0)	45 (48.4)	0.001	<0.001	0.116
18	29 (31.9)	34 (37.0)	45 (48.4)	0.020	0.010	0.116
24	16 (17.6)	35 (38.0)	30 (32.3)	0.007	0.022	0.410
Secondary outcome						
Mep use **	35 (38.5)	54 (58.7)	53 (57.0)	0.010	0.012	0.814
Add **	41 (45.1)	49 (53.3)	46 (49.5)	0.539	0.549	0.605
Post-op complication **						
N/V	7 (7.7)	10 (10.9)	15 (16.1)	0.195	0.078	0.295
Distension	25 (27.5)	24 (26.1)	22 (23.7)	0.835	0.533	0.702
Itching	10 (11.0)	3 (3.3)	7 (7.5)	0.130	0.417	0.199

*: mean ± standard deviation, **: n (%)

Abbreviations: D: dexamethasone group, L: lidocaine with adrenaline group, C: control group, Mep use: number of cases of meperidine use within 24 hours, Add: additional pain relieve after 24 hours post operation, N/V: nausea and vomiting

Furthermore, the frequency of measuring pain scores, pain level categorization, and meperidine use among the three groups was observed in our study, potentially enhancing the effectiveness of the results.

There was a limitation in our research due to the inability to blind the surgeon in the process, as the medication dosages are not equal. Furthermore, comparing dexamethasone to lidocaine was not feasible since the dosage of lidocaine is higher than that of dexamethasone, potentially leading to increased edema and pain. Additionally, the meperidine dose was fixed, making it challenging to assess whether patients use less of the opioid. Reevaluating the study design of patient-controlled anesthesia is necessary to evaluate the dosage of meperidine used accurately.

In conclusion, the local infiltration of dexamethasone among postoperative cesarean delivery showed to be effective in prolonging pain relief and reducing the moderate to severe pain and minimizing opioid use within 24 hours after cesarean delivery due to the reduction of inflammatory process. The findings of this study highlight the clinical benefits of implementing this approach.

What is already known on this topic

The incidence of cesarean delivery has been steadily rising globally and reaching nearly half of the parturients in 2023. Spinal anesthesia with hyperbaric bupivacaine and opioids is common practice in modern aesthetic. Adverse side effect of the opioid that commonly cause discomfort problems, include nausea, vomiting, and sedation. Various of medications namely, lidocaine, and dexamethasone are used to alleviate postoperative pain and minimize opioid-related adverse effects.

What does this study add

Local dexamethasone infiltration in post-cesarean delivery effectively prolonged pain relief, reduced moderate to severe pain, and minimized opioid use.

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Author Contributions

Conceived and designed the analysis, A.C., R.S.; Collected the data, R.S., Y.C.; Contributed data or analysis tools, D.P., K.S.; Performed the analysis, D.P., K.S.; Wrote the paper, R.S., Y.C., S.B., A.C. All authors have read and agreed to the final version of the manuscript.

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