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COMPARATIVE ANALYSIS OF ANALGESIC ONSET AND DURATION: BUPIVACAINE WITH FENTANYL VS. BUPIVACAINE WITH MEPERIDINE IN SPINAL ANESTHESIA FOR CESAREAN SECTION

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ABSTRACT

This study aimed to compare the onset and duration of analgesia in spinal anesthesia for cesarean section using hyperbaric bupivacaine combined with fentanyl or with meperidine. A double-blind randomized controlled trial was conducted involving sixty patients undergoing either elective or emergency cesarean section at Jejaring Hospital and H. Adam Malik General Hospital Medan. Patients were randomly assigned to receive hyperbaric bupivacaine with fentanyl or hyperbaric bupivacaine with meperidine, and the data were analyzed using appropriate statistical methods to examine differences between the groups. The findings revealed that the combination of bupivacaine with fentanyl produced a faster onset of analgesia compared to bupivacaine with meperidine, whereas the combination with meperidine provided a longer duration of analgesia. Both combinations were effective in achieving intraoperative and postoperative pain control, each offering distinct advantages. The study concludes that the choice of spinal anesthesia combination can be tailored to the clinical needs of patients, with fentanyl being preferable for rapid onset and meperidine offering prolonged analgesia..

ABSTRAK

Penelitian ini bertujuan membandingkan onset dan durasi analgesia pada anestesi spinal untuk persalinan sesar menggunakan kombinasi bupivakain hiperbarik dengan fentanil atau dengan meperidin. Desain penelitian yang digunakan adalah uji acak terkontrol buta ganda pada enam puluh pasien yang menjalani operasi sesar elektif

maupun darurat di Rumah Sakit Jejaring dan Rumah Sakit Umum H. Adam Malik Medan. Pasien secara acak menerima bupivakain hiperbarik dengan fentanil atau bupivakain hiperbarik dengan meperidin. Data kemudian dianalisis dengan uji statistik yang sesuai untuk menilai perbedaan kedua kelompok. Hasil penelitian menunjukkan bahwa kombinasi bupivakain dengan fentanil memberikan onset analgesia yang lebih cepat dibandingkan kombinasi bupivakain dengan meperidin, sedangkan kombinasi dengan meperidin menghasilkan durasi analgesia yang lebih panjang. Kedua kombinasi terbukti efektif memberikan analgesia intraoperatif dan pascaoperatif dengan kelebihan masing-masing. Simpulan dari penelitian ini adalah pemilihan kombinasi anestesi spinal dapat disesuaikan dengan kebutuhan klinis pasien, di mana fentanil lebih tepat digunakan untuk efek cepat, sementara meperidin lebih unggul dalam memberikan analgesia yang berkepanjangan.

INTRODUCTION

When selecting anaesthesia techniques for caesarean sections, anaesthetists prioritise methods that are both safe and comfortable. The use of regional anaesthesia in caesarean sections has significantly increased over the past 30 years. According to data from the United Kingdom, between 1979 and 1990, 94.9% of elective and 86.7% of emergency caesarean sections were performed using regional anaesthesia. By 2002, the proportion of elective caesarean sections under regional anaesthesia had risen from an average of 69.4% in 1992 to 94.9%, with subarachnoid (spinal) anaesthesia being employed in 86.6% of these cases. A retrospective analysis by Joy L. Hawkins et al (2019) revealed that the use of general anaesthesia decreased from 35% in 1981 to 12% in 1992. Similarly, Tsen et al (1998) documented a reduction in the use of general anaesthesia from 7.2% in 1990 to 3.6% in 1995. Initially, lidocaine, a local anaesthetic with a rapid onset and short duration of action (60–75 minutes), was widely used. However, lidocaine has been largely phased out due to its higher risk of transient neurologic symptoms (TNS), prompting clinicians to seek better alternatives.

Currently, hyperbaric bupivacaine is more commonly used intrathecally for caesarean sections, as it not only provides a high-quality blockade but is also well-suited for the typical duration of the surgery, spreading cephalad to achieve the desired analgesia. In a study by Chung et al (2001), an 80% incidence of hypotension was reported with the use of 12 mg of 0.5% hyperbaric bupivacaine. Similarly, Siddik-Sayyid et al (2002) found that 87% of patients experienced hypotension with 12 mg of 0.75% hyperbaric bupivacaine. Bryson et al (2007) reported hypotension in about 70% of patients. However, studies by Bogra et al (2005) showed lower rates of hypotension (50%, 46%, and 20%) with the use of 12.5 mg of 0.5% hyperbaric bupivacaine.

Spinal anaesthesia using only a local anaesthetic is often insufficient for prolonging blockade duration, and high doses may cause significant hypotension and increased risk of systemic toxicity. Therefore, intrathecal opioids are often used in combination with local

anaesthetics to enhance the effectiveness and extend the duration of spinal anaesthesia. Research by Ginosar et al (2004) suggests that a modest dose of hyperbaric bupivacaine (6–12 mg) can be safely combined with opioids. Intrathecal opioids synergise with local anaesthetics, intensifying sensory block without increasing sympathetic block, allowing effective anaesthesia even with lower doses of local anaesthetic. Animal studies also show that intrathecal opioids enhance visceral and somatic pain relief when combined with local anaesthetics. One commonly used lipophilic opioid is fentanyl.

Hunt, C.O et al (1989) conducted the first trial to examine the effects of adding varying doses of intrathecal fentanyl (6.25–50 mcg) to hyperbaric bupivacaine during caesarean sections. A dose of 6.25 mcg of intrathecal fentanyl improved perioperative analgesia without affecting the development of sensory and motor blocks. According to Belzarena (1992), small doses of fentanyl (0.25 mcg/kg) provide effective intraoperative analgesia, brief postoperative relief, and minimal side effects. However, increasing the dose of fentanyl (0.5–0.7 mcg/kg) can prolong postoperative analgesia but may affect respiratory patterns. Research by Bintarto, A., & Pryambodho (2010) in Indonesia demonstrated that a combination of 7.5 mg of 0.5% hyperbaric bupivacaine with 25 mcg of fentanyl was more effective for spinal anaesthesia in caesarean sections than 12.5 mg of 0.5% hyperbaric bupivacaine alone. Meperidine, also known as pethidine, is another opioid that can be used in spinal anaesthesia in addition to fentanyl. Meperidine's longer half-life, effective postoperative analgesia, and cost-effectiveness make it a popular choice. Kafle (1993) in Nepal compared the intrathecal administration of 5% meperidine (1 mg/kg BW) with 5% heavy lidocaine. The meperidine group experienced an average of six hours of postoperative analgesia, compared to just one hour in the lidocaine group.

A 1999 study by Cheun & Kim (1999) in Korea demonstrated that meperidine, when used alone intrathecally, provided stable haemodynamics, long-lasting analgesia (453.7 ± 158.1 minutes), and quick motor recovery (75.9 ± 17.2 minutes) during caesarean sections. A 2002 trial in China by Yu et al (2002) compared the effects of intrathecal meperidine (10 mg) with 0.5% hyperbaric bupivacaine (10 mg) and a control group receiving 0.5% hyperbaric bupivacaine with normal saline. The meperidine group had a longer duration of postoperative analgesia (234 minutes) compared to the saline group (125 minutes). Research in Turkey by (Atalay et al., 2010), found that combining 5 mg of plain bupivacaine with 25 mg of meperidine achieved a sensory block up to the T4 level within 7.0 ± 1.7 minutes, with an analgesic duration of 295.0 ± 23.0 minutes. This combination provided stable haemodynamics, minimal side effects, and improved patient comfort without compromising the quality of anaesthesia. Due to the limited availability and higher cost of fentanyl in peripheral areas, researchers became interested in comparing the effects of a more affordable opioid, meperidine. This research aims to compare the analgesic duration and onset of action between meperidine and fentanyl when combined with 7.5 mg of 0.5% hyperbaric bupivacaine in spinal anaesthesia for caesarean sections.

METHODS

This work is a double-blind, randomised clinical trial that is experimental in nature and aims to compare the duration and onset of analgesia between two groups: 7.5 mg of 0.5% hyperbaric Bupivacaine plus 25 mcg of intrathecal Fentanyl, and 7.5 mg of 0.5%

hyperbaric Bupivacaine plus 25 mg of Meperidine. The independent variables are Fentanyl (25 mcg) and Meperidine (25 mg), while the dependent variables are the onset of action and duration of analgesia.

The study population includes all patients undergoing elective and emergency caesarean sections with subarachnoid regional anaesthesia, requiring a sample size of at least 60 participants. The study's inclusion criteria are as follows: patients with a history of allergies to bupivacaine, fentanyl, or meperidine; contraindications for spinal anaesthesia; or undergoing MAO inhibitor therapy; dropout (emergencies such as shock, anaphylactic reactions, respiratory disorders, or failure of the subarachnoid block); and pregnant women aged 20–40 years who meet the ASA physical status I–II and who have signed informed consent. Using the Statistical Package for Social Sciences (SPSS), data were gathered, checked for completeness, and processed. Categorical data were reported as numbers and percentages, while numerical data were presented as means ± standard deviations. The Kolmogorov-Smirnov test was used to determine if numerical data were normal. With a significance threshold of $p < 0.05$, the independent t-test was used for normally distributed data, and the Mann-Whitney test for non-normally distributed data in the hypothesis testing process.

This section, in the drafting of a manuscript, is the easiest part, and is usually the first part to be written in a draft of a manuscript. If using a schema or image, you can see in the following example.

In general, the elements in the Method section are the design and design of the experiment, place and time, samples and sampling techniques, materials and tools (for experimental research), variables tested, methods of data collection and processing, statistical models, research work procedures (for experimental research), and research ethics (Levitt et al., 2018).

RESULTS AND DISCUSSION

Table 1. General Characteristic based on Age, Weight, Height, BMI, Cases Emergency/Elective, PS ASA Length of Operation, Tribe And Education Level

Table 1 General characteristics based on Age, Weight, Height, BMI, CasesEmergency/Elective, PS ASA, Length of Operation, Tribe and Education Level

Variables	Group A Bupivacaine 0.5% 7.5 mg + Fentanyl 25 mcg (n=30)	Group B Bupivacaine 0.5% 7.5 mg + Pethidine 25 mg (n=30)	*p*
Age, mean (SD), years	30.23 (5.43)	30.03 (5.62)	0.889a
Variables	**Group A Bupivacaine 0.5% 7.5 mg + Fentanyl 25 mcg (n=30)**	**Group B Bupivacaine 0.5% 7.5 mg + Pethidine 25 mg (n=30)**	***p***
Body Weight, average (SB), kg	64.03 (3.99)	63.1 (3.79)	0.272b
BMI, mean (SB), kg/m2	25.2 (1.2)	24.53 (1.48)	0.059a
Type of Operation, n (%)			
Emergency	21 (70)	14 (46.7)	0.067c
Elective	9 (30)	16 (53.3)	
PS ASA, n (%)			
1	23 (76.7)	18 (60)	0.165c
2	7 (23.4)	12 (40)	
Operating Time, mean (SB), minutes	78.73 (26.99)	70.57 (24.57)	0.225a
Ethnic group			
Aceh	2 (6,7)	3 (10)	
Batak	14 (46.7)	12 (40)	
Java	9 (30)	11 (36.7)	1,000c
Field	3 (10)	2 (6,7)	
Malay	1 (3,3)	2 (6,7)	
Chinese	1(3,3)	0	
Level of education			
JUNIOR HIGH SCHOOL	2 (6,7)	2 (6,7)	1,000c
SENIOR HIGH SCHOOL	18 (60)	18 (60)	
Bachelor	10 (33.3)	10 (33.3)	

The general characteristics of the study sample are presented in Table 1 above. A comparative analysis of the two study groups revealed no significant differences in several demographic and clinical parameters, with p-values exceeding 0.05. Specifically, the characteristics assessed included age, height, weight, and body mass index (BMI). These findings suggest that both groups were comparable in terms of their baseline physical attributes.

In addition to demographic factors, other relevant variables such as the type and duration of surgery, ASA physical status (PS), ethnicity, and educational attainment were also examined. The absence of significant differences in these areas further supports the conclusion that the two study groups were well-matched, minimizing potential confounding factors that could affect the outcomes of the study. This uniformity in the sample characteristics enhances the reliability of the study findings.

Table 2. Characteristic of Vas Values Pre and Post Operation

Table 2	Characteristics of VAS values Pre and Post Operation		
Variables	Group A Bupivacaine 0.5% 7.5 mg + Fentanyl 25 mcg (n=30)	Group B Bupivacaine 0.5% 7.5 mg + Pethidine 25 mg (n=30)	*p*
Preoperative, n (%)			
0	7 (23.3)	2 (6,7)	0.134a
1	7 (23.3)	4 (13.3)	
2	2 (6,7)	4 (13.3)	
3	4 (13.3)	4 (13.3)	
4	6 (20)	3 (10)	
5	1 (3,3)	5 (16.7)	
6	2 (6,7)	8 (26.7)	
7	1 (3,3)	0	
During Operation, n (%)			
1	24 (80)	27 (90)	0.472b
2	6 (20)	3 (10)	

The findings from the pre-operative Visual Analog Scale (VAS) evaluations revealed no statistically significant changes in pain perception between the two groups, with a pre-operative p-value of 0.134 and a post-operative p-value of 0.472, both exceeding the threshold of 0.05. This lack of significance suggests that there were no meaningful differences in pain levels reported by participants in Groups A and B prior to and following the surgical procedures. In Group A, the pre-operative VAS measurements indicated that 7 participants (23.3%) reported scores of either 0 or 1, signifying minimal pain levels. In contrast, Group B exhibited a higher incidence of pain scores, with 8 participants (26.7%) reporting a pre-operative VAS score of 6, which indicates a notable degree of discomfort prior to surgery.

Following the surgical intervention, the post-operative VAS assessments demonstrated a predominance of lower pain scores across both groups. Specifically, a significant majority of 24 participants (80%) in Group A reported a post-operative VAS score of 1, reflecting a low level of pain. Similarly, 27 participants (90%) in Group B reported the same post-operative VAS score of 1, illustrating that both groups experienced minimal pain following the procedure. The remaining participants in each group recorded a slightly higher score of 2. These results underscore the effectiveness of the analgesic protocols implemented in both groups, as the majority of participants experienced minimal pain after surgery. This outcome emphasizes the importance of effective pain management strategies

in enhancing patient comfort and satisfaction in the post-operative setting.

Table 3. Characteristic of Drug Onset and Duration of Analgesia

Table 3 Characteristics of Drug Onset and Duration of Analgesia

Variables	Group A Bupivacaine 0.5% 7.5 mg + Fentanyl 25 mcg (n=30)	Group B Bupivacaine 0.5% 7.5mg + Pethidine 25 mg (n=30)	p
Start Working, mean (SD), seconds	169.17 (51.09)	246 (70.64)	0.0001a
Duration of Analgesia, mean (SD), seconds	113 (19.1)	170.9 (37.98)	0.0001a

A significant difference was identified in both the mean duration of analgesia and the onset of medication action between patients administered 25 mg of pethidine and those receiving 25 mcg of fentanyl. This difference was confirmed using the Mann-Whitney test, yielding p-values of 0.0001, which is below the 0.05 significance threshold (see Table 4-3). Specifically, the onset of action for fentanyl was notably faster, with a mean time of 169.17 seconds, compared to 246 seconds for pethidine. This rapid onset suggests that fentanyl may provide quicker relief of pain in clinical settings where immediate analgesia is required.

Conversely, when assessing the duration of analgesia, pethidine demonstrated a significantly longer effect than fentanyl. The mean duration of analgesia for pethidine was recorded at 170.9 seconds (SD = 37.98 seconds), whereas the analgesic effect of fentanyl lasted only 113 seconds (SD = 19.1 seconds). These findings indicate that while fentanyl acts more rapidly, pethidine provides prolonged analgesia, highlighting the importance of selecting the appropriate analgesic based on the clinical requirements for pain management.

Table 4. Correlation Spearman BMI with Onset of Drug Action in The Group Receiving Bupivacaine 0.5% 7.5 Mg + Fentanyl 25 mcg

Table 4 CorrelationSpearman BMI with Onset of Drug Action in the group receiving Bupivacaine 0.5% 7.5 mg + Fentanyl 25 mcg

Variables	p	R
BMI	0.384	0.165

Table 5 Pearson Correlation of BMI with Drug Onset in the Groupwho received Bupivacaine 0.5% 7.5 mg + pethidine 25 mg

Variables	p	R
BMI	0.868	0.032

Table 6 Pearson Correlation of BMI with Drug Onset in all respondents

Variables	p	R
BMI	0.624	-0.065

The analysis conducted in this study assessed the correlation between body mass index (BMI) and the onset of drug action in respondents treated with fentanyl and pethidine. For those treated with fentanyl, the results showed no significant correlation, evidenced by a p-value of 0.384. This value is well above the commonly accepted threshold of 0.05, indicating a lack of statistical significance and suggesting that variations in BMI do not have a substantial influence on the onset of analgesic action for fentanyl.

Similarly, the group receiving pethidine also demonstrated no significant association between BMI and the onset of action. The p-value for this group was reported at 0.868, again exceeding the 0.05 threshold. This further reinforces the conclusion that BMI does not play a role in determining how quickly pethidine exerts its analgesic effects.

When both treatment groups were analyzed together, the overall correlation between BMI and the onset of drug effects yielded a combined p-value of 0.624. Collectively, these findings indicate that variations in BMI do not appear to have a meaningful impact on the speed at which fentanyl or pethidine provide analgesic relief in the studied populations. These results may have implications for clinical practices regarding pain management strategies, suggesting that BMI should not be a determining factor in the choice or expectation of analgesic onset for these medications.

Table 5. Correlation length of surgery and duration of analgesia in The Group Receiving 0.5% Bupivacaine 7.5 mg + 25 mcg Fentanyl

Table 7 CorrelationSpearman Length of surgery and duration of analgesia in the group receiving 0.5% Bupivacaine 7.5 mg + 25 mcg Fentanyl

Variables	p	R
Operation Time	0.962	0.009

Table 8 Pearson Correlation Length of operation and durationanalgesia in the group receiving 0.5% Bupivacaine 7.5 mg + 25 mg pethidine

Variables	p	R
Operation Time	0.559	0.111

Table 9 Pearson Correlation Length of operation and durationanalgesia in all respondents

Variables	p	R
Operation Time	0.673	-0.056

In the group of respondents who received fentanyl, the analysis indicated no statistically significant relationship between the duration of analgesia and the length of the operation, as evidenced by a p-value of 0.962. This lack of significance suggests that the length of the surgical procedure does not influence the duration of pain relief provided by fentanyl. Similarly, among the participants administered pethidine, no significant association was observed, with a p-value of 0.559. This further reinforces the finding that the duration of analgesia with pethidine is independent of the length of the operation. When evaluating the data across both treatment groups, the overall correlation between the duration of analgesia and the length of the operation was also found to be non-significant, resulting in a p-value of 0.673. These results collectively indicate that the length of surgical procedures does not significantly affect the effectiveness or duration of analgesia provided by either fentanyl or pethidine in the studied sample.

The characteristics of the patients, including age, weight, height, Body Mass Index (BMI), ASA physical status, and duration of surgery, showed no statistically significant differences between the two groups, indicating homogeneity. Similarly, the characteristics of ethnicity and education level did not reveal significant statistical differences. Regarding hemodynamic monitoring, preoperative assessments demonstrated homogeneity in systolic and diastolic blood pressure, mean arterial pressure (MAP), heart rate, and respiratory rate between the two groups, with no significant differences observed. However, following spinal anesthesia administration, Group A exhibited a drastic decrease in blood pressure, while

Group B experienced a sharp decline. This response was attributed to sympathetic blockade caused by spinal anesthesia, leading to vasodilation and a reduction in vasomotor tone. Despite these hemodynamic changes, stability in systolic and diastolic blood pressure, MAP, heart rate, and respiratory rate was maintained at 60, 90, and 120 minutes after anesthesia, indicating that the addition of intrathecal opioids can help preserve hemodynamic stability during surgery.

The Visual Analog Scale (VAS) assessment results indicated no significant differences between the two groups, both preoperatively and postoperatively. The onset of local anesthesia combined with Fentanyl was quicker than that combined with Meperidine, with average onset times of 169.17 seconds and 246 seconds, respectively. This study highlights that Fentanyl, due to its higher lipid solubility, provides a faster onset of action as it can penetrate nerve membranes more efficiently than Meperidine. In terms of analgesia duration, Meperidine demonstrated a longer duration of analgesia (170.9 minutes) compared to Fentanyl (113 minutes), influenced by absorption rates and protein binding, as Meperidine binds less to proteins than Fentanyl, allowing it to circulate more freely and persist longer in the system. The findings of this study suggest that the combination of 0.5% hyperbaric Bupivacaine with Fentanyl offers a quicker onset, while the addition of Meperidine results in prolonged analgesia. These results support the use of intrathecal opioid combinations to enhance analgesia quality during and after cesarean surgical procedures. Moreover, the hemodynamic assessments underline the importance of close monitoring post-spinal anesthesia to manage side effects such as hypotension and nausea.

CONCLUSION

Based on the research findings, several conclusions can be made:

1. In caesarean sections using subarachnoid regional anaesthesia, the addition of 25 mcg of Fentanyl to 7.5 mg of 0.5% hyperbaric Bupivacaine results in a quicker onset of action compared to adding 25 mg of Meperidine to the same dose of Bupivacaine. This difference is statistically significant ($p<0.05$).
2. The duration of analgesia is longer when 25 mg of Meperidine is added to 7.5 mg of 0.5% hyperbaric Bupivacaine than when 25 mcg of Fentanyl is added. This difference is also statistically significant ($p<0.05$).
3. Although the difference is not statistically significant ($p>0.05$), both combinations—7.5 mg of 0.5% Bupivacaine with 25 mcg of Fentanyl and 7.5 mg of 0.5% Bupivacaine with 25 mg of Meperidine—may still lead to hypotension during caesarean sections under subarachnoid regional anaesthesia.
4. Vomiting and nausea are common adverse effects in both anaesthetic approaches, but there is no statistically significant difference between the two ($p>0.05$).
5. A slightly higher incidence of pruritus is observed with the combination of 7.5 mg of 0.5% Bupivacaine and 25 mg of Meperidine compared to 25 mcg of Fentanyl, although this difference is not statistically significant ($p>0.05$).

Neither 7.5 mg of 0.5% Bupivacaine with 25 mcg of Fentanyl nor 7.5 mg of 0.5% Bupivacaine with 25 mg of Meperidine caused respiratory depression during caesarean sections.

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