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Efficacy of Intrathecal Buprenorphine or Clonidine as an Adjuvant to Bupivacaine versus Bupivacaine alone in Spinal Anaesthesia

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ABSTRACT

Background: Spinal anesthesia is widely used for lower limb and abdominal surgeries due to its simplicity, rapid onset, and effective sensory–motor block. Bupivacaine remains the most common agent; however, its limited duration of action necessitates the use of adjuvants. Buprenorphine and clonidine have been evaluated as intrathecal additives to enhance analgesia and block quality.

Methods: A prospective, randomized comparative study was conducted on 129 patients (ASA I–II), aged 18–50 years, scheduled for lower abdominal or lower limb surgeries under spinal anesthesia. Participants were divided into three equal groups: Group BB received 0.5% hyperbaric bupivacaine (15 mg) with buprenorphine (60 mcg), Group BC received bupivacaine with clonidine (30 mcg), and Group BN received bupivacaine alone. All solutions were diluted to 3.2 ml. Patients and observers were blinded to group allocation. Demographic variables and intraoperative parameters were recorded. Outcomes assessed included onset, spread, regression of block, and side effects.

Results: Demographic characteristics and ASA status were comparable among groups. Clonidine as an adjuvant resulted in faster onset of sensory block, earlier attainment of highest dermatomal level, and quicker two-segment regression compared to buprenorphine and control. Buprenorphine produced prolonged regression time, suggesting extended postoperative analgesia. Incidence of side effects such as bradycardia, hypotension, nausea, and dryness of mouth did not differ significantly across groups.

Conclusion: Clonidine enhances block onset and spread, while buprenorphine prolongs regression and analgesia. Both agents improve the efficacy of intrathecal bupivacaine without significant adverse effects. Choice of adjuvant should be individualized based on surgical and patient needs.

Key-words: Spinal anesthesia, Bupivacaine, Clonidine, Buprenorphine, Adjuvant

INTRODUCTION

Spinal anesthesia, also known as spinal block, is a type of regional anesthesia commonly used in lower limb and lower abdominal surgeries as well as childbirth procedures. It involves injecting an anesthetic medication directly into the cerebrospinal fluid in the subarachnoid space of the spinal cord.[1,2]

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Any surgeries performed below the umbilicus, such as groin hernia repair, Haemorrhoid surgery, Hysterectomy, Caesarean section, Prostate surgery, and genital surgery, are customarily performed under spinal anaesthesia. Additionally, spinal anaesthetics are used for orthopaedic surgery on the limbs, including the joints and bones. This technique has demonstrated good effectiveness, predictability, increased patient satisfaction, low complication rate, superior pain control compared to intravenous narcotics, earlier recovery of bowel function, reduced requirement for systemic opioids, easier breathing as a result of improved pain control, and easier participation in physical therapy.[3,4] While spinal anesthesia is generally safe, there are potential complications, including headache, nerve damage,

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infection, allergic reactions, and respiratory depression. Headaches are a common side effect, often caused by leakage of cerebrospinal fluid from the injection site. These headaches are usually positional and can be managed with conservative measures. When it comes to spinal anaesthesia, the most common drugs that are employed are local anaesthetics [3]. Rapid start of action and rapid cessation of action without side effects or with minimum side effects are the characteristics of the optimum local anaesthetic for spinal anaesthesia in day surgery. These traits are essential for the day surgery procedure. At present, bupivacaine is the local anaesthetic that is utilised the most frequently for spinal anaesthesia [4] .

The standard doses of Bupivacaine are linked to a sustained and powerful block of sensory and motor function, as well as a severe block of sympathetic function. Additionally, compared to Morphine, Buprenorphine is approximately thirty times more powerful than the agonist-antagonist opioid. In addition to having analgesic effects on the spinal and supraspinal regions, it is a lipid-soluble analogue of the alkaloid thebaine that acts on the central nervous system [5]. Furthermore, it has a counteracting effect on respiratory depression, although it does not affect analgesia. The ability of buprenorphine to have an antihyperalgesic effect contributes to the prevention of central sensitization. As a result of its high lipid solubility, high affinity for opioid receptors, and long duration of action, buprenorphine is an excellent choice for use as an adjuvant to intrathecal LA in the management of moderate to severe painful symptoms following surgical procedures [6]. Buprenorphine is widely available in a preparation that does not contain any preservatives and is compatible with the cerebrospinal fluid (CSF). Intrathecal doses are substantially less than parenteral doses, ranging from 30 µg to 150 µg. It is well known that these dosages prolong analgesia without impairing motor or sensory function. Following neuraxial injection, the purpose of this study was to investigate whether or not the administration of intrathecal Buprenorphine or Clonidine as an adjuvant to 0.5% hyperbaric Bupivacaine is more effective than the administration of hyperbaric Bupivacaine alone in the context of spinal anaesthesia [7].

MATERIALS AND METHODS

Study Design and Setting- This prospective, randomized comparative study was conducted at SNR District Hospital, Kolar, on patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia, during the period from October 2022 to January 2024.

Inclusion criteria

- All patients between the ages of 18 and 50 years.
- Male and female genders.
- Patients belonging to ASA grade I-II status.
- Patients scheduled for lower abdominal and lower limb surgeries.
- Patients with written informed consent.

Exclusion Criteria

- Patients having local infection, allergy to local anaesthetics, bleeding diathesis, neurological disorder and raised intracranial tension.
- Pregnant women and lactating mothers.
- ASA grade 3, 4 or 5.
- Body weight more than 100 kg and height less than 130 cm.
- Spinal deformity, post-spinal surgeries.

Methodology- Demographic details like age, height, weight, sex and BMI were recorded. Patients were randomly divided into three groups. All the patients underwent a thorough preanesthetic checkup. After the routine preoperative assessment, patients were kept nil per oral from midnight the day before surgery. Routine investigations like complete hemogram, Blood group, BT, CT, Renal function test (RFT), Random blood sugar (RBS), HbsAg, and HIV were done. ECG and Chest x-ray were done depending upon the age of the patient, clinical conditions. After shifting to the preoperative room, baseline vital parameters were recorded.

Statistical Analysis- Data were analyzed using SPSS version 12. Continuous variables were presented as mean±standard deviation (SD) and compared using one-way ANOVA. Categorical variables were expressed as frequencies and percentages, and compared using the Chi-square test. A p-value<0.05 was considered statistically significant.

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RESULTS

In group BB, 48.8% were males and 51.2% were females. Whereas both in group BC and group BN, 51.2% were males and 48.8% were females each. There was no significant difference observed between the groups in terms of gender distribution (p=0.96) (Fig. 1).

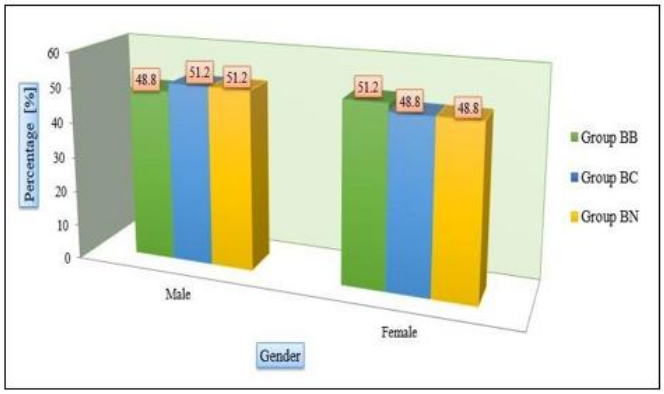

Fig. 1: Distribution graph of gender in three respective study groups

In comparison of the age groups, the majority of the subjects in all three groups were in the age range of 36-50 years, i.e., 65.1% in group BB, 62.8% in group BC and 65.1% in group BN. 34.9% in group BB, 37.2% in group BC and 34.9% in group BN fall in the age group of 18-35 years. There was no significant difference observed between the groups in terms of age group distribution (p=0.96) (Fig. 2).

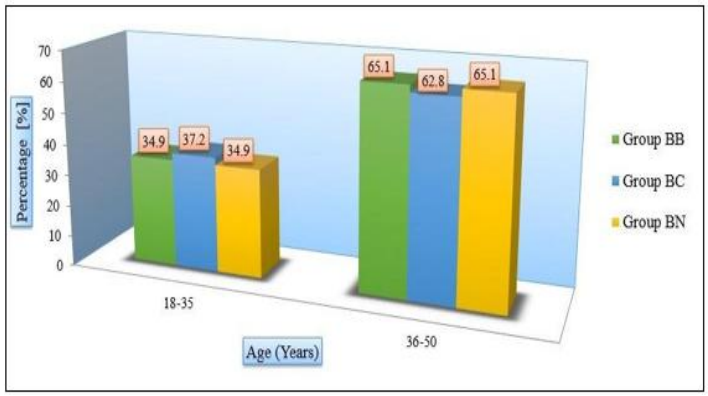

Fig. 2: Distribution Graph of age group in three respective study groups.

The mean age in the group BB, group BC and group BN was 39.8±8.6 years, 38.3±9.3 years and 39.4±9.4 years, respectively. The mean BMI in group BB was 24.4±1.6 kg/m2, group BC was 24.2±1.7 kg/m2 and group BN was 24.0±1.5 kg/m^2 (Table 1).

Table 1: Demographic details of subjects in respective groups.

Study group	Group BB (N=43)	Group BC (N=43)	Group BN (N=43)
Mean Age (years)	39.8±8.6	38.3±9.3	39.4±9.4
Mean BMI (kg/m^2)	24.4±1.6	24.2±1.7	24.0±1.5

Fig. 3 shows the distribution of patients according to the ASA physical status classification across the three study groups. The majority of patients in all groups belonged to ASA class II, with a smaller proportion in ASA class I. The distribution was comparable and did not show significant differences between groups.

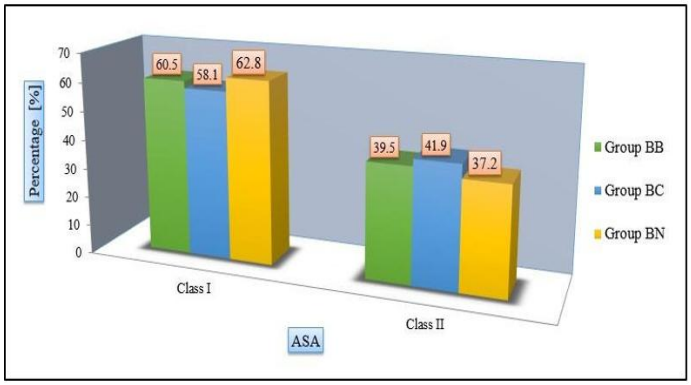

Fig. 3: Distribution graph of ASA class in respective groups.

Complications were observed in 32%, 37% and 39% of the subjects in group BB, group BC and group BN, respectively. Bradycardia was observed in 7% of subjects in group BB and group BC. 9.3% of the subjects in group BN had bradycardia. There was no significant difference in the incidence of bradycardia between the three groups (p=0.89). The use of clonidine (Group BC) or buprenorphine (Group BN) as adjuvants (Fig. 4).

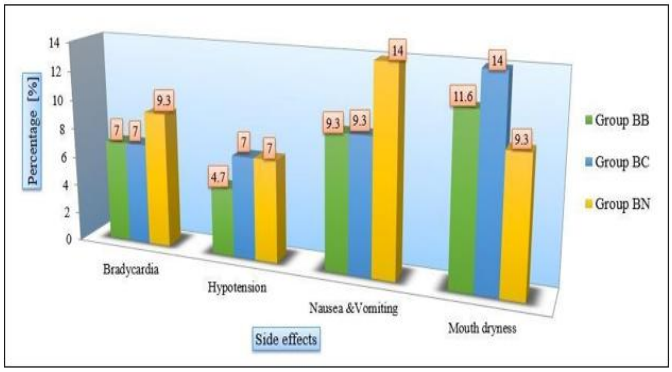

Fig. 4: Distribution graph of side effects observed in three respective study groups.

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DISCUSSION

Spinal anesthesia has gained widespread acceptance for its straightforwardness, ease of acquisition, and ability to create optimal surgical conditions while mitigating risks such as aspiration and intraoperative blood loss [7]. Its utility extends into the postoperative period, providing sustained pain relief with minimal complications [8]. This technique is highly favored for lower limb and lower abdominal surgeries, owing to its capacity to induce both sensory and motor block [9]. Although local anesthetics serve as the cornerstone of spinal anesthesia, their limited duration of action and potential adverse effects, such as hemodynamic instability and short-lived blockade, pose challenges [10]. Bupivacaine, the predominant choice for subarachnoid block, often falls short in maintaining adequate anesthesia and postoperative analgesia when used alone [11]. To address these shortcomings, researchers have explored the augmentation of intrathecal bupivacaine with adjunctive agents such as Buprenorphine or Clonidine [12]. These adjuncts aim to extend the duration of anesthesia and postoperative pain relief, yet their efficacy is hindered by the emergence of various early and late side effects [13]. Considering these considerations, this study aims to evaluate the effectiveness of combining intrathecal Buprenorphine or Clonidine with 0.5% hyperbaric Bupivacaine compared to using hyperbaric bupivacaine alone in spinal anesthesia [14].

Buprenorphine, a synthetic partial agonist opioid, targets the μ opioid receptors located in the substantia gelatinosa of the dorsal horn of the spinal cord [15]. Intrathecal administration of buprenorphine has demonstrated enhancements in both the duration and quality of postoperative analgesia [16]. When administered in low doses intrathecally, buprenorphine extends sensory block duration and analgesia without impeding motor block, while also exhibiting minimal side effects [17]. Research studies have indicated that a dose of 75 μg of intrathecal buprenorphine provides a rapid onset of analgesia without the side effects associated with higher doses [18]. Clonidine, on the other hand, is a selective partial agonist for α2 adrenoreceptors and acts by activation of post-synaptic α2 adrenoreceptors in the substantia gelantinosa of the spinal cord [19]. It prolongs the action of locally administered anesthetics intrathecally and possesses potent antinociceptive properties [20]. Preliminary investigations have shown that small doses of intrathecal clonidine (ranging from 15–75 μg) significantly increase the duration of postoperative analgesia [21]. Consequently, we selected a dose of 30 mcg for clonidine and 60 mcg for buprenorphine in this study [22,23]. Our study was a prospective, randomized comparative analysis, wherein patients were categorized into three groups, each comprising 43 subjects. Group BB received 3cc of 0.5% hyperbaric bupivacaine (15 mg) along with buprenorphine (60 mcg), while Group BC received the same dose of bupivacaine with clonidine (30mcg). Group BN served as the control, receiving only 3cc of 0.5% hyperbaric bupivacaine (15 mg). Analysis of demographic data revealed comparable gender distribution across all groups, with a male-to-female ratio of 0.9:1 in Group BB and 1.0:1 in both Groups BC and BN [24-28].

CONCLUSIONS

We concluded that clonidine emerges as a compelling adjunct to spinal bupivacaine, offering distinct advantages over buprenorphine. Its addition resulted in swifter sensory block onset compared to buprenorphine or bupivacaine alone, alongside a rapid spread of anesthesia, as evidenced by the shortest time to reach the highest dermatomal level. Moreover, the clonidine group exhibited faster recovery or regression of anesthesia effects, indicated by a quicker time to two-segment regression. Conversely, buprenorphine demonstrated a longer time to regression, implying a potentially prolonged anesthesia effect. Furthermore, the addition of clonidine to bupivacaine prolonged both sensory and motor block durations compared to buprenorphine or bupivacaine alone, leading to an extended duration of anesthesia. In clinical practice, the choice between clonidine and buprenorphine as adjuncts to bupivacaine should be guided by careful consideration of efficacy, safety profiles, and patient-specific factors.

Future research exploring long-term outcomes and optimizing dosages will further enhance our understanding and utilization of these adjuncts in spinal anesthesia.

CONTRIBUTION OF AUTHORS

Research concept- Madhura N, Mahadevaiah M
Research design- Madhura N, BM Chandrakumar
Supervision- Mahadevaiah M, BM Chandrakumar
Materials- Madhura N, Mahadevaiah M

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Data collection- Madhura N, BM Chandrakumar
Data analysis and interpretation- Madhura N
Literature search- Mahadevaiah M, BM Chandrakumar
Writing article- Madhura N, BM Chandrakumar
Critical review- Mahadevaiah M, BM Chandrakumar
Article editing- Madhura N, Mahadevaiah M
Final approval- Mahadevaiah M, BM Chandrakumar

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