PAIN MANAGEMENT

ЛЕЧЕНИЕ БОЛИ

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Effect of intrathecal opioid dose variation on patient outcomes in cesarean sections on a remote Indonesian island: a randomized controlled trial

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Abstract

INTRODUCTION: Intrathecal opioids are routinely used as adjuvants to spinal anesthesia for cesarean section to improve postoperative analgesia. While intrathecal morphine is considered the gold standard, the optimal dose that balances analgesic efficacy and adverse effects remains controversial, particularly in resource-limited and remote settings. **OBJECTIVE:** This study aimed to evaluate the effect of different intrathecal opioid regimens on postoperative pain control, mobilization, need for rescue analgesia, and postoperative nausea and vomiting in patients undergoing cesarean section in a remote Indonesian island hospital. **MATERIALS AND METHODS:** This randomized controlled trial was conducted from March to May 2025 at Wakatobi Regional General Hospital, Southeast Sulawesi. Eighty-four parturients undergoing cesarean section under spinal anesthesia were randomly assigned to four groups receiving hyperbaric bupivacaine 10 mg combined with either intrathecal fentanyl 25 µg, morphine 50 µg, morphine 100 µg, or morphine 150 µg. Postoperative pain was assessed using the Wong-Baker FACES Pain Rating Scale at 6, 12, 24, and 48 hours. Mobilization milestones, total rescue analgesic consumption, and incidence of postoperative nausea and vomiting were recorded up to 48 hours postoperatively. Non-parametric statistical analyses were applied, with $p < 0.05$ considered significant. **RESULTS:** Intrathecal morphine at all studied doses provided significantly better postoperative analgesia and reduced the need for rescue analgesics compared with intrathecal fentanyl, particularly at 6, 12, and 48 hours. No significant differences in pain scores or rescue analgesic requirements were observed among the three morphine doses. Mobilization was largely comparable between groups, although patients receiving morphine 150 µg achieved earlier ambulation than those receiving fentanyl. A significant dose-dependent increase in vomiting was observed with higher morphine doses.

Влияние различных доз интратекального опиоида на исходы у пациенток при кесаревом сечении на отдаленном индонезийском острове: рандомизированное контролируемое исследование

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Реферат

АКТУАЛЬНОСТЬ: Интратекальные опиоиды рутинно применяются в качестве адъювантов к спинальной анестезии при кесаревом сечении для улучшения послеоперационной анальгезии. Хотя интратекальный морфин считается эталонным средством, оптимальная доза, обеспечивающая баланс между эффективностью анальгезии и побочными эффектами, остается предметом дискуссий, особенно в условиях ограниченных ресурсов и отдаленных территорий. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Оценить влияние различных режимов дозирования интратекальных опиоидов на адекватность послеоперационного обезболивания, мобилизацию пациенток, потребность в дополнительной анальгезии, а также частоту послеоперационной тошноты и рвоты у пациенток, перенесших кесарево сечение в больнице на отдаленном острове Индонезии. **МАТЕРИАЛЫ И МЕТОДЫ:** Рандомизированное контролируемое исследование проводилось с марта по май 2025 г. в Региональной больнице общего профиля Вакатоби (Юго-Восточный Сулавеси). Восемьдесят четыре роженицы, перенесшие кесарево сечение под спинальной анестезией, были рандомизированы на четыре группы, получавшие 10 мг гипербарического бупивакаина в комбинации с интратекальным фентанилом в дозе 25 мкг, морфином в дозе 50, 100 или морфином 150 мкг. Послеоперационную боль оценивали по шкале Вонга—Бейкера FACES через 6, 12, 24 и 48 ч. Регистрировали сроки мобилизации, общее применение дополнительной анальгезии и частоту послеоперационной тошноты и рвоты до 48 ч после операции. Применялись непараметрические статистические методы; значимость устанавливалась при $p < 0{,}05$. **РЕЗУЛЬТАТЫ:** Интратекальный морфин во всех изученных дозах обеспечивал значительно лучшую послеоперационную анальгезию и снижал потребность в дополнительном обезболивании по сравнению с фен-

CONCLUSIONS: Intrathecal morphine offers superior and more sustained postoperative analgesia than fentanyl for cesarean section, and lower doses (50–100 µg) provide comparable efficacy to higher doses while minimizing opioid-related adverse effects.

KEYWORDS: cesarean section, intrathecal morphine, spinal anesthesia, postoperative pain, opioid adverse effects, postoperative nausea and vomiting

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танилом, особенно в 6, 12 и 48 ч. Значимых различий в баллах боли или потребности в дополнительном обезболивании между тремя дозами морфина не выявлено. Мобилизация была в целом сопоставима между группами, хотя пациентки, получавшие 150 мкг морфин, достигали ранней мобилизации быстрее, чем получавшие фентанил. Отмечался значимый дозозависимый рост частоты рвоты при более высоких дозах морфина. **ВЫВОДЫ:** Интратекальный морфин обеспечивает более выраженную и длительную послеоперационную анальгезию по сравнению с фентанилом при кесаревом сечении; низкие дозы (50–100 мкг) дают сопоставимую эффективность с высокими дозами при меньшей выраженности опиоид-индуцированных побочных эффектов.

КЛЮЧЕВЫЕ СЛОВА: кесарево сечение, интратекальный морфин, спинальная анестезия, послеоперационная боль, побочные эффекты опиоидов, послеоперационная тошнота и рвота

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Introduction

Cesarean delivery is performed when vaginal birth is not possible. Higher cesarean delivery rates are associated with lower maternal and neonatal mortality rates [1]. Spinal anesthesia remains the preferred technique for cesarean section due to its rapid onset, effective block, technical simplicity, and cost efficiency [2, 3]. Neuraxial morphine is widely used for its strong analgesic effects and cost-effectiveness, with intrathecal morphine (ITM) being the only Food and Drug Administration approved opioid for intrathecal use[1]. ITM provides prolonged analgesia of up to 36–48 hours after cesarean section and is recognized as the gold standard in post-cesarean pain management [4–6].

Postoperative pain is a common problem that can affect maternal mobility, bonding, breastfeeding, and newborn care [2, 5]. Inadequate pain control may increase thromboembolic events and delay recovery, while adequate postoperative analgesia means higher dose of opioid adjuvant and could increase incidence of postoperative opioid adverse effects such as nausea, vomiting, pruritus and respiratory depression, those adverse effects are associated with poor patient satisfaction, more complications, prolonged hospital stay, and higher medical expenses [5]. The optimal ITM dose, however, remains under debate. While most studies recommend 100–200 µg, some reports showed an effective analgesia effect can be achieved with 25–100 µg ITM [5, 7]. Underlining the increased risk of High dose ITM adverse effect, the goal of our study is to find the most favorable ITM dose for post cesarean section analgesia.

Objective

This study aimed to evaluate the effect of different intrathecal opioid regimens on postoperative pain control, mobilization, need for rescue analgesia, and postoperative nausea and vomiting in patients undergoing cesarean section in a remote Indonesian island hospital.

Materials and methods

Study Design and Participants

This study was an experimental research with a randomized controlled trial design. Participants were randomly distributed into several treatment groups, each receiving a different dose of intrathecal opioids. The research was conducted at Wakatobi Regional General Hospital (RSUD Kabupaten Wakatobi) in Southeast Sulawesi, from March to May 2025. The Hospital Ethics Committee has approved this study with registration number: 77.a/800/III/2025. The independent variable was the variation in intrathecal opioid doses, which were fentanyl 25 mcg, morphine 50 mcg, morphine 100 mcg, and morphine 150 mcg. The dependent variables were post-operative pain score, rate of mobilization, the need for additional analgesic rescue, and the occurrence of post-operative nausea and vomiting (PONV).

The samples were patients who had cesarean section during the study period and met the inclusion criteria without meeting any of the exclusion criteria. The inclusion criteria were all pregnant women aged between 18 and 40 years, experiencing cesarean section using spinal anesthesia, with a physical status of American Society of Anesthesiologists (ASA) classification II or III, able to communicate verbally to provide informed consent for spinal anesthesia, and undergo a surgical procedure that lasted no longer than 120 minutes without conversion to general anesthesia. Patients were excluded from the study if they had absolute contraindications to spinal anesthesia, known allergies to bupivacaine, fentanyl, morphine, or refused to undergo spinal anesthesia.

Anesthesia Procedure

All patients in the study received spinal anesthesia using 10 mg of hyperbaric bupivacaine. The type and dose of intrathecal opioid adjuvant were given according to each group. These procedures were carried out by trained anesthesia professionals under sterile clinical conditions and in accordance with standard operating procedures established at the hospital.

Data Collection

Descriptive characteristics of the patients and the clinical outcomes were collected. Baseline clinical data were collected to characterize the study population and ensure comparability between groups. These included the patient's age and body weight at the time of surgery, neonatal Apgar scores at one and five minutes after delivery, the parity status, the presence of anemia, obesity, and severe pre-eclampsia, and patient's preoperative condition that was classified using the American Society of Anesthesiologists Physical Status system.

Postoperative pain was evaluated using the Wong-Baker FACES Pain Rating Scale, which ranges from 0 to 10 and was recorded at 6, 12, 24, and 48 hours after surgery. Mobilization was evaluated based on how fast the patient can turn in bed, sit, stand, and walk. This was also recorded at 6, 12, 24, and 48 hours after surgery. The need for additional analgesic rescue was determined by calculating the total number of 30 mg of ketorolac administered intravenously until 48 hours postoperatively. Adequate pain control was defined as a Wong-Baker Score of 3 or lower. In addition, the incidence of PONV was recorded based on whether the patient experienced any episode of nausea or vomiting or required rescue antiemetics (ondansetron 4 mg administered via the intravenous route) until 48 hours after surgery.

Statistical Analysis

All statistical analyses were performed using SPSS version 27.0 for Windows. Descriptive statistics were used to summarize the data in univariate tables. To test for normality in the distribution of data, the Shapiro-Wilk test was applied. Comparisons between different dosage groups with pain scores, mobilization, and additional analgesic rescue were analyzed using one-way analysis of variance (ANOVA) if the data were parametric. If the data were non-parametric, the Kruskal-Wallis test was used instead. The incidence of PONV was analyzed with a chi-square test for trend when its assumptions were met. If the assumptions were not met, the Fisher's exact test was employed. The comparison was statistically significant if the p-value was less than 0.05.

Results

A total of 84 pregnant women were approached, and all were enrolled in the study. They were evenly divided into four treatment groups. The majority of participants in each group were multiparous, ranging from 52 to 62 %, while primiparous women comprised 38 to 48 % of the groups. Anemia was relatively uncommon: none of the participants in the fentanyl or morphine 100 μg groups had anemia, whereas 9 to 24 % of participants in the morphine 50 and 150 μg groups had anemia. Obesity was identified in 14 %

of the fentanyl group, 24 % of the morphine 100 μg group, and 19 % of the morphine 150 μg group, while no cases of obesity were observed in the morphine 50 μg group. Severe pre-eclampsia was absent in the fentanyl group but present in 9 to 24 % of participants in the morphine groups. Regarding physical status according to the ASA, all patients in the fentanyl group were classified as ASA II. In the morphine groups, the majority were ASA II (86–91 %), with a small proportion (9–14 %) classified as ASA III (Table 1).

The mean age of participants ranged from 27.7 ± 9.0 years in the morphine 100 μg group to 31.3 ± 6.6 years in the morphine 50 μg group. Mean body weight varied between 66.7 ± 7.4 and 71.5 ± 7.8 kg across the groups (Table 2).

The Shapiro-Wilk normality test showed that all tested variables had p-values < 0.001, including pain scores at 6, 12, 24, and 48 hours, the time required for patients to turn in bed, sit, stand, and walk as well as the 1-minute and 5-minute Apgar Score (Table 3). These results indicate that the data were not normally distributed. Therefore, subsequent analyses were conducted using the non-parametric Kruskal-Wallis test.

At 6 hours, a significant difference was observed among the groups ($p = 0.019$). Patients receiving fentanyl reported higher pain scores compared to those given morphine, with the most prominent difference found in the morphine 150 mcg group ($p = 0.021$). These findings suggest that fentanyl is less effective than high-dose morphine. At 12 hours, a similar pattern was observed ($p < 0.001$). Fentanyl consistently showed the highest mean pain scores, while all morphine groups demonstrated better pain reduction. No significant differences were found among the morphine doses, indicating comparable efficacy. At 24 hours, no significant differences were found between

Table 1. Patient demographic characteristics (categorical)

Таблица 1. Демографические характеристики пациентов (категориальные)

No	Variable	Fentanyl	Morphine, mcg		
			50	100	150
1	Parity Status:				
	■ Primipara	8 (38 %)	8 (38 %)	10 (48 %)	8 (38 %)
	■ Multipara	13 (62 %)	13 (62 %)	11 (52 %)	13 (62 %)
2	Anemia:				
	■ Anemia	0 (0 %)	2 (9 %)	0 (0 %)	5 (24 %)
	■ No	21 (100 %)	19 (91 %)	21 (100 %)	16 (76 %)
3	Obesity:				
	■ Obesity	3 (14 %)	0 (0 %)	5 (24 %)	4 (19 %)
	■ No	18 (86 %)	21 (100 %)	16 (76 %)	17 (81 %)
4	Severe pre-eclampsia:				
	■ Yes	0 (0 %)	2 (9 %)	3 (14 %)	5 (24 %)
	■ No	21 (100 %)	19 (91 %)	18 (86 %)	16 (76 %)
5	PS ASA:				
	■ 2	21 (100 %)	18 (86 %)	19 (91 %)	18 (86 %)
	■ 3	0 (0 %)	3 (14 %)	2 (9 %)	3 (14 %)

Note: PS ASA — Physical Status according to the American Society of Anesthesiologists.

Примечание: PS ASA — физический статус пациента по классификации Американского общества анестезиологов.

Table 2. Patient demographic characteristics (numerical)

Таблица 2. Демографические характеристики пациентов (количественные)

No	Variable	Fentanyl	Morphine, mcg		
			50	100	150
1	Age (years)	29.5 ± 6.6	31.3 ± 6.6	27.7 ± 9.0	30.6 ± 6.4
2	Weight (kg)	71.5 ± 7.8	66.7 ± 7.4	70.2 ± 14.5	67.8 ± 13.2
3	Apgar Score 1	7.0 ± 0.0	6.0 ± 1.5	6.70 ± 0.78	6.8 ± 0.7
4	Apgar Score 5	8.0 ± 0.0	7.4 ± 1.1	7.90 ± 0.43	8.0 ± 0.4

Table 3. Shapiro-Wilk normality test

Таблица 3. Тест Шапиро—Уилка для оценки нормальности распределения данных

No	Variable	Shapiro-Wilk Test
1	Pain at 6 hour	$p < 0.001$
2	Pain at 12 hour	$p < 0.001$
3	Pain at 24 hour	$p < 0.001$
4	Pain at 48 hour	$p < 0.001$
5	Turning in bed	$p < 0.001$
6	Sit	$p < 0.001$
7	Stand	$p < 0.001$
8	Walk	$p < 0.001$
9	AS 1	$p < 0.001$
10	AS 5	$p < 0.001$

Note: AS — Apgar Score.

Примечание: AS — шкала Апгар.

the groups ($p = 0.440$). By 48 hours, however, significant differences reappeared ($p < 0.001$) (Table 4). Fentanyl showed the highest mean rank, followed by morphine 50, 100 and 150 mcg. While there were no significant differences among the morphine doses, all morphine groups differed significantly from fentanyl (Table 5).

The Kruskal-Wallis test showed no significant differences among the groups in the time required for patients to mobilize into the lateral position ($p = 0.590$), sitting ($p = 0.327$), or standing ($p = 0.305$). However, a significant difference was observed in walking ability ($p = 0.018$) (Table 6). Pairwise analysis revealed that the difference was only between the morphine 150 mcg and fentanyl groups ($p = 0.012$) with no significant differences observed among the other doses (Table 7).

There was a highly significant difference among the groups in the need for additional analgesics ($p < 0.001$). The fentanyl group had the highest mean rank, indicating more frequent use of additional analgesics compared to the morphine groups. Pairwise analysis confirmed no significant differences among the morphine groups ($p = 1.00$ for all comparisons) (Table 8). However, all morphine groups differed significantly from fentanyl ($p < 0.001$ for all comparisons) (Table 9). These results demonstrate that all

Table 4. Relationship between pain scale assessment intervals and adjuvant dosage

Таблица 4. Взаимосвязь между интервалами оценки боли по шкале и дозами адъювантов

No	Pain scale assessment intervals	Adjuvant Dosage	Mean Rank	*P*-value
1	At 6 hour	Fentanyl	55.52	0.019*
2		Morphine 50 mcg	37.17	
3		Morphine 100 mcg	43.12	
4		Morphine 150 mcg	34.19	
5	At 12 hour	Fentanyl	69.64	< 0.001*
6		Morphine 50 mcg	32.45	
7		Morphine 100 mcg	37.10	
8		Morphine 150 mcg	30.81	
9	At 24 hour	Fentanyl	45.62	0.440
10		Morphine 50 mcg	44.95	
11		Morphine 100 mcg	44.29	
12		Morphine 150 mcg	35.14	
13	At 48 hour	Fentanyl	60.40	< 0.001*
14		Morphine 50 mcg	40.55	
15		Morphine 100 mcg	38.83	
16		Morphine 150 mcg	30.21	

Note: * Kruskal-Wallis.

Примечание: * Критерий Краскела—Уоллиса.

Table 5. Pairwise relationship between pain scale assessment intervals and adjuvant dosage

Таблица 5. Парная зависимость между интервалами оценки боли по шкале и дозами адъювантов

No	Pain scale assessment intervals	Adjuvant Dosage	*P*-value
1	At 6 hour	Morphine 50 Morphine 100	1.000
		Morphine 50 Morphine 150	1.000
		Morphine 100 Morphine 150	1.000
		Morphine 50 Fentanyl	0.073
		Morphine 100 Fentanyl	0.540
		Morphine 150 Fentanyl	0.021*
2	At 12 hour	Morphine 50 Morphine 100	1.000
		Morphine 50 Morphine 150	1.000
		Morphine 100 Morphine 150	1.000
		Morphine 50 Fentanyl	0.000*
		Morphine 100 Fentanyl	0.000*
		Morphine 150 Fentanyl	0.000*
3	At 48 hour	Morphine 50 Morphine 100	1.000
		Morphine 50 Morphine 150	0.860
		Morphine 100 Morphine 150	1.000
		Morphine 50 Fentanyl	0.029*
		Morphine 100 Fentanyl	0.013*
		Morphine 150 Fentanyl	0.000*

Note: * Pairwise.

Примечание: * Попарное сравнение.

Table 6. Relationship between mobilization and adjuvant dosage

Таблица 6. Связь между уровнем мобилизации пациента и дозами адъювантов

No	Mobilization	Adjuvant Dosage	Mean Rank	*P*-value
1	Turning in bed	Fentanyl	37.86	0.590
2		Morphine 50 mcg	45.55	
3		Morphine 100 mcg	44.24	
4		Morphine 150 mcg	42.36	
5	Sit	Fentanyl	37.33	0.327
6		Morphine 50 mcg	42.05	
7		Morphine 100 mcg	49.36	
8		Morphine 150 mcg	41.26	
9	Stand	Fentanyl	47.43	0.305
10		Morphine 50 mcg	43.43	
11		Morphine 100 mcg	44.00	
12		Morphine 150 mcg	35.14	
13	Walk	Fentanyl	53.83	0.018*
14		Morphine 50 mcg	43.40	
15		Morphine 100 mcg	39.60	
16		Morphine 150 mcg	33.17	

Note: * Kruskal-Wallis.

Примечание: * Критерий Краскела—Уоллиса.

studied doses of morphine, reduced the need for additional analgesics more effectively than fentanyl, with similar efficacy among the three morphine doses.

Trend analysis using the Chi-Square for Trend test revealed a significant association between higher morphine doses and the incidence of vomiting ($p = 0.014$). The proportion of vomiting increased with higher doses: 28.5 % in the 50 mcg group, 43 % in the 100 mcg group, and 66 % in the 150 mcg group (Table 10). This finding suggests a clear dose-related trend in vomiting associated with morphine use.

Table 7. Pairwise relationship between mobilization and adjuvant dosage

Таблица 7. Парная зависимость между мобилизацией пациента и дозами адъювантов

No	Mobilization	Adjuvant Dosage	*P*-value
1	Walk	Morphine 50 Morphine 100	1.000
		Morphine 50 Morphine 150	0.756
		Morphine 100 Morphine 150	1.000
		Morphine 50 Fentanyl	0.715
		Morphine 100 Fentanyl	0.200
		Morphine 150 Fentanyl	0.012*

Note: * Pairwise.

Примечание: * Попарное сравнение.

Table 8. Relationship between analgesic rescue and adjuvant dosage

Таблица 8. Взаимосвязь между обезболиванием и дозировками адъювантов

No	Intervention	Adjuvant Dosage	Mean Rank	*P*-value
1	Total analgesic doses administered	Fentanyl	66.71	0.001*
2		Morphine 50 mcg	33.52	
3		Morphine 100 mcg	35.43	
4		Morphine 150 mcg	34.33	

Note: * Kruskal-Wallis.
Примечание: * Критерий Краскела—Уоллиса.

Discussion

Patients' parity status (primiparous versus multiparous) appears to be a significant factor in postoperative pain experience and analgesic response after a cesarean delivery under spinal or intrathecal anesthesia. A study by Yang et al. (2020) showed that multiparas who had repeated cesarean sections had a significantly higher risk of inadequate analgesia compared to primiparas (OR ~1.53, 95% CI 1.19–1.97) [8]. These findings showed that multiparas may require either higher or more sustained analgesic regimens to achieve equivalent pain relief.

Pain intensity and analgesic response are influenced by other clinical factors such as anemia, obesity, severe pre-eclampsia, and higher ASA status. Anemia may impair oxygen delivery and tissue recovery, thereby lowering pain thresholds and leading to higher postoperative pain scores. Patients with a BMI ≥ 30 kg/m^2 (obesity) require higher opioid consumption compared with those with a BMI < 30 kg/m^2, and despite this increased use, their pain control tends to be slightly less effective too [9]. In contrast,

Table 9. Pairwise relationship between analgesic rescue and adjuvant dosage

Таблица 9. Парная зависимость между дозировкой дополнительного аналгетика и адъюванта

No	Adjuvant Dosage	*P*-value
1	Morphine 50 Morphine 150	1.00
2	Morphine 50 Morphine 100	1.00
3	Morphine 100 Morphine 150	1.00
4	Morphine 50 Fentanyl	0.00*
5	Morphine 100 Fentanyl	0.00*
6	Morphine 150 Fentanyl	0.00*

Note: * Pairwise.

Примечание: * Попарное сравнение.

Table 10. Chi-Square for Trend (Linear-by-Linear Association)

Таблица 10. Критерий χ^2 для выявления тренда (линейная зависимость)

No	PONV	Adjuvant Dosage			*P*-value
		Morphine 50 mcg	Morphine 100 mcg	Morphine 150 mcg	
1	Yes	6 (28,5 %)	9 (43 %)	14 (66 %)	0.014
2	No	15 (71,5 %)	12 (57 %)	7 (33 %)	

Note: PONV — Postoperative Nausea and Vomiting.

Примечание: PONV — послеоперационная тошнота и рвота.

some studies found that women with pre-eclampsia tend to experience lower postoperative pain scores and reduced analgesic needs, probably due to altered pain perception and neurohumoral changes [10]. Additionally, older age and patients with ASA physical status III have a slower pain resolution following surgery [11].

Neuraxial opioids act through the direct uptake of the drug into the spinal cord and cerebrospinal fluid, resulting in a strong analgesic response. Opioids bind to pre- and post-synaptic receptors in the spinal cord and brainstem, which inhibits the transmission of pain signals [12]. The lipophilicity of neuraxial opioids plays a key role in determining the onset, spread, and duration of analgesia [12]. Lipophilic opioids such as fentanyl and sufentanil have a rapid onset and a shorter duration of action because they can easily cross the blood–brain barrier and tend to retained in fat-rich tissues, such as epidural fat and white matter, resulting in lower concentrations and more rapid clearance from the cerebrospinal fluid [4, 12, 13]. Hydrophilic opioids, such as morphine and hydromorphone, have a slower onset but a wider spread and longer duration of analgesia. They cross the blood–brain barrier more slowly, bind less to fat, but have a stronger affinity for receptors in the grey matter — particularly in the dorsal horn — and remain longer in the cerebrospinal fluid [4]. Intrathecal morphine has an onset time of 45–75 minutes and provides analgesia lasting 13–33 hours, whereas fentanyl or sufentanil takes effect within 5–20 minutes but lasts only 1–6 hours [14–16].

The results of this study showed that morphine provided better postoperative analgesia in Cesarean section patients compared to fentanyl. At the 6th-hour evaluation, patients receiving fentanyl reported significantly higher pain scores than patients in the morphine 150 mcg group ($p = 0.021$). At the 12-hour and 48-hour evaluations, the fentanyl group consistently showed the highest pain scores compared to all morphine doses. However, at 24 hours, no significant differences were found between these groups ($p = 0.440$). These findings are consistent with those reported by Botea et al. (2023), where only 77.2 % of patients in the fentanyl group achieved adequate pain control, while all patients receiving morphine (100 %) achieved satisfactory pain control [17]. Another study by El Aish et al. (2018) also supports these results. They found significantly lower VAS pain scores than fentanyl from the first postoperative hour up to 24 hours (e.g., 1.84 *vs* 5.08 at 6 hours; $p < 0.0001$) [18].

In this study, no significant differences were found among the three morphine doses at all postoperative pain score evaluation times, indicating that all three doses were equally effective in providing analgesia. This result is consistent with Carvalho and Tenório (2013) and Fei et al. (2023), who found that a low dose of ITM (50–60 mcg) provided a similar quality of postoperative analgesia compared to 100 mcg ITM, while causing fewer side effects [5, 19]. However, Karnjanawanichkul et al. (2022) reported that although a very low dose of 50 mcg ITM still provided analgesia, it was inferior to 100 and 200 mcg for postoperative pain control [7]. Hess and Smiley (2025) also showed that ITM doses of 100 mcg or less provided analgesia comparable to doses higher than 100 mcg [20]. On the other hand, a meta-analysis of eleven studies by Sultan et al. (2016) showed that higher doses of morphine (> 100–250 μg) prolonged analgesia after cesarean delivery compared to lower doses (50–100 μg) [21].

Postoperative mobilization is closely linked with pain intensity. Rivas et al. (2022) conclude that lower scores of pain are linked with increased mobility regardless of opioid intake [22]. Consistent with this, our study found a significant difference only between the morphine 150 μg and fentanyl groups ($p = 0.012$) during the walking phase, indicating that patients receiving intrathecal fentanyl required significantly more time to walk compared with those administered 150 μg of morphine. However, differences were not statistically significant among the various morphine doses. Furthermore, even when pain was minimal, some patients refrained from mobilizing or expressed fear, indicating that psychological factors may also influence early ambulation.

Our study showed that as the dose of morphine increased, the incidence of vomiting also increased. According to the systematic review and meta-analysis by Gonvers et al. (2021), increasing the dose of ITM increases the frequency of opioid-related side effects, including vomiting [23]. The authors reported a threshold effect, indicating that morphine doses above 100 μg do not significantly improve analgesic efficacy but substantially elevate the risk of PONV. Hence, the data collected in this study demonstrate that the dosage of intrathecal administered to cesarean patients should be adjusted carefully i.e., to maintain optimal levels of pain relief while causing a minimum of adverse effects.

Conclusion

Overall, the results of this study support the use of intrathecal morphine as the primary choice for post-caesarean section analgesia. Lower doses are as effective as higher doses in giving adequate pain relief, while also minimizing the risk of side effects.

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