COMPARATIVE STUDY BETWEEN INTRATHECAL FENTANYL AND MIDAZOLAM AS ADJUVANT TO LOCAL ANESTHETICS IN SPINAL ANESTHESIA IN ELECTIVE CESEAREAN SECTION IN POST-OPERATIVE ANESTHESIA AND POST-OPERATIVE ANALGESIA

Ahmed Ali Fawaz, Tamer Youssef Elie, Wael Abd Elmoneim Mohamed Abdelwahab and Abdelrahman Ali Ali Gad Mattar

Anesthesia, Intensive Care and Pain Management Department, Faculty of Medicine, Ain Shams University

Corresponding:

Abdelrahman Ali Ali Gad Mattar
Mobile: (+2) 01093736019
Email:
dr_bedo_mattar@yahoo.com

ABSTRACT:

Background: Subarachnoid block achieved a wide spread popularity as a simple and effective method of anesthesia for elective cesarean sections. Among the local anesthetics, bupivacaine is the most commonly used drug for subarachnoid block.

Aim of the Work: This study was conducted to evaluate and compare the effects of intrathecal midazolam and fentanyl as additives to intrathecal hyperbaric bupivacaine with regards to onset and duration of sensory block, duration of complete and effective analgesia and side effects associated with the drug.

Patients and Methods: This study included 90 women aged between 18-35 years scheduled to undergo elective cesarean section under spinal anesthesia. Patients were subdivided randomly into 3 groups (30 patients each) on the basis of the adjuvant added to the anesthetic used; group A (Fentanyl + bupivacaine), group B (Midazolam + bupivacaine) and group C (Bupivacaine).

Results: Demographic data did not differ between the three study groups (p > 0.05). Group A showed a significantly earlier onset of sensory block (p =0.005), motor block (p = 0.009), as well as late regression to L1 sensory level (p <0.001). Additionally, longer analgesia (p < 0.05) and longer time before the first call for analgesics (p = 0.005) was associated with group A. The required dose of paracetamol and pethidine within the first day were significantly lower in group A and group B in comparison to group C. However, complications encountered did not differ between the three study groups (p > 0.05). Also, the state of the neonates didn't show significant difference between the three groups.

Conclusion: Intrathecal adjuvants are associated with improving out comes after CS as revealed by delayed onset and longer duration of sensory and motor block in addition to longer duration of complete and effective analgesia. Intrathecal fentanyl revealed better outcomes in terms of delayed onset and longer duration of sensory and motor block in addition to longer duration of complete and effective analgesia as compared with midazolam.

Keywords: Intrathecal Fentanyl, Midazolam, Local Anesthetics, Spinal Anesthesia, Elective Cesearean Section, Post-Operative Anesthesia, Post-Operative Analgesia.

INTRODUCTION:

Spinal or intrathecal anesthesia has a long history of success and more popular, mostly because of an increasing number of ambulatory procedures and interventions, for which the ideal spinal anesthetic would provide rapid and adequate surgical anesthesia together with early ambulation and early discharge[1].

More studies on bupivacaine have shown that it produces predictable and reliable spinal anesthesia for surgery[2].

Various intrathecal adjuvants to local anesthetics are used. When local anesthetics are combined with opioids, the duration of analgesia is prolonged[3].

Fentanyl, a short-acting lipophilic opioid, is known to augment the quality of subarachnoid block. It was also shown that the addition of fentanyl to hyperbaric ropivacaine increased the intraoperative quality of spinal anesthesia in patients undergoing anorectal surgery, cesarean section, and transurethral resection of the prostate[4].

However, worrisome adverse effects such as pruritus, urinary retention, postoperative vomiting, and respiratory depression limit the use of opioids[5].

Midazolam is a benzodiazepine with unique properties when compared with other benzodiazepines[6].

It is water soluble in its acid formulation but is highly lipid soluble *in vivo*. It has been reported to have a spinally mediated antinociceptive effect. Previous studies have shown that intrathecal administration of midazolam added to bupivacaine improves the duration and quality of spinal anesthesia[2].

AIM OF THE WORK:

This study is undertaken to evaluate and compare the effects of intrathecal midazolam (2 mg) and fentanyl (25 micrograms) as additives to intrathecal hyperbaric bupivacaine (0.5 %) with regards to: onset and duration of sensory block, duration of complete and effective analgesia, side effects associated with the drug.

PATIENTS AND METHODS:

- **Type of Study:** Prospective randomized double-blind study.
- **Study Setting:** Ain Shams University Hospital, Cairo, Egypt.
- **Study Period:** From July 2019 to January 2020.
- **Study Population:**

The study included 90 patients scheduled for elective CS under SA and fulfilling all the inclusion criteria were enrolled in the study and randomly allocated into three equal groups of 30 each.

Patienst Method: patients were subdivided randomly into 3 groups (30 patients each) on the basis of the adjuvant added to the local anesthetic used.

1. Group (A): 2 ml of hyperbaric bupivacaine 0.5% + 0.25 ml of fentanyl (12.5 µg) + 0.25 ml normal saline.
2. Group (B): 2 ml of hyperbaric bupivacaine 0.5% + 0.4 ml of midazolam (2mg) + 0.1 ml of normal saline.
3. Group (C): 2 ml of hyperbaric bupivacaine 0.5% + 0.5 ml of normal saline.

Selection criteria for cases:

Inclusion Criteria:

1. ASA physical status I and ASA II
2. Age from 18-35 years
3. Scheduled to undergo elective cesarean section under spinal anesthesia.

Exclusion Criteria:

1. ASA III or IV patients.
2. Patients refuse spinal anesthesia.
3. Patients physically dependent on narcotics or benzodiazepine.

4. Patients with history of drug allergy to fentanyl and midazolam
5. Patients with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis or neurological involvement/ diseases and any contraindication for spine.
6. Head injury cases.
7. Patients with cardiac, pulmonary, hepatic or renal disorders.
8. Patients with peripheral neuropathy.
9. Patients having inadequate subarachnoid blockade and who are later supplemented by general anesthesia.
10. Chronic pain at puncture site.
11. Patients who are unable to communicate.

Patients Consent:

A written informed consent was obtained from all participants before inclusion in the study, explaining the value of the study, plus the procedures details.

Ethical consideration:

The whole study design was approved by the Institutional review board, Faculty of Medicine, Ain -Shams University. Confidentiality and personal privacy will be respected in all levels of the study. Patients feel free to withdraw from the study at any time without any consequences. Collected data will not be used for any other purpose.

Patients:

In the operating room, a wide bore peripheral intravenous access was secured with 18G cannula. On arrival to the operating room, routine monitoring devices were attached and baseline blood pressure, ECG and pulse oximetry values were recorded. All patients were preloaded with Ringer's lactate solution at 15 ml/kg before SA. Dural puncture was performed at L3–L4 interspace with a 25G spinal needle in the left lateral decubitus position by an anesthesiologist who was not involved in the patient care.

The patients were randomly allocated into three groups to receive one of the medications intrathecally. The study solutions were constituted as mentioned before. Midazolam used as adjuvant to spinal anesthesia is available in our country in 5 mg/ml concentrations. In this study, we used 5 mg/ml concentration. Fentanyl is available as 50 µg/ml. After injection of the study solution, the patients were turned to the supine position with a 15 degree wedge under the right hip for left uterine displacement. Oxygen (3 L/min) was administered via facemask. Cardiorespiratory parameters, e.g. oxygen saturation, respiratory rate, non-invasive blood pressure and ECG were monitored.

Outcome measures:

VAS score was the primary outcome and it was measured at different time points (1h, 2h, 4h, 6h, 8h, 12h, 18h, and 24 hours postoperatively). The secondary outcome included the effect of these adjuvants on sensory and motor blockade. If the postoperative VAS was higher than 3, it was treated by analgesics such as pethidine.

Complications:

Hypotension was defined as a mean arterial blood pressure (MAP) < 60 mmHg, and it was managed by bolus doses of ephedrine 5 mg and fluids. Bradycardia was defined as heart rate (HR) < 60 b/min, and it was managed by atropine 0.5 mg increments. Vomiting was treated with metoclopramide 10 mg or granisetron 1 mg if persistent.

Statistical Methods:

Results were statistically analyzed by using statistical package of social sciences (SPSS 22.0, IBM/SPSS Inc., Chicago, IL) Two types of statistical analysis were conducted. In all applied tests, the *P*-values associated with test statistics indicated the significance level at which the null-hypothesis (the hypothesis of no difference) was rejected and it was set at 0.05 so that a *P*-values $\geq$ 0.05 are statistically non-significant, *P*-values < 0.05 are significant, and *P*-values < 0.01 are highly significant.

RESULTS:

Table 1: General characteristics of cases in the studied groups:

Variable	Group A (Fentanyl+ bupivacaine) (n= 30)	Group B (Midazolam+ bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	p-value
Age	27.24 ± 2.693	26.76 ± 2.457	27.55 ± 2.647	0.251
BMI	24.26 ± 3.71	25.83 ± 3.24	25.36 ± 3.31	0.354
ASA score				
1	27 (90%)	25 (83.3%)	25 (83.3%)	0.942
2	3 (10%)	5 (16.7%)	5 (16.7%)	

Continuous data expressed as mean±SD. Categorical data expressed as Number (%)
*: p is significant when <0.05

The demographic criteria of the pregnant females. There was no statistically significant difference in the mean age or the mean BMI among the cases of the three groups (p= 0.251 and 0.354). Most of the cases within the three groups were classified as ASA 1 score (90%, 83.3% and 83.3% in group A, B and C respectively) with no significant difference between the three groups (p=0.942).

Table 2: Sensory block characteristics

	Group A (Fentanyl + bupivacaine) (n= 30)	Group B (Midazolam + bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	*P value*
Mean onset time of sensory blockade at T10 (min)	4.52±0.9	6.86±0.6	8.45±1.3	0.005*
Maximum sensory level achieved	T5	T6	T6	0.824
Time to achieve maximum sensory level (min)	9.95±0.6	12.91±0.9	15.25±2.03	0.001*
Mean time to regression to L1 dermatome (min)	302.44±39.2	215.9±41.5	196.9±33.2	<0.001*

Continuous data expressed as mean±SD. Categorical data expressed as Number (%)
*: p is significant when < 0.05

Group A experienced earlier time of onset regarding sensory blockade at T 10 level (p = 0.005). Moreover, time needed to reach the maximum sensory level was significantly shorter in the same group (p 0.001). Nevertheless, the maximum sensory level achieved did not differ significantly between the three groups. Group A experienced a significantly longer time for regression of sensory block down to L1 dermatome (p < 0.001).

Table 3: Motor block characteristics.

	Group A (Fentanyl+ bupivacaine) (n= 30)	Group B (Midazolam+ bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	*P value*
Mean onset time of motor block (min)	9.35±0.7	12.04±1.96	13.09±2.84	0.009*
Maximum Bromage scale	3	3	3	1
Total duration of motor block (min)	229.2±35.4	181.3±22.5	167.89±29.05	<0.001*

Continuous data expressed as mean±SD; Categorical data expressed as Number (%); *: p is significant when < 0.05.

The mean onset of motor block was also earlier in group A (p = 0.009). Maximum Bromage score did not differ between the three study groups. The total duration of motor blockade was also significantly longer in group A when compared the other two groups (p < 0.001).

Table 4: Basal and post-operative VAS score during rest in the studied groups:

	Group A (Fentanyl + bupivacaine) (n= 30)	Group B (Midazolam + bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	p-value
At PACU	1 (1, 1)	1 (1, 1)	1 (1, 1)	1
One hour	1 (1, 2)	1 (1, 1)	1 (1, 1)	0.44
Two hours	1 (1, 1) c	2 (2, 3) c	2 (2, 3) a,b	<0.001*
Four hours	3 (2, 3.50) c	3 (3, 4) c	5 (4, 5) a,b	<0.001*
Six hours	3 (2, 4) b, c	4 (3.50, 4) a,c	4 (3.50, 5.50) a,b	<0.001*
Eight hours	4 (3, 4) b,c	5 (4, 5) a,c	4 (3, 5) a,b	<0.001*
12 hours	4 (3, 4.50) c	4 (4, 5) c	4 (3, 4) a,b	0.037*
18 hours	4 (3, 5) c	4 (4, 5) c	4 (3, 5) a,b	0.010*
24 hours	3 (3, 4)	4 (3, 4)	3 (3, 4)	0.47

Continuous data expressed as median (range); *: p is significant when < 0.05
a: significance in relation to group A; b: significance in relation to group B; c: significance in relation to group C.

There was a statistically significant difference between the females in the three groups in the VAS score after CS. The difference was manifested at two hours up to 18 hours following CS, but no significant difference was detected at 24 hours after the surgery. There was a significant difference between group A and group B at six hours and eight hours with decreased VAS score in group A (Fentanyl + bupivacaine).

Table 5: Post-operative recovery and analgesic requirements in the studied groups:

	Group A (Fentanyl + bupivacaine) (n= 30)	Group B (Midazolam + bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	p-value
Ambulation (hours)	3.91 ± 1.45	4.09 ± 1.05	3.83 ± 0.72	0.67
Hospital stay (hours)	14.90 ± 6.54	13.86 ± 4.84	14.07 ± 4.88	0.75
Pethidine in mg	70.59 ± 11.23 b	80.98 ± 13.54 a	150.31 ± 18.11 a,b	0.003*

Continuous data expressed as mean±SD. *: p is significant when <0.05
a: significance in relation to group A; b: significance in relation to group B.

There was no significant difference between the females in the three study groups in the ambulation time after surgery, hospital stay (p=0.67 and 0.75). However, there was a statistically significant difference in the mean dose of pethidine in the first day between the three study groups with the least amount required in group A.

Table 6: Neonatal outcomes in the studied groups:

Variable	Group A (Fentanyl + bupivacaine) (n= 30)	Group B (Midazolam + bupivacaine) (n= 30)	Group C Bupivacaine (n= 30)	p
APGAR score (1 min)	7.29 ± 0.53	7.66 ± 0.65	7.51 ± 0.47	0.338
APGAR score (5 min)	9.45 ± 0.25	9.62 ± 0.16	9.52 ± 0.19	0.276

Continuous data expressed as mean ±SD. Categorical data expressed as Number (%)
*: p is significant when < 0.05

The mean 1 min APGAR score in group A was 7.29 ± 0.53, in group B 7.66 ± 0.65 and 7.51 ± 0.47 in group C with no significant difference between the three groups. The mean 5 min APGAR score in group A was 9.45 ± 0.25, in group B 9.62 ± 0.16 and 9.52 ± 0.19 in group C with no significant difference between the three groups.

DISCUSSION:

Spinal anesthesia is preferred over general anesthesia (GA) in cases of cesarean section (CS) delivery, as it avoids the risk of aspiration that may occur with GA, avoids the neonatal depressant effect of GA, and provides postoperative analgesia. However, it also has disadvantages, as it provides a relatively fixed short duration of anesthesia, causes sympathetic block with subsequent hypotension and bradycardia, lesser control on the level of blockade, may give insufficient visceral block with visceral pain, and the possible occurrence of nausea and vomiting especially during uterine manipulation and peritoneal closure [7].

Bupivacaine, which is the most commonly used drug for spinal anesthesia, has slow onset, high potency, and relatively short postoperative analgesia. The intrathecal (IT) dose of hyperbaric bupivacaine for CS ranges from 12 to 15 mg [8].

Peritoneal traction and handling of intraperitoneal organs during cesarean delivery lead to intraoperative visceral pain. Increasing the dose of hyperbaric bupivacaine leads to reduction of the incidence of intraoperative visceral pain, but on the expense of the possibility of the risk of higher blockade and its adverse effects.

To avoid these drawbacks, a number of adjuvants have been used. The commonly used adjuvants include opioids such as fentanyl and nalbuphine; α_2 stimulants such as clonidine and dexmedetomidine; NMDA receptor antagonist such as ketamine; GABA receptor agonists such as midazolam [9].

Opioids are the most popular used adjuvants added to bupivacaine in spinal blockade to obtain a sufficient intraoperative visceral analgesia and increase the duration and quality of postoperative analgesia, with less sympathetic block and hemodynamic effect [10].

Fentanyl is a strong μ-opioid receptor agonist. It is a lipophilic opioid, has fast onset of action after IT administration, provides better intraoperative analgesia, and is more safe than morphine for management of early postoperative pain as it does not spread to the fourth ventricle in sufficient

concentration to cause delayed depression of the respiratory center after IT administration [11].

Midazolam is a relatively water-soluble benzodiazepine and is extensively used in both critical care medicine and in the operating room for its sedative, anxiolytic, and amnesic effects[12].

Midazolam exerts its analgesic activity through benzodiazepine receptors, which are distributed in the gray matter of the cervical, thoracic, lumbar, and sacral regions of the spinal cord; the highest densities of receptors were localized within lamina II of the dorsal horn. The segmental analgesia produced by intrathecal midazolam is mediated by the benzodiazepine GABA receptor complex, which is also involved in other benzodiazepine actions[13].

This study was conducted at Ain Shams University Hospitals aiming to evaluate and compare the effects of intrathecal midazolam and fentanyl as additives to intrathecal hyperbaric bupivacaine as regards onset and duration of sensory block, duration of complete and effective analgesia and side effects associated with the drug. To the best of our knowledge, this is the first study to compare midazolam and fentanyl as adjuvants to bupivacaine in management of postoperative pain following CS.

Starting with demographics in the current study, no significant difference was detected regarding age either while comparing the three groups, or when every two groups are compared separately (p > 0.05). In our study, mean time of onset of sensory blockade in the fentanyl group was 4.52 minutes and it was significantly shorter than the other two groups (p = 0.005) which is 6.86 minutes in midazolam group and 8.45 minutes in bupivacaine group. Moreover, time elapsed till reaching the maximum level of sensory blockade was 9.95 minutes in fentanyl group and 12.9 minutes in midazolam group and 15.25

minutes in bupivacnce group (p = 0.001). In addition, mean time to regression to L1 dermatome was 302.44 minutes in fentanly group (p < 0.001) and 215.9 minutes in midazolam group and 196.9 in bupivance group. Accordingly, time for request of the first analgesia was significantly longer in both adjuvant groups compared to bupicane group the third group (p < 0.001), with high superiority of fentanyl against midazolam (p < 0.001).

The extension of the duration of effective analgesia has been well-described before. Prolonged periods of effective analgesia, ranging from 40 to 120minutes, have been observed for intrathecal fentanyl 6.25 to 12.5mg in several studies [14].

Nonetheless, most of the research on higher doses of fentanyl has been in agreement, and a prolongation of effective analgesia averaging 3 to 5 hours is in line with our result, has been reported for intrathecal fentanyl at doses of 15 to 25mg [15, 16].

As regards midazolam, *Dodawad et al.* [17] reported that postoperative analgesia was significantly better and longer in the midazolam group as demonstrated by its significantly longer time until the first request for analgesia and also the lower need for rescue analgesics.

Regarding motor block in our study, mean onset of block was achieved after 9.35 minutes in the fentanyl group (p = 0.009) and 12.04 minutes in midazolam group and 13.9 minutes in bupivacaine group. Furthermore, total duration of motor block was significantly longer in fentanyl group which is 229.2 mintues (p < 0.001) and 181.3 minutes in midazolam group and 167.89 mintues in in bupivacaine group.

Bharti et al. [18] reported a prolonged motor block in their midazolam group. The result in our study was in accordance with *Muller et al.* who reported an antispasticity

effect of intrathecal midazolam with little effect on normal motor function.

In our study, both basal and post-operative heart rates and MAP did not differ between the three groups and all of these readings were within the normal heart rate levels. As regards postoperative pain and VAS score the differ between the three groups at PACU and 1-hour after operation (p > 0.05), the fentanyl group expressed significantly lower scores when compared to the other groups (p < 0.05) on the subsequent six readings. Again, no difference was detected 24 hours after operation between the three groups (p > 0.05). Due to longer block and lower VAS scores, the fentanyl group expressed a lower dosage of paracetamol and pethidine intake in the 1st post-operative day when compared to the other groups. The midazolam group received also a lower dose when compared to the third group.

One study reported that when 2 mg intrathecal midazolam were added to 1.5 mL of 5% lignocaine in women who underwent a caesarean section delivery, postoperative pain relief was evident[19]. A similar result was shown by Tucker and colleagues[20].

Kim and Lee[21], who reported that the addition of 1 or 2 mg of intrathecal midazolam prolonged the postoperative analgesic effect of bupivacaine by approximately 2 hours and 4.5 hours, respectively, compared with controls after hemorrhoidectomy and used fewer analgesics in the first 24 hours after surgery.

Prakash et al.[22] concluded that 2 mg intrathecal midazolam provided a moderate prolongation of postoperative analgesia in cesarean patients. Similar observations were reported by previous studies[23].

In our study, the detected complications (bradycardia, hypotension, as well as nausea and vomiting) did not differ significantly between the three groups. Moreover, they occurred with a low incidence as no one of

such complications occurred in more than 10% of cases in each group. In addition, these complications were properly managed as discussed in patients and methods. These findings are in agreement with *Weigl et al.*[24] who showed that the PONV was rare (2/29; 7%) among the patients who received intrathecal fentanyl.

Similar results have been reported in other studies [25, 26, 27]. *Weigl et al.*[24] observed a low incidence of pruritus among the women who received spinal anesthesia with local anesthetic alone, as has been reported in other studies[27].

The incidence of pruritus reached 10% among patients in the fentanyl group, which was also consistent with results of other studies that have reported rates of pruritus ranging from 10% to 24%[27].

Possibly, the most dangerous side effect of opioid analgesia is respiratory depression. Reports of respiratory depression after spinal administration of lipophilic opioids in obstetrics have mostly implicated sufentanil [28], however, no cases have reported the occurance of respiratory depression in our study. Talking about midazolam, this trend is consistent with studies by *Sanwal et al.*[23] who reported that this relationship may be due to the bupivacaine-sparing effect of midazolam and concluded that intrathecal midazolam may allow the dose of bupivacaine to be reduced while still providing the same surgical anesthesia with fewer episodes of bradycardia and hypotension. A similar observation was reported by previous studies[18, 29, 30].

In our study as regard of the fetal state as assessed by 1 and 5 minutes APGAR scores, there was no significant difference between the three groups. There was no relationship between intrathecal fentanyl administration and neonatal Apgar scores, and this finding is in agreement with those of other studies [15, 27, 14]. Adjunct intrathecal midazolam was shown to potentially provide

a more prolonged analgesia than opioids alone while also inhibiting their adverse effects, such as nausea and vomiting [31]. It has been postulated that a possible mechanism for the anti-emetic effect of benzodiazepines could be an action at the chemoreceptor trigger zone, which reduce the synthesis, release, and postsynaptic effect of dopamine[32].

Conclusion:

From these results we can conclude that:

- Intrathecal adjuvants are associated with improving out comes after CS as revealed by delayed onset and longer duration of sensory and motor block in addition to longer duration of complete and effective analgesia.

- Intrathecal fentanyl revealed better outcomes in terms of delayed onset and longer duration of sensory and motor block in addition to longer duration of complete and effective analgesia as compared with midazolam.

- Addition of intrathecal fentanyl and midazolam didn't affect the incidence of maternal and fetal complications as compared with bupivacaine alone.

REFERENCES:

1. Liu, S. S. and McDonald, S. B. (2001): "Current issues in spinal anesthesia." Anesthesiology: The Journal of the American Society of Anesthesiologists, 94 (5): 888-906.

2. Gunaydin, B. and Tan, E. D. (2010): "Intrathecal hyperbaric or isobaric bupivacaine and ropivacaine with fentanyl for elective caesarean section." The journal of maternal-fetal & neonatal medicine, 23(12): 1481-1486.

3. Obara, M., Sawamura, S., Satoh, Y., Chinzei, M., Sekiyama, H., Tamai, H., et al. (2003): "The effect of intrathecal fentanyl added to hyperbaric bupivacaine for caesarean section." Masui. The Japanese journal of anesthesiology, 52(4): 378-382.

4. Shahriari, A., Khooshideh, M. and Heidari, M. H. (2009): "Prevention of nausea and vomiting in caesarean section under spinal anesthesia with midazolam or metoclopramide." J Pak Med Assoc, 59(11): 756-759.

5. Chhabra, A. R., Jagtap, S. R. and Dawoodi, S. F. (2013): "Comparison of clonidine versus fentanyl as an adjuvant to intrathecal ropivacaine for major lower limb surgeries: A randomized double-blind prospective study." Indian Journal of Pain, 27(3): 170.

6. Sadeh, S. S., Tanha, F. D. and Sadeghi, S. (2012): "Prevention of postoperative nausea and vomiting by administration of sub hypnotic doses of propofol and midazolam during spinal anesthesia for Cesarean section: 1AP3-2." European Journal of Anaesthesiology (EJA): 29, 11.

7. Gauchan, S., Thapa, C., Prasai, A., Pyakurel, K., Joshi, I. and Tulachan, J. (2014): "Effects of intrathecal fentanyl as an adjunct to hyperbaric bupivacaine in spinal anesthesia for elective caesarean section." Nepal Medical College journal: NMCJ, 16(1): 5-8.

8. Choi, D. H., Ahn, H. J. and Kim, M. H. (2000): "Bupivacaine-sparing effect of fentanyl in spinal anesthesia for cesarean delivery." Reg Anesth Pain Med, 25(3): 240-245.

9. Yallapragada, S. V., Vemuri, N. N. and Shaik, M. S. (2016): "Effect of adding clonidine to intrathecal bupivacaine on the quality of subarachnoid block: A prospective randomized double-blind study." Anesthesia, essays and researches, 10(3): 451.

10. Shukla, D., Verma, A., Agarwal, A., Pandey, H. and Tyagi, C. (2011): "Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine." Journal of anaesthesiology, clinical pharmacology, 27(4): 495.

11. Gehling, M. and Tryba, M. (2009): "Risks and side‐effects of intrathecal morphine combined with spinal anesthesia: a meta‐analysis." Anesthesia, 64(6): 643-651.

12. Olkkola, K. T. and Ahonen, J. (2008). Midazolam and other benzodiazepines Modern anesthetics (pp. 335-360): Springer.

13. Barik, A. K., Paswan, A., Prakash, S., Meena, R., Singh, Y., Loha, S., et al. (2016): "Dose-response effects of spinal midazolam added to bupivacaine intrathecal anesthesia in lower segment caesarean section: Randomized control clinical trial." Indian Journal of Preventive & Social Medicine, 47(3-4): 7-7.

14. Bogra, J., Arora, N. and Srivastava, P. (2005): "Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section." BMC anesthesiology, 5(1): 5.

15. Dahl, J. B., Jeppesen, I. S., Jorgensen, H., Wetterslev, J. and Moiniche, S. (1999). Intraoperative and postoperative analgesic efficacy and adverse effects of intrathecal opioids in patients undergoing cesarean section with spinal anesthesia: a qualitative and quantitative systematic review of randomized controlled trials Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]: Centre for Reviews and Dissemination (UK).

16. Siti, G. S. and Choy, Y. C. (2009): "Comparison of morphine with fentanyl added to intrathecal 0.5% hyperbaric bupivacaine for analgesia after caesarean section." The Medical journal of Malaysia, 64(1): 71-74.

17. Dodawad, R., Sumalatha, G., Pandarpurkar, S. and Jajee, P. (2016): "Intrathecal midazolam as an adjuvant in pregnancy-induced hypertensive patients undergoing an elective caesarean section: A clinical comparative study." Anesthesiology and pain medicine, 6(5).

18. Bharti, N., Madan, R., Mohanty, P. and Kaul, H. (2003): "Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anesthesia." Acta anaesthesiologica scandinavica, 47(9): 1101-1105.

19. Sen, A., Rudra, A., Sarkar, S. K. and Biswas, B. (2001): "Intrathecal midazolam for postoperative pain relief in caesarean section delivery." Journal of the Indian Medical Association, 99(12): 683-684, 686.

20. Tucker, A. P., Lai, C., Nadeson, R. and Goodchild, C. S. (2004a): "Intrathecal midazolam I: a cohort study investigating safety." Anesthesia & Analgesia, 98(6): 1512-1520.

21. Kim, M. and Lee, Y. (2001): "Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy." British journal of anesthesia, 86(1): 77-79.

22. Prakash, S., Joshi, N., Gogia, A. R., Prakash, S. and Singh, R. (2006a): "Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patients undergoing cesarean delivery."

23. Sanwal, M. K., Baduni, N. and Jain, A. (2013): "Bupivacaine sparing effect of intrathecal midazolam in sub-arachnoid block for cesarean section." Journal of Obstetric Anesthesia and Critical Care, 3(1): 27.

24. Weigl, W., Bierylo, A., Wielgus, M., Krzemień-Wiczyńska, S., Szymusik, I., Kolacz, M., et al. (2016): "Analgesic efficacy of intrathecal fentanyl during the period of highest analgesic demand after cesarean section: A randomized controlled study." Medicine, 95(24).

25. Hunt, C. O., Naulty, J. S., Bader, A. M., Hauch, M. A., Vartikar, J. V., Datta, S., et al. (1989): "Perioperative analgesia with subarachnoid fentanyl-bupivacaine for cesarean delivery." Anesthesiology, 71(4): 535-540.

26. Grant, G. J., Susser, L., Cascio, M., Moses, M. and Zakowski, M. I. (1996): "Hemodynamic effects of intrathecal fentanyl in nonlaboring term parturients." Journal of clinical anesthesia, 8(2): 99-103.

27. Biswas, B., Rudra, A., Bose, B., Nath, S., Chakrabarty, S. and Bhattacharjee, S. (2002): "Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period." Indian J anaesth, 46(6): 469-472.

28. Ferouz, F., Norris, M. C. and Leighton, B. L. (1997): "Risk of respiratory arrest after intrathecal sufentanil." Anesthesia & Analgesia, 85(5): 1088-1090.

29. Tucker, A. P., Mezzatesta, J., Nadeson, R. and Goodchild, C. S. (2004b): "Intrathecal midazolam II: combination with intrathecal fentanyl for labor pain." Anesthesia & Analgesia, 98(6): 1521-1527.

30. Salimi, A., Nejad, R. A., Safari, F., Mohajaerani, S. A., Naghade, R. J. and Mottaghi, K. (2014): "Reduction in labor pain by intrathecal midazolam as an adjunct to sufentanil." Korean journal of anesthesiology, 66(3): 204.

31. Rodola, F. (2006): "Midazolam as an anti-emetic." European review for medical and pharmacological sciences, 10(3): 121.

32. Agrawal, N., Usmani, A., Sehgal, R., Kumar, R. and Bhadoria, P. (2005): "Effect of intrathecal midazolam bupivacaine combination on post operative analgesia." Indian J anaesth, 49(1): 37-39.

دراسة مقارنة بين اضافه الفينتانيل والميدازولام الى ادوية التخدير الموضعي في التخدير الشوكي في عمليات الولادة القيصرية الاختيارية وتسكين الألم بعد التدخل الجراحي

أحمد علي فـواز، تـامر يـوسف إيـلي، وائل عبد المنعم محمد عبد الوهاب،
عبد الرحمن علي علي جاد مطر

قسم التخدير والرعاية المركزة وعلاج الألم، كلية الطب، جامعة عين شمس

مقدمة البحث: يتسم التخدير القطني أو التخدير داخِل القِراب بتاريخ طويل من النجاح حيث أصبح هو الأكثر شيوعاً حيث يرجع ذلك في الغالب إلى زيادة عدد الإجراءات والتدخلات المتنقلة التي قد يوفر لها التخدير القطني أو النخاعي تخديراً جراحياً سريعاً ومناسباً جنباً إلى جنب مع سير المريض مبكراً والخروج المبكر من المستشفى. أظهرت الدراسات التي تم إجرائها على البيوبيفاكيين أنه ينتج تخدير قطني يمكن التنبؤ به وموثوق فيه بالنسبة للعمليات الجراحية.

الهدف من البحث: تهدف هذه الدراسة لإجراء تقييم ومقارنة لآثار الحقن بالميدازولامداخِل القِراب (٢مجم) والحقن بالفينتانيل (٢٥ ميكروجرام) كمواد مساعدة كإضافات للحقن بالبُوبيفاكايينمُفْرِط الضَّغْطداخل القِراب (٠,٥%) فيما يتعلق ببداية ومدة الاحصار الحِسّي، مدة التسكين الكامل والفعال، الآثار الجانبية المرتبطة بالحقن بعقاقير التخدير.

طريقة البحث: لقد شمل هذا البحث ٩٠ سيدة (الاصحاء الطبيعيات تبعاً للحالة البدنية والسيدات اللائي تعانين من مرض جهازي خفيف وفقاً لتصنيف الجمعية الأمريكية لأطباء التخدير)اللائي تتراوح أعمارهن بين ١٨-٣١ عام المحدد لهن الخضوع للولادة القيصرية الاختيارية تحت التخدير القطني. تقسيم المريضات عشوائياً إلى ٣ مجموعات(٣٠ مريضة لكل مجموعة) على أساس المواد المساعدة المصافة إلى عقاقير التخدير المستخدمة: **المجموعة الأولى:** ٢مل من البُوبيفاكايينمُفْرِط الضَّغْط ٠,٥% + ٠,٤مل من محلول الملح الطبيعي، **المجموعة الثانية:**٢مل من البُوبيفاكايينمُفْرِط الضَّغْط ٠,٥% + ٠,٤مل من الميدازولام (٢مجم) + ٠,١مل من محلول الملح الطبيعي، **المجموعة الثالثة:**٢مل من البُوبيفاكايينمُفْرِط الضَّغْط ٠,٥% + ٠,٢٥مل من الفينتانيل (١٢,٥ ميكروجرام) + ٠,٢٥مل من محلول الملح الطبيعي.

نتائج البحث: لم تظهر البيانات الديموغرافية أي اختلاف بين مجموعات الدراسة الثلاث.أظهرت المجموعة (أ) بداية مبكرة للوصول للتسكين الحسي ، وكذلك الانحدار المتأخر إلى المستوى الحسي عند الفقرة القطنية الأولى. أظهرت المجموعة الأولى أيضا مدة أطول في تسكين الألم ووقت أطول قبل استدعاء الأول لمسكنات. كانت الجرعة المطلوبة من الباراسيتامول والبيثيدين خلال اليوم الأول أقل بكثير في المجموعة (أ) والمجموعة (ب) مقارنة بالمجموعة (ج). ومع ذلك ، لم تظهر المجموعات الثلاث أي اختلاف من حيث المضاعفات التي واجهتها السيدات بعد الولادة. وأيضا لم تظهر حالة المواليد أي اختلاف بين المجموعات الثلاث.

خلاصة الدراسة: يتم إجراء العملية القيصرية بمعدل مرتفع في مصر مع تفضيل التخدير القطني عن التخدير العام، يتم استخدام العديد من المواد المساعدة داخِل القِراب لعقاقير التخدير الموضعي، ارتبط استخدام المواد المساعدة داخل القِراب بالتحسن بعد القيصريات كما يتضح من تأخر البدء وطول مدة الحسية والحركية بالإضافة إلى فترة أطول من تسكين كامل وفعال، أظهر استخدام الفينتانيل داخل القِراب عن نتائج أفضل من حيث التأخر في البدء وطول مدة الحسية والحركية بالإضافة إلى فترة أطول من التسكين الكامل والفعال مقارنةً بالميدازولام، إن إضافة الفنتانيل داخل القِراب والميدازولام لم يؤثر على حدوث مضاعفات الأم والجنين مقارنة مع بوبيفاكايين وحده.