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ORIGINAL RESEARCH **OBSTETRIC ANESTHESIA**

Comparative evaluation of intrathecal hyperbaric bupivacaine alone versus combined with dexmedetomidine for cesarean sections

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ABSTRACT

Background & Objective: This study examined the use of dexmedetomidine 5 µg as an adjuvant to 10 mg of intrathecal hyperbaric 0.5% bupivacaine in elective cesarean sections and aimed to assess dexmedetomidine's impact on block characteristics and post-operative pain management. As spinal anesthesia is commonly employed for cesarean deliveries, the study seeks to determine whether the addition of dexmedetomidine as an adjuvant can prolong the duration and enhance the quality of the block, leading to improved post-operative pain relief.

Methodology: This randomized controlled trial included 100 parturients undergoing elective cesarean section over a period of six months. Participants were allocated to either Group B or Group D using a non-random consecutive sampling technique. In Group D, 2 mL of 0.5% bupivacaine mixed with 0.05 mL of dexmedetomidine (5µg) was injected intrathecally, while Group B received 2 mL of 0.5% hyperbaric bupivacaine along with an equivalent volume of saline. Sensory and motor block assessments were conducted prior to the start of surgery. Post-operatively, the duration of motor block and post-operative pain relief were assessed.

Results: The addition of dexmedetomidine as an adjuvant to intrathecal bupivacaine resulted in significant reductions in the onset time of sensory block (4.22 ± 0.79 min vs 5.66 ± 1.21 min) and motor block (4.20 ± 0.81min vs 6.32 ± 1.20 min) ($P < 0.001$). Furthermore, the duration of motor block was longer in the dexmedetomidine + bupivacaine group compared to the bupivacaine alone group (7.32 ± 0.95 h vs 4.38 ± 1.27 h). Additionally, patients who received intrathecal dexmedetomidine as an adjuvant to bupivacaine experienced significantly longer durations of post-operative analgesia (7.32 ± 0.95 h) as compared to the bupivacaine alone group (4.38 ± 1.27 h) ($P < 0.001$).

Conclusion: Dexmedetomidine as an intrathecal adjuvant to hyperbaric bupivacaine extends the duration of analgesia and motor block, providing prolonged pain relief. Additionally, it exhibits an early onset of sensory and motor block, ensuring prompt pain relief and rapid anesthesia onset.

Clinical Trial Registration: [www.clinicaltrials.gov], identifier: ID NCT05469529

Abbreviations: CS - cesarean section; OT - Operation Theater; SA - Spinal anesthesia; VAS - visual analogue scale;

Keywords: cesarean section, dexmedetomidine, bupivacaine, spinal anesthesia

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1. INTRODUCTION

Global cesarean section (CS) rates have significantly increased from approximately 7% in 1990 to the current 21%, surpassing the WHO's recommended ideal CS rate of 10%-15%. Similarly, there has been a gradual rise in the cesarean deliveries in Pakistan over the past two decades, escalating from 3.2% in 1990 to 19.6% in 2018.[1]

Spinal anesthesia (SA) has become the technique of choice for cesarean deliveries as it offers superior pain management, facilitates early mobilization, and enables a quicker resumption of regular activities, when compared to general anesthesia. It also avoids the risks associated with general anesthetics and failed intubation and is better in terms of the APGAR scores of the babies.[2,3] Intrathecal hyperbaric bupivacaine is used for cesarean deliveries in most hospitals worldwide. However, it has been associated with certain challenges like intra-operative hypotension, nausea, inadequate visceral block, limited post-operative analgesia of short duration of action.[4-6] To address these concerns, various adjuvants such as opioids, benzodiazepines, alpha-2 agonists, neostigmine, and ketamine are being utilized to enhance the quality and prolong the duration of the block and analgesia.[4, 6-9]

Dexmedetomidine is a highly selective alpha$_2$ agonist with notable sedative and anesthetic properties. Its mechanism of action involves the activation of G-proteins in the brainstem, resulting in the inhibition of norepinephrine release.[10] Although not FDA-approved for intrathecal use, dexmedetomidine is commonly employed as an adjuvant in clinical settings.

This study was designed to evaluate the effects of adding dexmedetomidine 5 µg as adjuvant to intrathecal hyperbaric 0.5% 10 mg in elective CS. The primary focus was to evaluate how this combination affects the characteristics of the block as well as the effectiveness of post-operative analgesia.

2. METHODOLOGY

The study protocol was approved by the Ethical Review Committee of Khan Research Laboratories Hospital, Islamabad, Pakistan (Ref ERC: KRL-HI-ERC/Apr21/18) and was registered on ClinicalTrials.gov (ID NCT05469529). Written informed consent was obtained from all enrolled participants. A total of one hundred pregnant, full-term, parturients, with singleton pregnancy; ASA physical status II-III; aged between 18 and 45 y, scheduled for elective CS under SA from 15 April 2022 to 15 Sep 2022 were enrolled in the study. Parturients with contraindications to regional anesthesia, allergy to dexmedetomidine, any pre-existing non-obstetric medical comorbidities, e.g., hypertension, cardiopulmonary disease, epilepsy, chronic kidney disease; pre-existing obstetrical comorbidities (such as insulin-dependent diabetes mellitus, uncontrolled pregnancy induced hypertension, pre-eclampsia, eclampsia, placenta previa, placenta accreta), HR < 60 bpm and systolic BP < 100 mmHg were excluded. Patients were allocated to either of the two groups - Group B and Group D, according to non-random consecutive sampling technique, with every third patient in the elective surgery list being enrolled. The patients falling on odd numbers were assigned to Group B, while those falling on even numbers were assigned to Group D.

All parturients were premedicated with tab omeprazole 20 mg at 6:00 hours. Two 18G IV cannulas were inserted in Operation Theater (OT). Pre-hydration was performed with lactated ringer's solution at a rate of 20 mL/kg. Standard monitoring including pulse oximeter, non-invasive blood pressure (NIBP) and ECG was initiated upon arrival in the OT, with baseline readings recorded. The researcher prepared intrathecal drugs followed by aseptic preparation of the patient's back and identification of L3-L4 space. Local anesthetic was infiltrated and spinal puncture was performed with 25-gauge pencil point spinal needle. Group D received 2 mL of 0.5% hyperbaric bupivacaine (10 mg) combined with 0.05 mL of dexmedetomidine (5µg). while Group B received 2 mL of 0.5% hyperbaric bupivacaine combined with an equivalent volume of saline, injected over a duration of 20 seconds. The parturients were positioned supine with 15% left tilt after the injection and the timer was started. Intraoperative hypotension and bradycardia were managed by using phenylephrine and atropine, respectively. Post-operatively, tramadol 50 mg and paracetamol 1 g were used as rescue analgesia. Injection paracetamol 1 g IV was given every 6 h after the first dose for 24 h.

Data collection was conducted by fellow colleagues who had similar professional experience and were blinded to the administered drugs. Sensory blockade was assessed using the pinprick method with a blunt 27G hypodermic needle every minute until loss of sensation at the xiphoid (T6 level) was achieved. The quality of motor blockade was assessed using the modified Bromage scale, initially at 3 min and then at one-minute intervals until Bromage I motor block was attained. Post-operative analgesia was evaluated every half hour during the first 3 h and then hourly using a visual analogue scale (VAS). The assessments were continued until a VAS score of 4 or more was achieved or the time of the request for the first analgesic was made by the patient; whichever occurred first. The duration of motor block was determined using the Bromage score along with VAS score. The time

Table 1: Demographic profile of the patients in two groups

Parameter	Group B (n = 50)	Group BD (n = 50)	P-value
Age (y)	28.90 ± 4.86	28.02 ± 5.13	0.381*
BMI (kg/m^2)	30.31 ± 5.53	30.76 ± 3.61	0.633*
ASA Status			
II	25 (50)	27 (54)	0.689**
III	25 (50)	23 (46)	

*Values are presented as mean ± SD or n (%); * P > 0.05 (Independent Samples t Test); ** P > 0.05 (Fischer Exact Test)*

taken to regain full flexion of the knees and hips was also recorded.

2.1. Sample size

Sample size of 50 in each group was determined using the WHO sample size calculator for a hypothesis test on two sample proportions (one-sided test) with a significance level of 5% and 90% power. The calculation was based on a study by Sushruth MR et al.[5] The study reported peak sensory levels at 3.98 ± 1.8 min for the dexmedetomidine group and 4.98 ± 1.6 min for the control group.

2.2. Statistical analysis

Data obtained was tabulated and analyzed in Statistical Package for Social Science (SPSS version 22). Quantitative variables such as age, BMI, time to sensory and motor block and duration of analgesia were measured as mean ± standard deviation. Independent sample t-test was used to compare the two groups and P ≤ 0.05 was considered as significant. Qualitative variables like ASA status was measured as frequency and percentage by using Fischer Exact Test.

3. RESULTS

In the current study, 100 patients were enrolled and were assigned to two groups, i.e., Group B (n=50) and Group D (n=50). All participants completed the study. The two groups exhibited similar characteristics with regards to age, BMI, ASA status and baseline vital signs (P > 0.05) (Table 1).

Throughout the study, no patient encountered any instances of respiratory distress. Peripheral oxygen saturation levels consistently remained greater than 95% in all patients.

Group D demonstrated a significantly quicker onset of sensory block compared to Group B (P < 0.001) and significantly faster mean onset time of motor block compared to Group B (P < 0.001) (Table 2).

The study also evaluated duration of post-op pain relief and motor block in the two groups. Group D experienced a significantly longer mean duration of post-operative pain relief as well as the motor block in comparison to Group B (P < 0.001) (Table 2).

These findings indicate that 0.5% hyperbaric bupivacaine combined with 0.05 mL of dexmedetomidine outperformed 0.5% hyperbaric bupivacaine in terms of an earlier block and prolonged duration of pain relief.

4. DISCUSSION

In this prospective, randomized study, it was observed that the addition of 5 µg of dexmedetomidine to 0.5% bupivacaine intrathecally during cesarean section reduced the sensory and motor block onset time while prolonging the post-operative analgesia and motor blockade duration.

Anesthesiologists, across the world, use a variety of drugs in the subarachnoid and epidural spaces solely, as well as adjuvants to local anesthetics, to provide anesthesia and pain relief. Adjuvants are added to local anesthetics to improve efficacy, which includes a faster onset and a longer duration of the block. These effects lead to a decrease in the total dose of local anesthetics, thereby reducing their side effects.

Dexmedetomidine is a selective and potent α_2-adrenoceptor agonist that is used universally owing to its properties as an anxiolytic, sedative, and analgesic agent, and produces its clinical effects by binding to G-Protein-coupled α_2-AR receptors which are found throughout the central,

Table 2: Comparison of the block characteristics between the two groups

Parameters	Group B (n = 50)	Group BD (n = 50)	P value*
Time to sensory block (min)	5.66 ± 1.21	4.22 ± 0.79	< 0.001
Time to motor block (min)	6.32 ± 1.20	4.20 ± 0.81	< 0.001
Mean duration of post-op pain relief (h)	3.84 ± 0.99	6.50 ± .03	< 0.001
Mean duration of motor block (h)	4.38 ± 1.27	7.32 ± .95	< 0.001

*Values are presented as mean ± SD; *Independent Samples t test*

peripheral and autonomic nervous system, as well as vital organs and blood arteries. The spinal cord is the primary site for the analgesic activity whereas the locus ceruleus in the brain stem is the primary site for the sedative action. Compared with clonidine, which is also an α_2-agonist that has been in use for several decades, dexmedetomidine differs in the way that it has a greater selectivity for α_2-receptors (α_2:α_1 ratio of 1620:1 vs. 220:1). Dexmedetomidine is a more compelling sedative than clonidine because it blocks the effects of the sedative 2-adrenoceptors in the central nervous system. Patients who get dexmedetomidine-based sedation are nevertheless easily arousable, which is an important characteristic.

Dexmedetomidine is frequently combined with bupivacaine and ropivacaine during SA. Several studies used dexmedetomidine as an adjuvant to spinal anesthetics alone or in combination with other drugs but only a limited number of systematic reviews and meta-analyses have been done. As dexmedetomidine has become available in our region in only recent years we have evidence lacking to support the use of dexmedetomidine as an intrathecal adjuvant. To the best of authors' knowledge, there was no published report on the administration of bupivacaine plus dexmedetomidine in cesarean patients in this region to evaluate the onset or duration of the blocks.

Our study showed significant change in the block characteristics as it provided promising results in terms of quicker onset of sensory and motor block on the addition of low dose of dexmedetomidine (i.e. 5 µg) to the conventional dose of intrathecal bupivacaine (i.e. 10 mg) already being used. The addition resulted in longer duration of post-operative analgesia and time first request for analgesics.

Alam et al. studied 100 patients who underwent lower abdominal procedures. Their research demonstrated that the addition of 10 µg of dexmedetomidine to bupivacaine intrathecally, resulted in a rapid onset of both sensory and motor block. Despite the smaller dose used by us, similar results were achieved reflecting the significance of even a modest dose of dexmedetomidine in the obstetric population.[11] As studied by Li et al. intrathecal administration of 5 µg of dexmedetomidine has been observed to enhance the effectiveness of epidural labor analgesia. This results in a quicker onset of pain relief and a reduced need for epidural ropivacaine when compared to control group.[12] In a study by Azemati et al. involving ninety pregnant women, the research examined the impact of adding 5 µg of dexmedetomidine to 10 mg bupivacaine in comparison to other study group using bupivacaine alone and bupivacaine with meperidine. Interestingly, their findings indicated that the addition of dexmedetomidine did not significantly affect the onset times for sensory and motor blocks when compared to other treatment groups. This outcome stands in contrast to our study, where the dexmedetomidine group exhibited a faster onset. Furthermore, the bupivacaine + dexmedetomidine group displayed significantly longer block regression times ($P < 0.001$).[13] In another study by Sun et al., on 90 term parturients undergoing CS, three intrathecal approaches were compared: bupivacaine alone, bupivacaine plus fentanyl and bupivacaine plus dexmedetomidine. The bupivacaine group supplemented with dexmedetomidine exhibited a longer regression time to T10, prolonged sensory block duration and delayed onset of post-operative pain compared to the other groups. This aligns with our study's findings regarding post-operative pain relief but differs in terms of motor block.[14]

In our study, the onset time of sensory as well as motor block was considerably shorter in dexmedetomidine group compared to the bupivacaine group, aligning with previously published literature.[9,11,15] Furthermore, the dexmedetomidine group displayed an extended duration of motor block and post-operative analgesia, as shown by Zhang et al., where the addition of 5 µg of dexmedetomidine to ropivacaine prolonged both sensory and motor block durations.[16]

5. LIMITATIONS

The research lacked investigation of the adverse effects on the mother as well as on the newborn outcome. We excluded patients with pre-existing comorbidities, and administered only a single dose of dexmedetomidine. Further research into the potential side effects of intrathecal dexmedetomidine, the optimal dose of dexmedetomidine, and the best feasible minimum dose of bupivacaine required to accomplish the desired goal while minimizing the adverse effects is recommended.

6. CONCLUSION

It is concluded that addition of dexmedetomidine as an adjuvant to 0.5% bupivacaine in spinal anesthesia for cesarean sections improves both sensory and motor block characteristics, prolongs the postoperative analgesia duration and improves outcomes. Moreover, it may prove useful in emergency surgeries where urgent surgery is required as onset is quicker.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

RAQ: Study concept and design, conduction of study work, data collection and analysis, manuscript preparation

HJ: Literature Review, critical revision of content for improvement and intellectual input

MS: Literature Review, Data Analysis

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