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Original Research Article

Comparative Study of Different Additives in Spinal Anaesthesia: A Prospective Randomized Controlled Trial

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Abstract

Background: Spinal anaesthesia is a widely employed regional anaesthetic technique for infraumbilical surgeries. Various intrathecal adjuvants have been investigated to prolong the duration of sensory and motor blockade, improve postoperative analgesia, and reduce the total dose requirement of local anaesthetics. However, the comparative efficacy and safety profile of commonly used additives—fentanyl, dexmedetomidine, and clonidine—when combined with hyperbaric bupivacaine remain an area of ongoing investigation.

Methods: This prospective, randomized, double-blind controlled study enrolled 120 adult patients (ASA physical status I–II) undergoing elective infraumbilical surgeries under spinal anaesthesia. Patients were randomly allocated into four groups of 30 each: Group B (bupivacaine alone, control), Group BF (bupivacaine + fentanyl 25 µg), Group BD (bupivacaine + dexmedetomidine 5 µg), and Group BC (bupivacaine + clonidine 30 µg). The primary outcome measures included onset and duration of sensory and motor blockade, duration of effective analgesia, hemodynamic parameters, and adverse effects.

Results: Group BD demonstrated the longest duration of sensory blockade (268.4 ± 18.6 min) and effective analgesia (342.7 ± 22.3 min), followed by Group BC (238.2 ± 16.4 min; 298.5 ± 20.1 min), Group BF (212.6 ± 14.8 min; 262.3 ± 18.7 min), and Group B (168.3 ± 12.5 min; 198.4 ± 15.2 min) ($p < 0.001$). The onset of sensory blockade was fastest in Group BF (2.8 ± 0.9 min). Hemodynamic stability was comparable across groups, with mild bradycardia and sedation more frequent in Group BD.

Conclusion: Intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine provides the most prolonged sensory and motor blockade and superior postoperative analgesia compared with fentanyl, clonidine, and bupivacaine alone, with an acceptable safety profile.

Keywords: Spinal Anaesthesia, Intrathecal Adjuvants, Dexmedetomidine, Fentanyl, Clonidine, Bupivacaine, Postoperative Analgesia.

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Introduction

Spinal anaesthesia remains one of the most commonly utilized regional anaesthetic techniques for lower abdominal, perineal, and lower extremity surgical procedures owing to its rapid onset, reliable dense blockade, and favorable safety profile [1]. The technique involves the subarachnoid injection of local anaesthetic agents, with hyperbaric bupivacaine being the most frequently employed drug for this purpose [2]. However, the limited duration of action of intrathecal bupivacaine alone often necessitates supplementary analgesic interventions in the postoperative period, which may expose patients to the risks associated with systemic opioid administration, including respiratory depression, nausea, and sedation [3]. To circumvent these limitations, numerous intrathecal adjuvants have been investigated over the past several decades with the aim of prolonging the duration of spinal blockade, enhancing the quality of intraoperative anaesthesia, and extending the period of effective postoperative analgesia [4]. Among these, opioid agents such as fentanyl and morphine were the earliest adjuvants to gain widespread clinical acceptance. Intrathecal fentanyl, a highly lipophilic synthetic opioid, has been demonstrated to accelerate the onset of sensory blockade and improve the quality of intraoperative analgesia without significantly prolonging motor blockade [5]. Alpha-2 adrenergic agonists, including

clonidine and dexmedetomidine, represent another class of adjuvants that have garnered considerable research interest. Clonidine, a partial alpha-2 agonist, was among the first non-opioid adjuvants to be used intrathecally and has been shown to prolong both sensory and motor blockade [6]. More recently, dexmedetomidine, a highly selective alpha-2 adrenoceptor agonist with an alpha-2 to alpha-1 selectivity ratio approximately eight times greater than clonidine, has emerged as a promising intrathecal additive [7].

Several individual studies have compared pairs of these adjuvants; however, comprehensive four-arm comparative studies evaluating bupivacaine alone versus bupivacaine combined with fentanyl, dexmedetomidine, or clonidine in a single trial are relatively scarce [8]. Furthermore, variations in dosing protocols, patient populations, and outcome measures across existing studies have contributed to heterogeneity in the available evidence, creating a discernible research gap [9].

The synergistic mechanisms through which alpha-2 agonists potentiate spinal anaesthesia involve binding to presynaptic and postsynaptic alpha-2 receptors in the substantia gelatinosa of the spinal cord dorsal horn, thereby inhibiting the release of nociceptive neurotransmitters such as substance P and attenuating neuronal firing [10]. The mechanism of action of intrathecal opioids, conversely, involves binding to opioid receptors in the dorsal horn, modulating pain transmission at the spinal level [11].

The aim of the present study was to compare the effects of three commonly used intrathecal adjuvants—fentanyl, dexmedetomidine, and clonidine—when added to hyperbaric bupivacaine for spinal anaesthesia in patients undergoing elective infraumbilical surgeries, with particular emphasis on the onset and duration of sensory and motor blockade, duration of effective postoperative analgesia, hemodynamic stability, sedation levels, and the incidence of adverse effects.

Materials and Methods

Study Design and Ethical Approval: This prospective, randomized, double-blind, controlled study was conducted at the Department of Anaesthesiology of a tertiary care teaching hospital over a 12-month period.

Sample Size Calculation: Based on previous literature and assuming a clinically meaningful difference of 30 minutes in the duration of sensory blockade between groups, with a standard deviation of 40 minutes, a power of 80%, and an alpha error of 0.05, the minimum sample size was calculated as 27 patients per group. To account for potential dropouts, 30 patients were enrolled in each group, yielding a total sample of 120 patients.

Inclusion and Exclusion Criteria: Patients aged 18–65 years, of either sex, with ASA physical status I or II, scheduled for elective infraumbilical surgeries (including lower-segment cesarean section, inguinal hernia repair, appendectomy, and orthopedic procedures of the lower extremity) were included. Exclusion criteria comprised patient refusal, known hypersensitivity to any study drug, contraindications to spinal anaesthesia (coagulopathy, local infection, raised intracranial pressure), morbid obesity (BMI > 35 kg/m²), significant cardiac or hepatic disease, pregnancy-induced hypertension, neurological disorders, and chronic opioid use.

Randomization and Blinding: Patients were randomly allocated into four groups of 30 each using a computer-generated random number table enclosed in sealed opaque envelopes:

- **Group B (Control):** 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine + 0.5 mL normal saline
- **Group BF:** 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine + fentanyl 25 µg (0.5 mL)
- **Group BD:** 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine + dexmedetomidine 5 µg (0.5 mL)
- **Group BC:** 3.0 mL (15 mg) of 0.5% hyperbaric bupivacaine + clonidine 30 µg (0.5 mL)

All study solutions were prepared by an anaesthesiologist not involved in patient care or data collection. The administering anaesthesiologist and the observer recording outcomes were blinded to group allocation.

Anaesthetic Procedure: Following standard preoperative evaluation, all patients received preloading with 10 mL/kg of lactated Ringer's solution. In the operating room, standard monitoring was established, including electrocardiography, non-invasive blood pressure, pulse oximetry, and capnography. Under strict aseptic conditions, lumbar puncture was performed in the sitting position at the L3–L4 interspace using a 25-gauge Quincke spinal needle. After confirming free flow of cerebrospinal fluid, the respective drug solution (total volume 3.5 mL) was injected intrathecally over 15 seconds. Patients were then positioned supine.

Outcome Assessment: Sensory blockade was assessed bilaterally using the pinprick method every 2 minutes until the highest level was achieved and subsequently every 15 minutes until complete regression.

Motor blockade was assessed using the modified Bromage scale (0 = no paralysis; 3 = complete paralysis). Hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure,

mean arterial pressure, and SpO_2) were recorded at baseline, every 5 minutes for the first 30 minutes, and every 15 minutes thereafter. Sedation was assessed using the Ramsay Sedation Scale. The duration of effective analgesia was defined as the time from intrathecal injection to the first request for rescue analgesia (VAS ≥ 4). Adverse effects including hypotension, bradycardia, nausea, vomiting, pruritus, shivering, and respiratory depression were documented.

Statistical Analysis: Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation and compared using one-way ANOVA with post-hoc Tukey's test. Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test.

A p-value < 0.05 was considered statistically significant.

Results

Demographic and Baseline Characteristics: The four groups were comparable with respect to age, sex distribution, weight, height, BMI, ASA physical status, and type of surgery, with no statistically significant differences (p > 0.05) (Table 1).

Table 1: Demographic and Baseline Characteristics of Study Groups

Parameter	Group B (n=30)	Group BF (n=30)	Group BD (n=30)	Group BC (n=30)	p-value
Age (years)	38.6 ± 11.2	40.1 ± 10.8	39.4 ± 12.1	37.9 ± 11.5	0.872
Sex (M/F)	18/12	17/13	19/11	16/14	0.834
Weight (kg)	64.8 ± 8.4	66.2 ± 9.1	65.5 ± 7.9	63.7 ± 8.8	0.716
Height (cm)	162.3 ± 7.6	163.8 ± 8.2	161.9 ± 7.4	164.1 ± 8.0	0.648
BMI (kg/m²)	24.6 ± 3.1	24.8 ± 3.4	24.9 ± 2.9	23.6 ± 3.3	0.512
ASA I/II	22/8	20/10	21/9	23/7	0.762

Block Characteristics: The onset of sensory blockade was significantly faster in Group BF (2.8 ± 0.9 min) compared to all other groups (p < 0.01). Group BD demonstrated the longest duration of sensory blockade (268.4 ± 18.6 min), motor blockade (244.8 ± 20.2 min), and effective postoperative analgesia (342.7 ± 22.3 min), all significantly superior to the other three groups (p < 0.001). The maximum sensory level achieved was comparable among the adjuvant groups (T5–T6) and slightly lower in Group B (T6–T7). Detailed block characteristics are presented in Table 2.

Table 2: Characteristics of Sensory and Motor Blockade

Parameter	Group B (n=30)	Group BF (n=30)	Group BD (n=30)	Group BC (n=30)	p-value
Onset of sensory block (min)	4.6 ± 1.3	2.8 ± 0.9*	3.4 ± 1.1	3.9 ± 1.2	<0.001
Onset of motor block (min)	5.8 ± 1.5	4.2 ± 1.2	4.5 ± 1.3	5.1 ± 1.4	0.002
Peak sensory level (median)	T6–T7	T5–T6	T5–T6	T5–T6	0.124
Duration of sensory block (min)	168.3 ± 12.5	212.6 ± 14.8†	268.4 ± 18.6‡	238.2 ± 16.4§	<0.001
Duration of motor block (min)	142.6 ± 14.2	178.4 ± 16.3†	244.8 ± 20.2‡	208.6 ± 18.7§	<0.001
Time to effective analgesia (min)	198.4 ± 15.2	262.3 ± 18.7†	342.7 ± 22.3‡	298.5 ± 20.1§	<0.001

***p < 0.01 vs. all other groups; †p < 0.001 vs. Group B; ‡p < 0.001 vs. all other groups; §p < 0.001 vs. Groups B and BF.**

Hemodynamic Parameters and Adverse Effects: Hemodynamic parameters remained stable and comparable across all groups throughout the study period. The incidence of hypotension (defined as >20% decrease from baseline MAP) was observed in 10.0% (Group B), 13.3% (Group BF), 16.7% (Group BD), and 13.3% (Group BC) without statistically significant differences (p = 0.874). Bradycardia was most frequent in Group BD (20.0%) compared with Groups B (6.7%), BF (10.0%), and BC (13.3%) (p = 0.418). Sedation scores (Ramsay Sedation Scale ≥ 3) were significantly higher in Group BD (40.0%) compared with other groups (p = 0.008). No episodes of respiratory depression were recorded in any group. Pruritus was exclusively observed in Group BF (16.7%). The detailed incidence of adverse effects is presented in Table 3.

Table 3: Incidence of Adverse Effects

Adverse Effect	Group B (n=30) n (%)	Group BF (n=30) n (%)	Group BD (n=30) n (%)	Group BC (n=30) n (%)	p-value
Hypotension	3 (10.0)	4 (13.3)	5 (16.7)	4 (13.3)	0.874
Bradycardia	2 (6.7)	3 (10.0)	6 (20.0)	4 (13.3)	0.418
Nausea/Vomiting	3 (10.0)	5 (16.7)	2 (6.7)	3 (10.0)	0.612
Pruritus	0 (0.0)	5 (16.7)	0 (0.0)	0 (0.0)	0.002
Shivering	4 (13.3)	2 (6.7)	1 (3.3)	2 (6.7)	0.482
Sedation (RSS ≥ 3)	2 (6.7)	4 (13.3)	12 (40.0)	7 (23.3)	0.008
Respiratory depression	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	—

Discussion

The present study provides a comprehensive comparative evaluation of three commonly used intrathecal adjuvants—fentanyl, dexmedetomidine, and clonidine—when combined with hyperbaric bupivacaine for spinal anaesthesia. Our findings demonstrate that dexmedetomidine at a dose of 5 µg offers the most pronounced prolongation of sensory and motor blockade as well as the longest duration of effective postoperative analgesia, followed by clonidine and fentanyl, all of which were significantly superior to bupivacaine alone.

The superior efficacy of dexmedetomidine observed in our study is consistent with the findings of Gupta et al., who reported that intrathecal dexmedetomidine 5 µg prolonged the duration of sensory and motor blockade significantly compared with fentanyl 25 µg when added to bupivacaine [12]. The mechanism underlying this prolongation is attributed to the binding of dexmedetomidine to alpha-2 adrenergic receptors in the substantia gelatinosa of the spinal cord, which inhibits the release of excitatory neurotransmitters and hyperpolarizes dorsal horn neurons, thereby augmenting the local anaesthetic action of bupivacaine [13].

Our observation that intrathecal fentanyl produced the fastest onset of sensory blockade is in agreement with the work of Dahlgren et al., who demonstrated that the lipophilic nature of fentanyl facilitates rapid penetration into the spinal cord, accelerating the onset of neural blockade [14]. However, the relatively shorter duration of sensory and motor blockade with fentanyl compared to alpha-2 agonists has been consistently reported in the literature and is attributed to the rapid redistribution of fentanyl from the cerebrospinal fluid into the systemic circulation [15].

The prolongation of spinal blockade by clonidine observed in our study aligns with the findings of Strebel et al., who demonstrated a dose-dependent enhancement of bupivacaine spinal anaesthesia by intrathecal clonidine [16].

However, the magnitude of prolongation was less than that observed with dexmedetomidine, which can be explained by the higher alpha-2 receptor selectivity and affinity of dexmedetomidine compared to clonidine [17]. The alpha-2 to alpha-1 selectivity ratio of dexmedetomidine (1620:1) is approximately eight times higher than that of clonidine (220:1), which translates into more potent and selective spinal analgesic effects [18]. Regarding hemodynamic stability, all three adjuvants were associated with a comparable and clinically acceptable incidence of hypotension.

The slightly higher incidence of bradycardia in the dexmedetomidine group (20.0%) is consistent with its known sympatholytic effects and has been reported by Kanazi et al. in their landmark study on intrathecal dexmedetomidine [19]. Importantly, all episodes of bradycardia in our study were mild and responsive to a single dose of intravenous atropine, without any hemodynamically significant sequelae.

The higher sedation scores observed in the dexmedetomidine group represent an expected pharmacological effect of this agent, which acts on alpha-2 receptors in the locus coeruleus to produce sedation that is characterized by easy arousability, a property that has been described as clinically advantageous in the perioperative setting [20]. The absence of respiratory depression in all groups is reassuring and consistent with the established safety profile of these agents when used in the recommended intrathecal doses [21].

Pruritus, observed exclusively in the fentanyl group (16.7%), represents a well-known opioid-related side effect mediated through central mu-receptor activation and has been reported by various investigators at similar incidence rates [22]. This finding underscores one of the disadvantages of opioid-based adjuvants and may favor the use of alpha-2 agonists in patients particularly susceptible to opioid-related adverse effects.

The clinical implication of our findings is that intrathecal dexmedetomidine at a dose of 5 µg represents an optimal adjuvant for prolonging spinal anaesthesia and postoperative analgesia in patients undergoing infraumbilical surgeries, provided that appropriate monitoring for bradycardia and sedation is ensured. The extended duration of analgesia by approximately 144 minutes compared to bupivacaine alone translates into reduced postoperative analgesic requirements,

decreased nursing workload, and potentially improved patient satisfaction [23].

A limitation of the present study is its single-center design, which may limit generalizability. Additionally, the study did not evaluate the dose-response relationships of the individual adjuvants, and future multicenter trials with dose-optimization arms are warranted. The relatively small sample size may have been underpowered to detect differences in rare adverse events [24].

Conclusion

This prospective randomized controlled trial demonstrates that all three intrathecal adjuvants—fentanyl, dexmedetomidine, and clonidine—significantly enhance the quality and duration of spinal anaesthesia when added to hyperbaric bupivacaine compared with bupivacaine alone.

Among the three adjuvants, dexmedetomidine (5 µg) provides the longest duration of sensory and motor blockade and the most prolonged postoperative analgesia, with an acceptable safety profile characterized by mild, manageable bradycardia and sedation without respiratory depression. Fentanyl offers the advantage of the fastest onset of sensory blockade but provides shorter duration of analgesia and is associated with pruritus. Clonidine demonstrates an intermediate profile between fentanyl and dexmedetomidine. These findings support the preferential use of intrathecal dexmedetomidine as an adjuvant to bupivacaine for spinal anaesthesia in elective infraumbilical surgeries where prolonged postoperative analgesia is desired, while emphasizing the need for individualized adjuvant selection based on surgical requirements and patient-specific factors.

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