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Comparative Study of Fentanyl vs Dexmedetomidine as Adjuvants to Intrathecal Bupivacaine in Cesarean Section

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ABSTRACT

Background: Spinal anesthesia remains the preferred method for cesarean deliveries because of its deep sensory block and minimal negative consequences on the fetus and mother.

Objective: This research aimed to compare the impacts of dexmedetomidine and fentanyl when used as adjuvants to intrathecal bupivacaine during elective cesarean section, assessing their impact on period of spinal anesthesia, quality of analgesia, hemodynamic stability, incidence of side effects, and neonatal outcomes.

Methods: This was randomized, double-blind clinical research involving sixty parturients that were classified into 2 groups; every group included thirty parturients. Group (A): 30 patients were administered ten milligrams of hyperbaric bupivacaine 0.5% + 5 ug dexmedetomidine, and Group (B): 30 patients were administered ten milligrams of hyperbaric bupivacaine 0.5% + 25 ug fentanyl.

Results: An insignificant variance was recorded according to the pain score at the 1st hour, third hour, and sixth hour (P-value > 0.05), period of motor block and duration of operation, bradycardia, hypotension, shivering, nausea/vomiting, and respiratory depression, and Apgar score at one- and five-min (P>0.05). Statistically significant variance was recorded between the examined groups according to duration of analgesia (P-value < 0.05).

Conclusion: Dexmedetomidine (5 μg) is a more effective adjuvant for pain management following surgery within a cesarean section under spinal anesthesia compared to fentanyl. It prolongs analgesia and reduces the need for additional pain medication, with few opioid-related negative consequences involving respiratory depression and nausea, making it a more favorable choice.

Keywords: Fentanyl, Cesarean section, Dexmedetomidine, Effect.

INTRODUCTION

Spinal anesthesia remains the preferred method for cesarean delivery because of its deep sensory block and minimal negative impact on the mother and fetus. The technique is not capable of providing adequate analgesia following surgery, and it has a short period, regardless of its numerous advantages. Within cesarean sections, adequate analgesia following surgery is essential for the promotion of breastfeeding and the proper care of newborns[1].

The quality of spinal anesthesia was stated to be enhanced by the addition of opioids (including fentanyl, sufentanil, and morphine) and other medications (e.g., clonidine, dexmedetomidine, neostigmine, midazolam, and ketamine). The quality of early postoperative and intraoperative subarachnoid block is enhanced by the use of opioids, including fentanyl, in combination with bupivacaine. Fentanyl is correlated with many negative consequences, despite the fact that it provides a superior level of analgesia. This has directed research toward the application of more effective adjuvants for spinal anesthesia, including clonidine and dexmedetomidine [2].

Dexmedetomidine is a highly selective alpha-2 adrenoceptor agonist agent that is relatively new and produces sedative and analgesic impacts. It has additionally been utilized as an adjuvant in spinal anesthesia, leading to an extended period of block and better analgesia following surgery with no correlated hypotension or other negative consequences [3].

Fentanyl is a synthetic opioid that has central action and is frequently utilized for pain management.

Intrathecal fentanyl is frequently added into the mixture of other local anesthetics to enhance anesthesia and analgesia. This has enhanced spinal anesthesia and minimized the negative consequences of anesthetic drugs, such as vomiting, nausea, and pruritus[4].

The dosage of local anesthetics may be reduced, and motor and sensory block may be guaranteed by the addition of adjuvant medications to intrathecal bupivacaine. Intrathecal adjuvants, such as dexmedetomidine and fentanyl, are receptor agonists that contain hemodynamic-stabilizing sedative, anesthetic-sparing, perioperative sympatholytic, and analgesic features [5].

This research aimed to compare;

- ✓ Primarily the effects of dexmedetomidine and fentanyl when used as adjuvants to intrathecal bupivacaine during elective cesarean section, assessing their impact on the duration of spinal anesthesia, quality of analgesia, hemodynamic stability.
- ✓ Secondarily, the incidence of side effects, and neonatal outcomes.

PATIENTS AND METHODS

This was a randomized, double-blind clinical research involving sixty parturients who were classified into two groups; every group included thirty parturients.

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Group (A): 30 patients were administered ten milligrams of hyperbaric bupivacaine 0.5% + 5 ug dexmedetomidine, and Group (B): 30 patients were administered ten milligrams of hyperbaric bupivacaine 0.5% + 25 ug fentanyl.

Inclusion criteria: Participants consisted of participants in the childbearing duration between the ages of eighteen and forty, with a gestational age of thirty-seven weeks or more, and ASA 1 and 2 candidates with BMI 20 - 35 for elective cesarean delivery under spinal anesthesia.

Exclusion criteria: Cases with emergency disorders, contraindications for spinal anesthesia,
A previous diagnosis of valvular heart illness, sensitivity or allergy to the medications administered, and placenta previa, in addition to those who required injection of general anesthesia or unsuccessful blockade, have been removed.
All parturients have been exposed to as follows: Full history taking and complete physical investigation: General investigation: Vital signs (temperature, blood pressure, respiratory rate, heart rate) and signs of pallor, lymph node enlargement, and jaundice.

Anesthetic technique:
Basic standard follow-up, which included noninvasive blood pressure, electrocardiography, and pulse oximetry, has been conducted on cases upon their arrival in the operating room. Additionally, initial hemodynamic variables have been assessed. All cases have been administered a ten-milliliter per kilogram Ringer solution prior to the initiation of spinal block.

All cases have been equally and randomly classified into the following both groups:

The total volume of intrathecal administration within the two groups has been equal (2.5 milliliters). Group A were administered ten milligrams of hyperbaric bupivacaine 0.5% + 5 micrograms dexmedetomidine, while Group B were administered ten milligrams hyperbaric bupivacaine 0.5% + 25 micrograms fentanyl.

An anesthesiologist administered spinal anesthesia to all research participants within the sitting position at the L4-L5 intervertebral space using an aseptic method and a 25 G Quincke spinal needle. The intrathecal medications have been administered following the observation of a free flow of transparent cerebrospinal fluid. Afterward, cases have been placed within a supine position (slightly tilted to the left side), and a simple face mask has been utilized to deliver six liters per minute of oxygen. The pinprick test has been utilized to evaluate the sensory block, while the modified Bromage scale has been utilized to evaluate the motor block. The surgery has been permitted to commence upon the confirmation of an adequate level of sensory block (T4-T6).

Outcome measurement:
Hemodynamic following up, which encompassed heart rate (HR), mean arterial pressure (MAP), SBP and peripheral oxygen saturation level (SpO2), and DBP was documented both during and following the surgery. The modified Bromage scale (zero = no motor block, one = inability to flex the hip, two = inability to flex the knee, and three = complete motor block of limb) has been utilized for assessing motor block, and the onset of sensory block (time to reach T4-T6) has been evaluated every 2 minutes utilizing a pinprick test (by utilizing a blunt 25-gauge needle along the mid-clavicular line bilaterally). The patients' pain score was evaluated utilizing a visual analogue scale (VAS) throughout the recovery room (T0) and at 1, 3, and 6 h (T1, T3, and T6) in the duration following surgery. The scale measures pain from zero to ten, with zero considering no pain and ten considering the most severe pain imaginable. The period of the operation was documented. Throughout the 6 hours following the operation, the frequency of shivering, vomiting, and nausea, in addition to respiratory depression (respiratory rate less than ten per minute), has been assessed and documented. The Apgar scores of newborns have been additionally evaluated at 1- and 5-min following birth.

Sample size:
The sample size calculation was performed using Epi-Info 2002 software statistical package designed by World Health Organization (WHO) and by Centers for Disease Control and Prevention (CDC). The sample size was calculated based on the following considerations: input parameter was duration of analgesia, 95% confidence level and according to a previous study [1]. Resulting sample size was 55. Sample size increased to 60 and was divided into 30 in each group: Group A and Group B.

Ethical consideration:
The Ethics Committee of Faculty of Medicine, Sohag University accepted the research protocol [IRB No.: Soh-Med-24-06--09PD]. Prior to enrollment, cases or their legal representatives provided written informed consent in accordance with the condition of the case. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

Data generated by computers have been analyzed using IBM SPSS version 22.0. Percentages and numbers were used to express qualitative data which were compared by Chi-Square test. Mean ± SD were used to express quantitative data, which were compared by the independent t-test. A significant p-value was defined as one that is equal to or less than 0.05.

RESULTS
A statistically insignificant variance was recorded among examined groups according to age, weight, height, and ASA (Table 1).

Table (1): Distribution of general characteristics among the examined groups

	Group A Number=30	Group B Number =30	P value
Age (years)	27.53±4.8	27±3.7	0.667
Weight (kg)	71.03±9.8	70.6±12.2	0.860
Height (cm)	160.4±4.5	161.3±8.07	0.577
ASA			
I	23 (76.7%)	20 (66.7%)	0.39
II	7 (23.3%)	10 (33.3%)	

Data are presented as mean ±SD. P value <0.05 is statistically significant, P value >0.05: Not significant, SD: standard deviation,p<0.001 is highly significant.

A statistically significant variance was found among examined groups according to pain score (VAS) at T0, while a statistically insignificant variance was found as regard pain score (VAS) at T1, T3, and T6 (Table 2).

Table (2): Distribution of pain score following surgery between the studied groups

	Group A N=30	Group B N=30	P value
T0	0.83±0.73	0.41±0.62	**0.01***
T1	2.2±0.98	2.1±0.98	0.6
T3	4.5±1.45	4.9±1.18	0.2
T6	8.7±1.83	8.8±1.25	0.8

Data are presented as mean ±SD. P value <0.05 is statistically significant. T0: at baseline, T1: first hour, T3: third hour, T6: sixth hour.

A statistically insignificant variance was recorded among the examined groups according to period of operation and period of motor block, while there was a statistically significant variance between the examined groups according to duration of analgesia (Table 3).

Table (3): Distribution of operative data among the examined groups

	Group A (N=30)	Group B (N=30)	P value
Period of analgesia (min)	439.05±86.15	253.95±53.60	**<0.001**
Duration of motor block (min)	258.88±60.50	275.52±47.25	0.24
Duration of surgery (min)	52.33±12.48	50.32±8.03	0.46

Data are presented as mean ±SD. P value <0.05 is statistically significant.

A statistically insignificant variance was recorded among examined groups according to bradycardia, hypotension, shivering, nausea/vomiting, and respiratory depression (Table 4).

Table (4): Distribution of complications among the examined groups

	Group A (N=30)	Group B (N=30)	P value
Hypotension	16(53.30%)	20(66.70%)	0.292
Bradycardia	5(16.70%)	3(10.00%)	0.448
Respiratory depression	1(3.30%)	1(3.30%)	1
Shivering	2(6.70%)	5(16.70%)	0.228
Nausea/vomiting	2(6.70%)	3(10.00%)	0.64

Data are presented as number (%).

A statistically insignificant variance was recorded among the examined groups according to Apgar score at one- and five-minutes (Table 5).

Table (5): Distribution of Apgar score among the examined groups

	Group A (N=30)	Group B (N=30)	P value
Apgar score at 1 min	8.87±0.73	8.65±0.86	0.27
Apgar score at 5 min	9.69±0.43	9.63±0.49	0.58

Data are presented as mean ± standard deviation.

DISCUSSION

Cesarean section is a globally conducted obstetrical intervention that is becoming increasingly prevalent [6]. Cesarean section, frequently referred to as C-section, is now recognized as the primary alternative technique for delivery in pregnancies with life-threatening complications [7]. C-sections must only be performed when vaginal delivery is either impossible or poses a greater danger, and they must only be performed if there are specific fetal or maternal indications[8].

Intrathecal (IT) drug delivery systems (IDDS) are a choice for therapy for cases who are unable to deal with the negative consequences of systemic drugs or have pain that is refractory to it[9]. Life-threatening toxicity may result from therapeutic intrathecal injection. Although systemic symptoms are rarely stated as a result of intrathecal anesthetic injections, the utilization of intrathecal anesthetics for chronic pain is on the rise [10]. Several adjuvants were suggested as a means of extending the period of action and reducing the negative consequences of local anesthetic medications[11].

The results of our study were as follows:

The current research demonstrated that there was statistically insignificant variance among examined groups according to age, weight, height, and ASA.

Similarly, the present findings aligned with **Khosravi *et al.*** [1] who presented comparative research of fentanyl versus dexmedetomidine as adjuvants to

intrathecal bupivacaine during cesarean delivery, as statistically insignificant variance was discovered among studied groups according to age (p-value = 0.071), weight (p-value = 0.483), height (p = 0.103), and ASA (p = 0.254).

As well, the current findings agreed with **Sun *et al.*[12]** who aimed to compare the impacts of bupivacaine plus dexmedetomidine, bupivacaine plus fentanyl, and bupivacaine alone on analgesia following surgery in females who underwent cesarean delivery under spinal anesthesia. They reported that statistically insignificant variance was recorded among studied groups according to age (p-value = 0.47), weight (p-value = 0.23), height (p-value = 0.12), and ASA (p = 0.69).

The present findings demonstrated that statistically significant variance was recorded among examined groups according to pain score (VAS) at T0, while statistically insignificant variance was discovered with regard to pain score (VAS) at T1, T3, and T6.

As well, the current result agreed with **Khosravi *et al.*[1]** whose study involved 110 participants with gestational age ≥thirty-seven weeks and ASA I and II candidates for elective cesarean delivery under spinal anesthesia; statistically significant variance was discovered among the A group and B group according to pain score (VAS) at T0 (P-value = 0.004), whereas statistically insignificant variance was recorded according to pain score (VAS) at T1 (P-value = 0.811), T3 (P-value = 0.371), and T6 (P-value = 0.997).

Also, **Tsaroucha *et al.* [13]** who aimed to investigate the duration of motor and sensory block along with the hemodynamic parameters, neonatal Apgar scores, postoperative analgesia and maternal satisfaction of overall anesthetic/analgesic regimen in parturients under ropivacaine 0.75% plus dexmedetomidine or fentanyl spinal anesthesia, they revealed that patients on dexmedetomidine remained pain-free longer postoperatively.

In contrast, **Sun *et al.* [12]** whose study contained 90 term participants scheduled to have elective cesarean sections, revealed that a statistically significant variance was recorded according to pain score (VAS) at T1.

The observed results revealed that statistically insignificant variance was recorded according to period of motor block and period of operation, while statistically significant variance was discovered among the studied groups according to period of analgesia.

Similarly, the present study was in line with **Khosravi *et al.* [1]** who aimed to compare the analgesia following surgery and hemodynamic alterations following the intrathecal administration of bupivacaine in combination with dexmedetomidine or fentanyl. They demonstrated that statistically insignificant variance was recorded among the examined groups according to period of motor block (P-value=0.077) and period of surgery (P-value=0.165), while statistically significant variance was discovered among the examined groups according to duration of analgesia (P-value=<0.001).

The obtained findings showed that statistically insignificant variance was discovered among examined groups according to bradycardia, hypotension, shivering, nausea/vomiting, and respiratory depression.

Additionally, the current laboratorial findings aligned with **Khosravi *et al.*[1]** who concluded that in comparison to fentanyl, it appeared that the addition of five micrograms of dexmedetomidine to bupivacaine had a more favorable impact on the treatment of pain following surgery during a cesarean delivery under spinal anesthesia. They showed that statistically insignificant variance was discovered among both groups as regards hypotension (P-value=0.171), bradycardia (P-value=0.376), respiratory depression (P-value=1.000), shivering (P=0.140), and nausea/vomiting (P=0.716) between the A group and the B group.

Considering the study of **Boshoff *et al.* [14]** who presented a review aimed to comparing the efficacy of intrathecal dexmedetomidine and fentanyl as additives to hyperbaric bupivacaine in providing postoperative analgesia for patients undergoing cesarean sections, they found that the majority of the side effects associated with intravenous administration of dexmedetomidine are cardiovascular in nature, particularly bradycardia and hypotension. There are several known adverse effects of intrathecal opioids, but the four most prevalent ones are respiratory depression, pruritus, nausea and vomiting, and urine retention. These side effects are more likely when hydrophilic intrathecal opioids, like morphine, are administered.

Wang *et al.*'s[15] research comparing the effects of 5 mcg intrathecal dexmedetomidine with normal saline as an additive to intrathecal bupivacaine in CS found no increase in the incidence of bradycardia, hypotension, or nausea and vomiting.

Also, the present results agreed with **Sun *et al.*[12]** who concluded that the application of dexmedetomidine as an adjuvant to bupivacaine in cesarean operations results in improved during surgery and analgesia following surgery with insignificant impact on Apgar scores or the frequency of negative consequences. They recorded that statistically insignificant variance as regards hypotension (P-value=1.0), Bradycardia (P=0.45), and respiratory depression (P=1). Meanwhile, a statistically significant variance was recorded as regards shivering (P-value=0.037) and nausea/vomiting (P-value=0.04) among groups.

The current study showed that a statistically insignificant variance was discovered among the examined groups according to Apgar score at one and five minutes.

Similarly, the obtained findings agreed with **Khosravi *et al.*[1]** who indicated that a statistically insignificant variance was discovered among the examined groups according to Apgar score at one (P = 0.782) and five minutes (P = 0.982).

As well, the present results aligned with **Sun *et al.*[12]** who revealed that a statistically insignificant

difference was detected between the studied groups based on Apgar score at one (P=0.43) and five minutes (P-value=0.90).

Also, the results were supported by **Tsaroucha *et al.*** [13] when compared to fentanyl, their prospective, double-blind, randomized study examined whether intrathecal dexmedetomidine as an adjuvant to ropivacaine 0.75% improved the quality of anesthesia for cesarean sections. They found no statistically significant differences in neonatal Apgar scores (first and fifth minute).

CONCLUSION

Dexmedetomidine (5μg) is described as a more effective adjuvant for pain management following surgery during cesarean section under spinal anesthesia compared to fentanyl.

It reduces the need for additional pain medication and prolongs analgesia, with few opioid-related negative consequences involving respiratory depression and nausea, making dexmedetomidine a more favorable choice.

LIMITATIONS

1- Small sample size, we need more researches with larger populations.
2- Single center study, more researches should be done in multi-centers.
3- Research was limited to elective cesarean section.

No funding.

No conflict of interest.

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