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Research Article

Safety Profile of Intrathecal Morphine in Obese Parturients Undergoing Caesarean Delivery: A Retrospective Study

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Abstract

Background: The escalating prevalence of maternal obesity poses significant challenges in obstetric anaesthesia. Specifically, provider apprehension regarding opioid-induced respiratory depression frequently limits the utilisation of intrathecal morphine (ITM) in obese parturients undergoing caesarean delivery.

Objectives: To evaluate the safety and efficacy profile of ITM in this growing, high-risk population.

Methods: This was a retrospective cohort analysis conducted at a tertiary hospital, including 400 obese parturients who underwent caesarean delivery under spinal anaesthesia with a standard regimen including 0.1 mg of ITM. Data, including demographics, comorbidities, postoperative pain scores, side effects (nausea, vomiting, pruritus, respiratory depression) and neonatal Apgar scores, were collected up to 24 hours postoperatively.

Results: The cohort had a mean age of 31.22 ± 4.99 years and a mean body mass index of 36.13 ± 4.17 kg/m². No respiratory depression was observed at all time, with a peak incidence of 30.3% for nausea (at 1 hour) and 22.0% for pruritus (at 12 hours) postoperatively. There were no statistically significant differences in the incidence of any side effect across the different obesity classes. Analgesic efficacy was good, with a median visual analogue score of 0 in the first 4 hours, gradually increasing to a median of 3 at 24 hours. Neonatal Apgar scores were favourable.

Conclusion: A standard use of 0.1 mg dose of intrathecal morphine provides effective early postoperative analgesia with no incidence of respiratory depression and manageable non-life threatening side effects, even in parturients with morbid obesity.

Keywords: patient safety, intrathecal morphine, obesity, caesarean delivery, outcome

INTRODUCTION

Pain is a complex and subjective unpleasant sensation, modulated by a multitude of individual factors [1]. In the context of obstetrics, caesarean births present a unique clinical challenge. Unlike patients undergoing other major surgical procedures, parturients are expected to recover rapidly to care for their newborns within hours of the operation. This crucial early interaction can be significantly impaired if postoperative pain control is unsatisfactory [2, 3]. Furthermore, emerging evidence indicates that inadequately treated acute pain following a caesarean section is associated with a heightened incidence of adverse long-term outcomes, including chronic pain and post-traumatic stress syndrome [4-6]. The incidence of postoperative pain after caesarean section varies widely; reports suggest acute pain ranges from 0.5% to 20%, while chronic post-surgical pain is reported in 4% to 41.8% of patients, often influenced by the severity of initial postoperative pain [7, 8].

The lower segment caesarean section (LSCS) is the most frequently performed obstetric operation globally. Its incidence has risen markedly in recent decades, amplifying the need for optimised perioperative management [9]. Spinal anaesthesia has become the preferred anaesthetic technique for the majority of LSCS procedures [10]. To enhance the quality and duration of analgesia, intrathecal opioids are now routinely co-administered with local anaesthetics. This practice prolongs analgesia both intraoperatively and into the postoperative period [11].

Among the available opioids, intrathecal morphine (ITM) is recognised for providing a more prolonged and effective analgesic block compared to shorter-acting agents like fentanyl, with effective doses typically ranging from 0.1 to 0.25 mg [12-14]. However, the use of ITM is tempered by concerns regarding its potential side effects, which commonly include pruritus, nausea, vomiting, and urinary retention, and more rarely, the life-threatening complication of respiratory depression [13]. The reported incidence of these side effects varies considerably in the literature. For instance, postoperative nausea and vomiting have been reported in approximately 30% of patients, while pruritus incidence ranges from 0% to as high as 100% in some studies [15-20]. Conversely, the incidence of significant respiratory depression following ITM administration in parturients is low, generally reported between 0% and 0.9% [21-23], although several large retrospective studies have found the incidence to be between 0.26% and 3% [24, 25].

The global rise in obesity has led to a corresponding increase in the number of obese parturients presenting for caesarean delivery [26]. This patient population presents distinct anaesthetic challenges. Intrathecal morphine is administered with caution in obese patients,

especially those with higher STOP-Bang scores or with diagnosed obstructive sleep apnoea (OSA), due to concerns regarding a higher risk of side effects, necessitating more frequent monitoring [27-30]. This apprehension often leads to the under-treatment of pain or the complete avoidance of ITM despite the critical need for effective analgesia to facilitate early ambulation and mitigate the inherently higher risk of venous thromboembolism in this group [31, 32]. Despite the increasing prevalence of this clinical scenario, there is a paucity of literature specifically evaluating the safety and efficacy of standardised ITM doses in the obese parturient population. Clinical practice varies, and in many centres, the use of ITM in obese parturients is not standardised. This creates an evidence gap regarding the true risk-benefit profile of ITM in this specific patient demographic.

This study aims to evaluate the safety profile of a standard dose of ITM in obese parturients undergoing caesarean section. The primary focus is to determine the incidence of side effects, particularly nausea, vomiting, pruritus, and respiratory depression. Additionally, the study assessed the analgesic efficacy of ITM through postoperative pain scores and evaluate neonatal well-being via Apgar scores.

METHODOLOGY

This study was conducted as a retrospective cohort analysis of medical records from Selayang Hospital, a tertiary care centre in Selangor, Malaysia. The study period encompassed all LSCS procedures performed from January 2018 to December 2022. Ethical approval was obtained from the Research Ethics Committee, Universiti Kebangsaan Malaysia (UKM) (Ref No. JEP-2024-128), and the Medical Research and Ethics Committee (MREC), Ministry of Health, Malaysia (NMRR-24-02526-FDN). Participant data were handled in accordance with institutional ethical approval and confidentiality agreements.

The study population comprised all the data of obese parturients who underwent LSCS under spinal anaesthesia during the specified five-year period. Inclusion criteria were: the data of parturients aged between 18 and 50 years with a Body Mass Index (BMI) > 30 kg/m². Exclusion criteria were: the data of parturients with American Society of Anesthesiologists (ASA) physical status of IV or higher, pre-existing chronic pain conditions and LSCS performed under general or epidural anaesthesia.

Parturients data were retrieved from the Health Information Department of Selayang Hospital. A standardised data collection sheet was used to extract all relevant information, covering the intraoperative period up to 24 hours postoperatively. Records with significant missing data pertinent to the primary outcomes were excluded.

The study cohort consisted of the data of parturients who received a standardised spinal anaesthetic of 0.1 mg of ITM co-administered with 0.5% hyperbaric bupivacaine and 10-15 mcg of fentanyl, administered at the L3-L4 or L4-L5 interspace. All parturients received 4 mg of intravenous (IV) dexamethasone intraoperatively as an antiemetic and a 50-100 mg diclofenac sodium suppository postoperatively, unless contraindicated.

Key data points included demographics, comorbidities, intraoperative details, neonatal Apgar scores, and observations at 1, 4, 8, 12, and 24 hours postoperatively. Data was further classified into class 1 obesity (BMI 30 to 34.9 kg/m²), class 2 obesity (BMI 35 to 39.9 kg/m²) and class 3 obesity (BMI >40 kg/m²). Postoperative observations included pain assessment using the Visual Analogue Scale (VAS), haemodynamic monitoring, and the incidence of side effects. A VAS score > 4 typically triggered a request for rescue analgesia. Additional analgesic such as aliquot of IV tramadol and diclofenac were given by attending obstetrician. Nausea and vomiting were treated with 10 mg of IV metoclopramide. Respiratory depression was defined as a respiratory rate (RR) < 8 breaths per minute, hypotension as systolic blood pressure (SBP) reduction > 20% from the baseline, and desaturation as oxygen saturation (SpO₂) < 95%.

The sample size was determined using the Krejcie & Morgan formula for a finite population [33]. Based on a total population of 5,611 obese parturients undergoing LSCS at the participating hospital between the years 2018 and 2022, and an expected pruritus incidence of 45.7% [34], the minimum required sample size was 357. This was increased to 400 subjects to account for a potential 10% dropout rate. All data were analysed using SPSS for Windows, version 23.0 (IBM Corp, Armonk, NY, USA). Descriptive statistics were used to summarise the data. Continuous variables were presented as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR). Categorical variables were presented as frequencies and percentages. An independent t-test or Mann-Whitney U test was used for between-group analyses of continuous data, while the Chi-square or Fisher's exact test was used for categorical data. A p-value < 0.05 was considered statistically significant.

RESULTS

Out of 503 parturients' data, 400 met the inclusion criteria and included in the analysis. The remaining 103 data was excluded due to incomplete information, as depicted in Figure 1. The majority of participants were classified as having Class 1 obesity. The most common comorbidities were gestational diabetes mellitus (GDM) and pregnancy-induced hypertension (PIH). The demographic and clinical characteristics of the parturients are summarised in Table 1.

CONSORT Flow Diagram

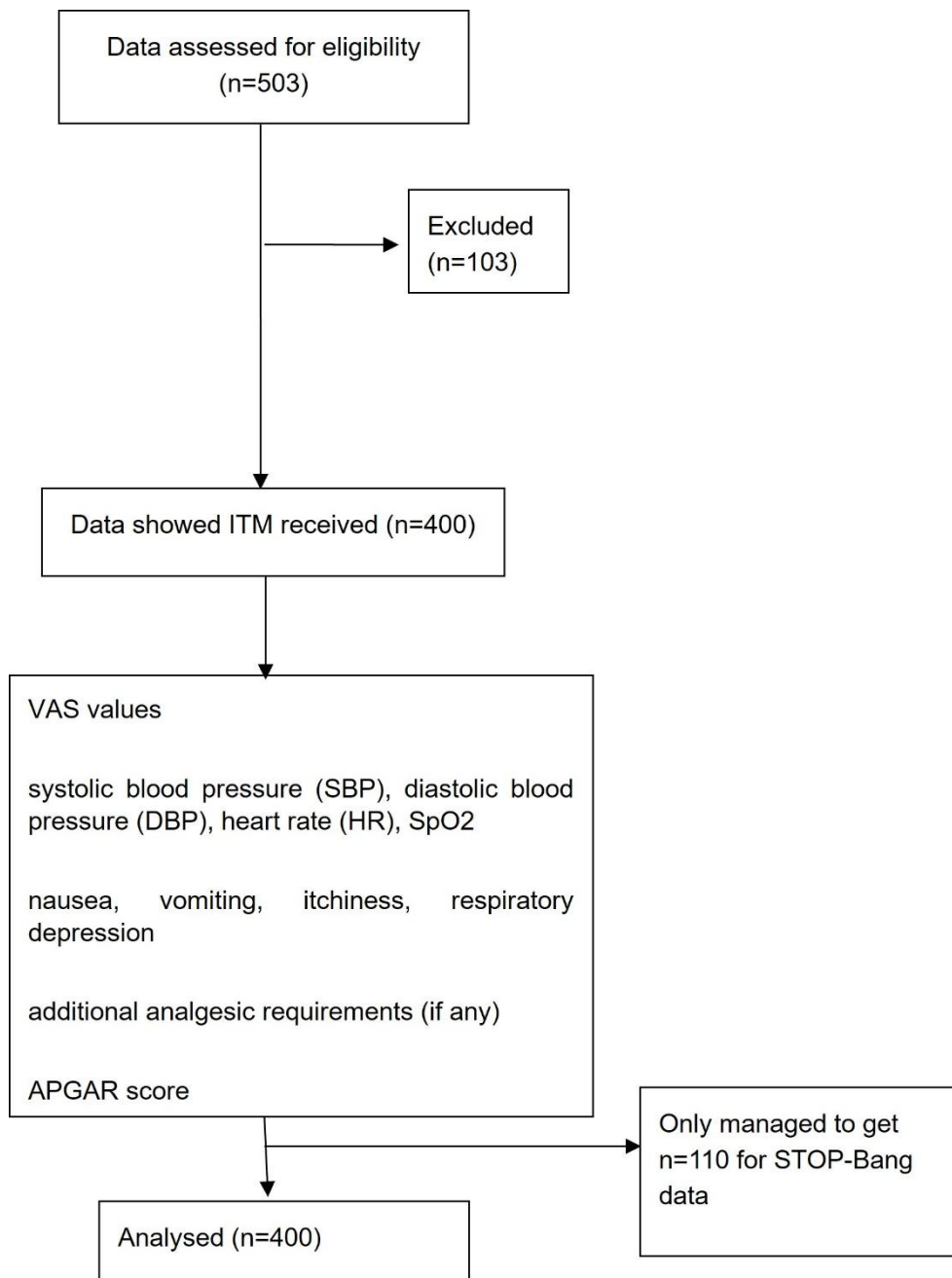


Figure 1 CONSORT flow diagram

Table 1 Demographic and clinical characteristics of the parturients

Characteristics		Total (n=400)
Age in years, mean $\pm$ SD		31.22 $\pm$ 4.99
BMI in kg/m ² , mean $\pm$ SD		36.13 $\pm$ 4.17
BMI category, n (%)	Class 1	170 (42.5)
	Class 2	146 (36.5)
	Class 3	84 (21.0)
Parity, median (IQR)		1 (0, 2)
Comorbidities, n (%)	Asthma	27 (6.8)
	GDM	88 (22.0)
	PIH	86 (21.5)
	Others	4 (1.0)
Duration of surgery in minutes, mean $\pm$ SD		55.47 $\pm$ 14.19
Estimated blood loss in ml, mean $\pm$ SD		527.86 $\pm$ 191.24

Values are expressed as mean SD

BMI Body mass index, SD standard deviation, IQR interquartile range, GDM gestational diabetes, PIH pregnancy induced hypertension

The incidences of postoperative side effects are shown in Table 2. Nausea was the most frequent side effect, about a third of patients in the first hour and gradually decreased to less than 10% by 24 hours. However, only half of quarter of parturients vomited within the first hour, reduced to 2.3% by 24 hours. Pruritus showed a delayed onset, with the incidence of 5.8% at 1 hour to a peak of almost a quarter of patients at 12 hours postoperatively. There were no statistically significant differences in the incidence of all the side effects measured across the different classes of obesity.

Table 2 Incidence of side effects following administration of intrathecal morphine

Side effects	Incidence	Obesity classes			<i>P</i> value
		Class 1	Class 2	Class 3	
		(n=170)	(n=146)	(n=84)	
Nausea					
1 hour	121 (30.3)	48 (28.2)	50 (34.2)	23 (27.4)	0.415 ^a
4 hours	88 (22.0)	42 (24.7)	31 (21.2)	15 (17.9)	0.446 ^a
8 hours	67 (16.8)	32 (18.8)	27 (18.5)	8 (9.5)	0.136 ^a
12 hours	46 (11.5)	22 (12.9)	13 (8.9)	11 (13.1)	0.467 ^a
24 hours	27 (6.8)	14 (8.2)	7 (4.8)	6 (7.1)	0.472 ^a
Vomiting					
1 hour	50 (12.5)	18 (10.6)	19 (13.0)	13 (15.5)	0.526 ^a
4 hours	49 (12.3)	23 (13.5)	17 (11.6)	9 (10.7)	0.782 ^a
8 hours	25 (6.3)	9 (5.3)	7 (4.8)	9 (10.7)	0.161 ^a
12 hours	15 (3.8)	7 (4.1)	5 (3.4)	3 (3.6)	0.945 ^a
24 hours	9 (2.3)	4 (2.4)	2 (1.4)	3 (3.6)	0.509 ^b
Itchiness					
1 hour	23 (5.8)	11 (6.5)	8 (5.5)	4 (4.8)	0.846 ^a
4 hours	41 (10.3)	20 (11.8)	14 (9.6)	7 (8.3)	0.661 ^a
8 hours	71 (17.8)	24 (14.1)	32 (21.9)	15 (17.9)	0.195 ^a
12 hours	88 (22.0)	40 (23.5)	28 (19.2)	20 (23.8)	0.586 ^a
24 hours	62 (15.5)	23 (13.5)	25 (17.1)	14 (16.7)	0.642 ^a

Data are presented as number (%).

^aPearson chi-squared test; ^bFisher Exact test.

As shown in Figure 2, none of the parturients experienced respiratory depression and desaturation throughout the study period.

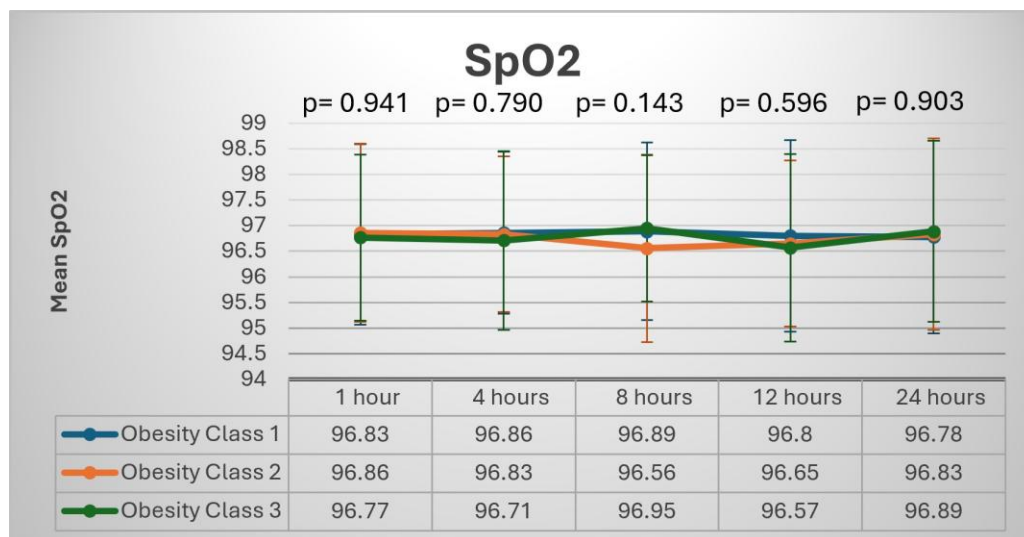


Figure 2 Respiratory profile of parturients after ITM

Figure 3 summarises the efficacy of ITM in pain management with regular post op analgesia. Postoperative pain was minimal in the initial hours, with a median VAS score of 0 at both 1 and 4 hours. The median pain score gradually increased to 3 (IQR: 2-4) by 24 hours. Correspondingly, the number of parturients requiring additional analgesia increased over time, from 2.5% at 1 hour to 35.5% at 24 hours. There were no significant differences in pain scores between the different obesity classes.

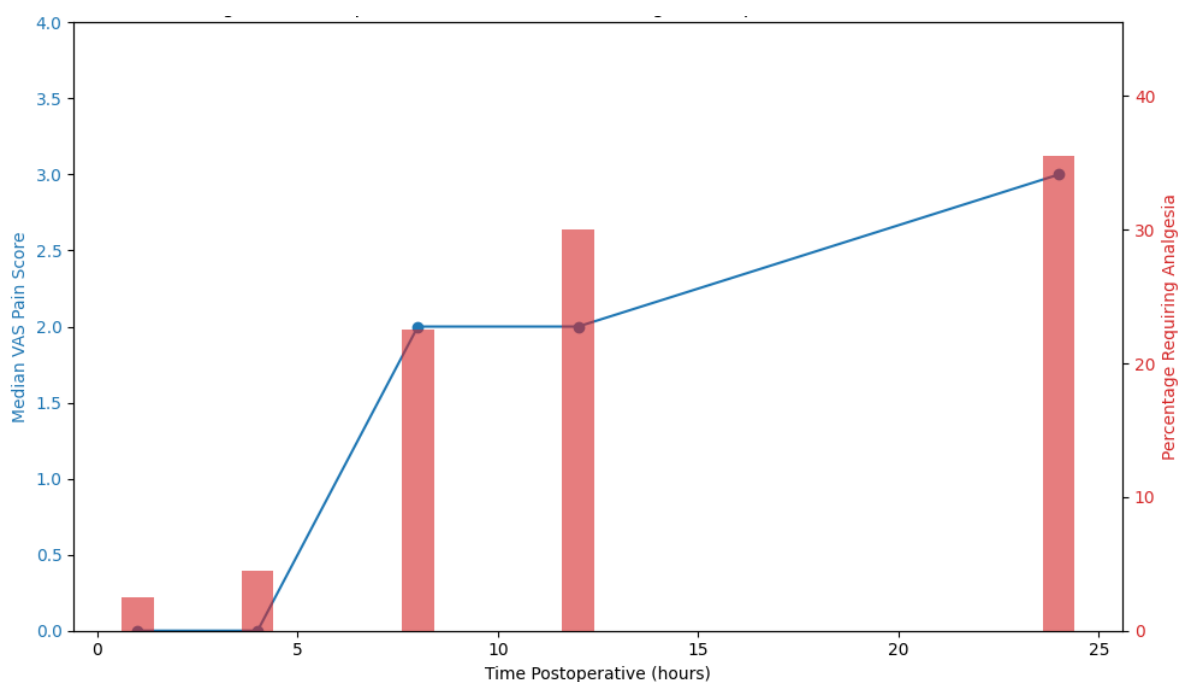


Figure 3 Postoperative pain scores and analgesic requirement over 24 hours

Figure 4 and 5 show the postoperative haemodynamic trend over 24 hours. Both SBP and diastolic blood pressure (DBP) remained stable over the study period maintaining between mean value $\pm$ SD 121-130 mmHg for SBP and 75-81 mmHg for DBP. There were no significant differences in haemodynamic parameters between the different obesity classes.

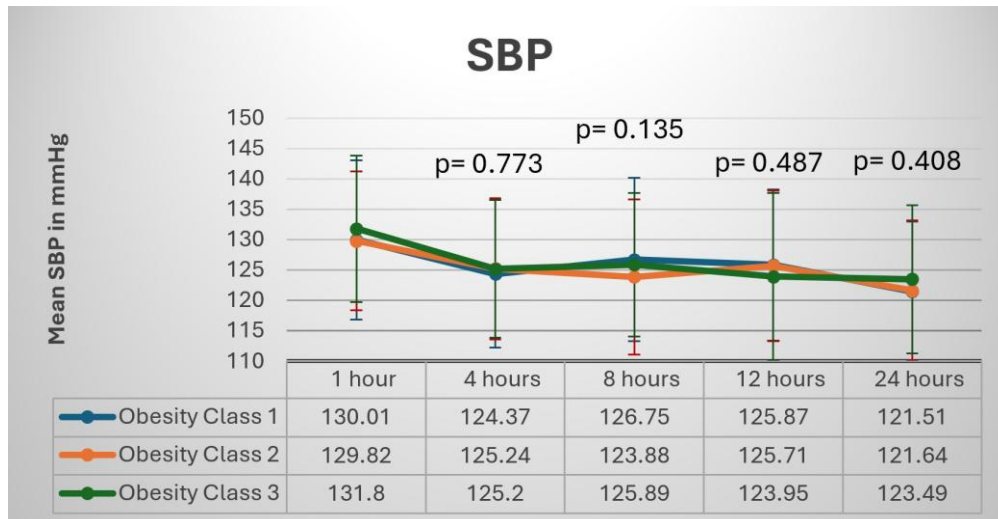


Figure 4 Postoperative SBP trend over 24 hours

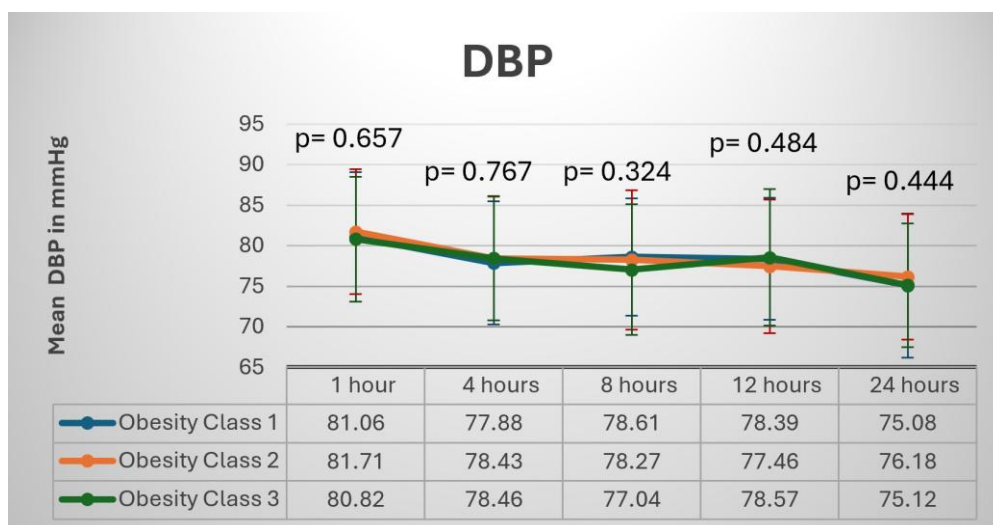


Figure 5 Postoperative DBP trend over 24 hours

As a surrogate of safety profile of the neonate, Apgar score was used. For the neonatal outcome following ITM, no significant difference in mean Apgar scores observed among the obesity classes as shown in figure 6.

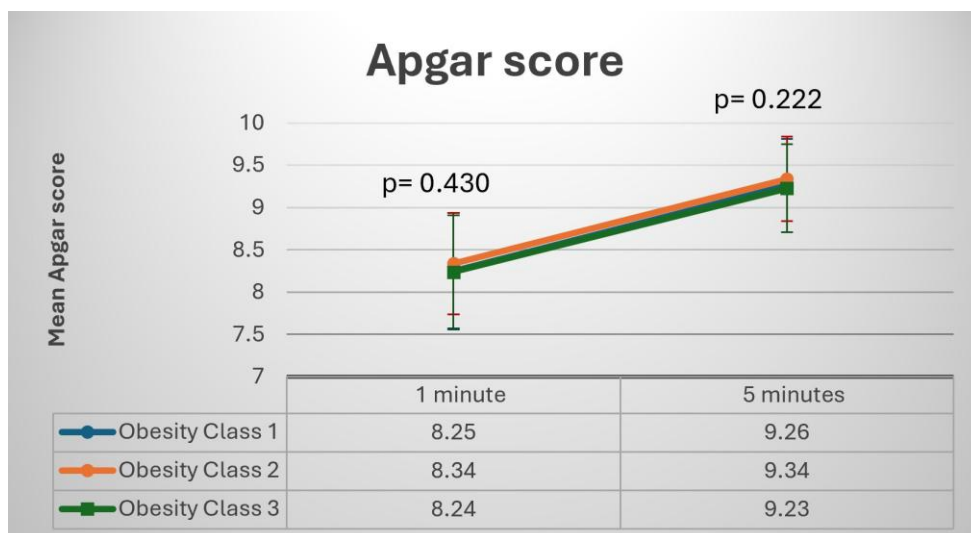


Figure 6 Outcome of neonate following intrathecal morphine

DISCUSSION

This retrospective study, conducted in a Malaysian tertiary hospital, provides valuable insight into the clinical safety and efficacy of a standard 0.1 mg dose of ITM in a large cohort of obese parturients undergoing caesarean section. The findings confirm safety profile of ITM as the study's hypothesis, demonstrating a predictable profile of manageable, non-life-threatening side effects alongside excellent early postoperative analgesia even in morbidly obese parturients. This is particularly significant given the high prevalence of comorbidities such as GDM and PIH in the local obstetric population, which adds a layer of clinical complexity.

The overall incidence of side effects aligns with established literature on ITM. The peak incidence of nausea is consistent with studies reporting rates of approximately 30% [18, 19], while the peak pruritus incidence of 22.0% falls within the lower end of the wide spectrum reported globally [16, 20]. The lower pruritus rate observed in this study compared with rate exceeding 40% in other studies may relate pharmacogenetic variations affecting opioid receptor expression, as previously postulated [35]. The difference of timing in peak of side effects has been reported by several studies [15, 20], which also noted that nausea typically precedes pruritus when low dose of ITM were used. The peak incidence of nausea and vomiting around the first hour postoperatively corresponds with central action of morphine on the chemoreceptor trigger zone once the drug equilibrates across the cerebrospinal fluid-brain barrier [36].

A key finding of this study is the lack of a statistically significant difference in the incidence of side effects across the three classes of obesity. Although not statistically

significant, there were minor numerical trends, such as a slightly higher incidence of vomiting in Class 3 parturients at the 1-hour and 8-hour marks. However, the absence of a clear relationship between increasing BMI and side effect frequency is a reassuring clinical finding. It suggests that for 0.1 mg dose of ITM, the physiological alterations associated with higher degrees of obesity do not appear to substantially increase the risk of common side effects, challenging the clinical fear that often leads to withholding this effective analgesic in parturients with obesity [27, 30].

The context of obesity classification in Asia warrants special consideration. While this study utilised the standard WHO classification ($\text{BMI} \geq 30 \text{ kg/m}^2$), clinical guidelines in Malaysia and across Asia often recommend lower BMI cutoffs for defining obesity ($\geq 27.5 \text{ kg/m}^2$) due to evidence that Asian populations experience obesity-related health risks at a lower BMI [37]. This implies that the entire study cohort, including those in the Class 1 category, represents a population with a significant clinical burden of obesity compared to local standards. The excellent safety profile observed across all classes in our study is therefore highly relevant and generalisable to the broader Malaysian parturient population, providing strong evidence to support the use of ITM in this group.

Importantly, the lack of significant differences in adverse effect incidence across obesity classes contrasts with the physiological expectation that higher BMI predispose patients to hypoventilation and opioid sensitivity. In this large cohort of 400 obese parturients, no respiratory depression was observed throughout the study period. This aligns with large-scale safety data indicating that clinically significant respiratory depression is a rare event with low-dose ITM [21, 24, 25]. Together, these results suggest that obesity per se should not prevent the use of neuraxial morphine when standard dosing and vigilant monitoring are applied.

In term of analgesic efficacy, the observed median VAS scores and rescue analgesia rates are comparable to those reported in other studies. Studies found similar VAS patterns with this dose of ITM, with minimal pain in first six hours and gradual increase after 8 hours [22], consistent with the pharmacological duration of morphine's hydrophilic action. The analgesic efficacy demonstrated was good, with median VAS scores of zero for the first four hours, allowing patients a crucial pain-free window to bond with their newborns [3]. The predictable duration of action, with pain scores gradually increasing after 8 hours, allows for a smooth transition to a multimodal oral analgesic regimen. This emphasizes the reliability of ITM as a key of spinal anaesthesia for caesarean delivery. Furthermore, the absence of haemodynamic instability supports previous observations that ITM at the standard dose provide stable perioperative physiology without compromising maternal safety [34].

Another aspect worth noting is the broader implication for postoperative recovery. Effective analgesia in the immediate postpartum period promotes early mobilisation, facilitates maternal-infant bonding, and reduce thromboembolic risk, which is particularly relevant in obese parturient population [31].

The Apgar scores were favourable, consistent with the established literature as it demonstrates that the low systemic absorption of a 0.1 mg ITM dose results in a low placental transfer and minimal impact on the neonate [38]. The reassuring maternal safety profile found in our study further supports the overall safety of this technique for both mother and baby.

The study is, however, limited by its retrospective nature, which carries an inherent risk of information bias from incomplete or inaccurate charting. Side effects like nausea and pruritus may be under-reported. The absence of a non-ITM control group also means that definitive causal conclusions cannot be drawn. Other confounding factors like STOP-Bang score, which is an important factor for the adverse event, is not included and analysed in this study as the data for this score was inadequate.

CONCLUSION

A standard use of 0.1 mg dose of intrathecal morphine provides effective early postoperative analgesia with no incidence of respiratory depression and manageable non-life threatening side effects, even in parturients with morbid obesity.

CLINICAL TRIAL REGISTRATION

Clinial trial number not applicable

Abbreviations

ASA- American Society of Anesthesiologists

BMI- body mass index

DBP- diastolic blood pressure

SBP- systolic blood pressure

ITM- intrathecal morphine

HR- heart rate

IQR- interquartile range

LSCS- lower segment caesarean section

VAS- visual analogue scale

GDM- gestational diabetes

PIH- pregnancy induced hypertension

HCTM- Hospital Canselor Tuanku Muhriz

SPSS- statistical package for social science

UKM- Universiti Kebangsaan Malaysia

Declarations

Ethics approval and consent to participate

This study was granted ethical approvals by the Research Ethics Committee of UKM (Ref No. JEP-2024-128) and the MREC, Ministry of Health, Malaysia (NMRR-24-02526-FDN). The study complied with the Declaration of Helsinki. Patient consent was waived by the institutional ethics committee due to the retrospective nature of this study, which utilised anonymised patient data extracted from the institutional Health Information Department without any direct patient intervention.

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AUTHORS CONTRIBUTIONS

Conception, design, data collection, data assembly, and drafting of the manuscript: Mohd Hamdi Che Yusoff and Azlina Masdar. Critical revision of the manuscript: Azlina Masdar, Mohd Hamdi Che Yusoff, Izzuddin Azaharuddin, Nadia Md Nor, Wan Rahiza Wan Mat, Iskandar Khalid, Mohd Khazrul Nizar Abd Kadir. All authors have read and approved the final version of the manuscript.

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DATA AVAILABILITY STATEMENT

The raw data supporting this article will be made available by the authors upon request, without undue reservation.

COMPETING INTERESTS

The authors declare no competing interests with respect to the authorship of this article.

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