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ORIGINAL ARTICLE

Comparison of Dexmedetomidine and Fentanyl as Adjuvants to Intrathecal Isobaric Levobupivacaine in Lower Segment Caesarean Section

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Abstract

Background/Aim: Caesarean section is one the most common surgeries encountered in the operating room worldwide in the younger demographic ages from 18-39 years of age. The objective of this study was to compare the efficacy of dexmedetomidine versus fentanyl as adjuvants to intrathecal levobupivacaine in the lower segment caesarean section.

Methods: This quasi-experimental study was carried out at the Anaesthesia Department, Combined Military Hospital, Rawalpindi, Punjab, Pakistan from July 2021 to July 2023. A total of 240 patients were studied. They were divided into the dexmedetomidine group (n = 120) and fentanyl group (n = 120) group. Patients in both groups received 2.5 mL of 0.5 % of isobaric levobupivacaine with the dexmedetomidine group receiving 5 mcg of the drug and the fentanyl group 25 mcg of fentanyl to a total volume of 3 mL. Primary variables measured were: time to complete sensory and motor block, total duration of the block, time to first rescue analgesia after block regression in the post anaesthesia care unit (PACU) and mean PACU stay. Secondary variables observed were hypotension, nausea, vomiting and shivering.

Results: The time on onset for a sensory block in the dexmedetomidine group was delayed compared to the fentanyl group (4.35 ± 0.14 min and 3.39 ± 0.11 min, respectively), ($p < 0.0001$). The duration of the block was longer for the dexmedetomidine group with a mean time of 327.26 ± 12.60 min versus 243.3 ± 22.75 min ($p < 0.0001$). When comparing the motor blockade, the time of onset to successfully reach Bromage score 3 was similarly delayed in the dexmedetomidine group with a mean time of onset of 3.33 ± 0.12 min versus 2.36 ± 0.09 min ($p < 0.0001$). A similar trend was seen in the duration of the block with a mean time of 262.17 ± 13.31 min versus 203.34 ± 1.47 min ($p < 0.0001$).

Conclusion: Dexmedetomidine offered advantages over fentanyl as an adjunct to levobupivacaine spinal anaesthesia with a longer block duration and less adverse effects profile. It is recommended to use dexmedetomidine due to its better safety profile, longer duration and better hemodynamic stability. Fentanyl should be reserved when the early onset of the block is required in emergency cases.

Key words: Levobupivacaine; Fentanyl; Dexmedetomidine; Spinal anaesthesia; Adjunct.

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Introduction

Caesarean section is one the most common surgeries encountered in the operating room worldwide in the younger demographic from 18-39 years of age.[1] With the increasing rates of caesarean section deliveries worldwide, local studies also confirm the increase in Pakistan over the last two decades from 3.2 % in the 1990s to 18-20 % by 2018-2019.[2] This translates to around 1 in 5 mothers being delivered through a caesarean section in the country. With such an increased burden, safety and success in the provision of anaesthesia becomes mandatory to ensure the health of the mother as well as the baby.

Spinal anaesthesia remains the modality of choice when compared to general anaesthesia in these patients.[3] With a better safety profile and the mother being awake, spinal anaesthesia provides better pain relief both pre and post-operatively reducing the need for intravenous (iv) medications for induction and analgesia resulting in a better anaesthesia profile.[4] However, even with all its advantages, the procedure is not without its deficiencies - hypotension, bradycardia[5] and a failure rate ranging from 1-17 %.[6] To improve upon the technique, various advances have been made to offer a better density of block, prolonged duration of action with decreased use of rescue analgesia with added benefits of sedation, anxiolysis and patient comfort.

Isobaric levobupivacaine (s-isomer of racemic bupivacaine)[7] is introduced in recent years as the choice drug for spinal anaesthesia in the obstetric age group due to its less neuro- and cardio- toxicity with an improved density of block and prolonged duration of action when compared to conventional racemic bupivacaine.[8] However, literature is scarce when combining it with adjuvants for better pain control, anxiolysis and prolongation of block time especially in presented demographic area where its use is still considered novel since its onset is slower than that of racemic bupivacaine. Due to its better adverse effect profile and longer duration of block, adjuvants should be sought to improve its onset time as well.[8, 9]

The two most common adjuvants used internationally in spinal anaesthesia have been the α-agonist dexmedetomidine and the opioid fentanyl. It can be hypothesised that compared to the opioid fentanyl, dexmedetomidine would provide effective and comparable analgaesia without the opioid-related adverse effects.

The objective of this study was to compare potential superiority and efficacy of dexmedetomidine versus fentanyl as adjuvants to intrathecal levobupivacaine in the lower segment caesarean section.

Methods

This quasi-experimental study was carried out at the Department of Anaesthesiology, Combined Military Hospital, Rawalpindi, Punjab, Pakistan from July 2021 to July 2023 after approval from the ethical review board. Two hundred forty patients requiring elective caesarean sections were included in the study after calculating the sample size using the WHO calculator keeping the confidence interval (CI) at 95 %, margin of error at 5 % and keeping the population proportion of caesarean sections in analysed local demographic area at 19 %.[2]

Inclusion criteria included all ASA-I and II (American Society of Anesthesiology) adult patients of 18-30 years of age with a weight between 50-90 kg presenting in the obstetric department for scheduled elective caesarean delivery under spinal anaesthesia. Non-inclusion criteria comprised of patients unwilling to spinal anaesthesia refused to be included in the study, patients with allergy to either fentanyl, levobupivacaine or dexmedetomidine, patients who underwent spontaneous labour and emergency lower (uterine) segment caesarean section (LSCS) before the operation, patients with failed spinal for the procedure and were given general anaesthesia and patients with known major respiratory or cardiovascular disease.

The patients were divided into the dexmedetomidine group (n = 120) and the fentanyl group (n = 120). The method of sampling was a non-probability consecutive type. This was a double-blind study and once the patients were divided into two groups, the anaesthetist on duty in the operating room unaware of the study protocol received sealed envelopes with the two adjuvant vials labelled 1 and 2 with the anaesthetist not knowing which vial had dexmedetomidine and

which one had fentanyl. Both groups received 500 mL of normal saline in the patient holding bay 15 min before being shifted to the operating room. Standard monitoring including non-invasive blood pressure, heart rate, capnography and ECG in both groups.

Patients in both groups received 2.5 mL of 0.5 % of isobaric levobupivacaine with the dexmedetomidine group and fentanyl group receiving 5 mcg of the dexmedetomidine and 25 mcg of fentanyl to a total volume of 3 mL, respectively. The patient was injected the study solutions in both groups in the L2-L3 or L3-L4 space by a standard needle (*Quincke*) with free flow confirmed by the barbotage method and the spinal solution injection and patient was placed in the supine position with a wedge placed underneath.

Sensory blockade till the T6 dermatome level was confirmed by loss of sensation to cold ethyl chloride spray in the mid-line bilaterally and motor blockade with Bromage score[10] of 3 was considered as a successful block and the surgery was then continued. The total duration of the block was calculated once the sensory level was at S1 dermatome and Bromage score of 0. Bradycardia was defined as a heart rate of < 60 beats per minute[11] and hypotension as mean arterial pressure (MAP) < 50 mm Hg[12] and was treated with 5 mg ephedrine and 600 mcg of glycopyrrolate when needed.

Primary variables measured were: time to complete sensory and motor block with total duration of the block, time to first rescue analgesia after block regression in the post anaesthesia care unit (PACU) and mean PACU stay as secondary variables. Adverse effects observed were hypotension, nausea, vomiting and shivering. Demographic data were statistically described in terms of mean ± standard deviation (SD), frequencies and percentages when appropriate. A p-value of < 0.05 was considered statistically significant. All statistical calculations were performed using SPSS 26.0.

Results

A total of 240 patients were studied divided into the dexmedetomidine group (n = 120) and fentanyl group (n = 120) group. The mean age of patients in the dexmedetomidine group was 24.12 ± 2.22 years versus 24.20 ± 2.17 years in the fentanyl group. Both groups were comparable in age. The mean weight of patients in the groups was 75.31 ± 9.30 kg for dexmedetomidine and 75.80 ± 9.56 kg for the fentanyl group (Table 1).

Table 1: Age and height characteristics of patients in both groups (n = 240)

Variable	Dexmedetomidine group (n = 120)	Fentanyl group (n = 120)
Mean age (years)	24.1 ± 2.22	24.2 ± 2.17
Mean weight (kg)	75.3 ± 9.30	75.8 ± 9.56

When the primary outcome variables were seen, the time on onset for a sensory block in the dexmedetomidine group was delayed compared to the fentanyl group (4.35 ± 0.14 min and 3.39 ± 0.11 min, respectively), (p < 0.0001). The duration of the block was longer for the dexmedetomidine group with a mean time of 327.26 ± 12.60 min versus 243.3 ± 22.75 min (p < 0.0001). When comparing the motor blockade, the time of onset to successfully reach Bromage score 3 was similarly delayed in the dexmedetomidine group with a mean time of onset of 3.33 ± 0.12 min versus 2.36 ± 0.09 min (p < 0.0001). A similar trend was seen in the duration of the block with a mean time of 262.17 ± 13.31 min versus 203.34 ± 1.47 min (p < 0.0001) in the dexmedetomidine and fentanyl group, respectively (Table 2).

Time to first rescue analgesia after cessation of sensory block in both groups showed that the mean time for patients requiring iv analgesia was 274.7 ± 12.92 min in the dexmedetomidine group versus 243.49 ± 2.64 min in the fentanyl group (p < 0.0001). The mean length of PACU stay was comparable between both groups (p = 0.806).

When talking about the adverse effect profile between both the groups, the frequency of hypotension was 21 (17.5 %) patients in the dexmedetomidine group versus 28 (23.3 %) in the fentanyl group. Six (5.0 %) patients had nausea and vomiting in both the dexmedetomidine group and the fentanyl group, respectively. There was no incidence of shivering and respiratory depression in

Table 2: Comparison of block onset, block regression and rescue analgesia (n = 240)

Variable	Dexmedetomidine group (n = 120)	Fentanyl group (n = 120)	p-value
Sensory block			
Mean time for onset of block (T6) (min)	4.35 ± 0.14	3.39 ± 0.11	< 0.0001
Mean time for block regression (S1) (min)	327.26 ± 12.60	243.3 ± 22.75	< 0.0001
Motor block			
Mean time for onset of block (Bromage: 3) (min)	3.33 ± 0.12	2.36 ± 0.09	< 0.0001
Mean time for block regression (Bromage: 0) (min)	262.17 ± 13.31	203.34 ± 11.47	< 0.0001
Mean time to first dose rescue analgesia (min)	274.7 ± 12.92	243.49 ± 2.64	< 0.0001
Mean PACU stay (h)	5.10 ± 0.25	5.11 ± 0.24	0.8060

PACU: post anaesthesia care unit; Bromage: Bromage score;

Table 3: Incidence of side effects between groups (n = 240)

Variable	Dexmedetomidine group (n = 120)	Fentanyl group (n = 120)
Hypotension	21 (17.5 %)	28 (23.3 %)
Nausea/vomiting	6 (5.0 %)	6 (5.0 %)
Shivering	0 (0.0 %)	9 (7.5 %)
Respiratory depression	0 (0.0 %)	14 (11.7 %)

the dexmedetomidine group, however, nine (7.5 %) of patients exhibited shivering and 14 (11.7 %) patients had an episode of respiratory depression after the procedure (Table 3).

Discussion

Even though many studies have been done on adjuvants and their role in spinal anaesthesia, the role of adjuvants in the new formulation of levobupivacaine has not been studied, especially in presented demographic area and setups. Since levobupivacaine is a relatively new formulation associated with less cardiotoxicity and prolonged duration of action, it is preferable over precious regimes due to good patient safety and satisfaction.

Dexmedetomidine is a selective 2 agonist[13] and its effects on the spinal cord *via* subarachnoid administration are explained by stimulation of α2 receptors at the *substantia gelatinosa* of the dorsal horn leading to inhibition of the release of substance P.[14] The spinal mechanism is principal for the analgesic effects of dexmedetomidine even though there is evidence for both supraspinal and peripheral sites of action. Fentanyl is a pure μ receptor agonist and exerts its effects by binding to opioid receptors at the spinal cord level as well as para-spinal when absorbed.[15] Studies carried out by Khosravi et al[16] and Davis et al[17] concluded that dexmedetomidine was a better alternative to fentanyl when it came to the duration of the blockade and haemodynamic stability. However, when talking about the onset of the block, fentanyl was better at the initial onset for both sensory and motor blockade. This was confirmed by studies carried out by Hamed et al.[18]

When talking about mean PACU stay due to pain, there was no difference in the length of stay, however, the patient required more rescue iv analgesia in the PACU in the fentanyl group. This was also observed in a study carried out by Sun et al.[19]

A study carried out by Liu et al[20] also confirmed that dexmedetomidine was better at preventing shivering than other adjuncts. This effect was seen in presented study where no patients exhibited the adverse effect when administered with the drug as an adjunct. When assessing the degree of respiratory depression, fentanyl was observed to cause more respiratory depression than its counterpart. This is closely related to its spinal depressing effects as discussed above.

The limitations are that the study is single-centre only. A multi-centre study would result in a wider demographic area with more confirmative results. This study doesn't consider high-risk ASA III and IV cases.

Conclusion

Dexmedetomidine offers advantages over fentanyl as an adjunct to spinal anaesthesia with longer block duration and less adverse effects profile. It is recommended to use dexmedetomidine its better safety profile, longer duration and better hemodynamic stability. Fentanyl should be reserved when the early onset of the block is required in emergency cases.

Ethics

This study was approved by the local Ethics Committee at the Combined Military Hospital, decision No 241, dated 15 June 2021.

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None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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