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Original Research Article

Evaluating the Efficacy of Intrathecal Dexmedetomidine, Clonidine, and Fentanyl as adjuvants to Hyperbaric Bupivacaine for Lower Limb Procedures

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Abstract

Background and Aim: Spinal anaesthesia involves the use of various adjuvants in conjunction with local anaesthetics to effectively reduce both intraoperative visceral and somatic pain, while also providing prolonged postoperative analgesia. This study aimed to evaluate the differences in the onset and duration of sensory and motor block, haemodynamic effects, postoperative analgesia, and adverse effects associated with the intrathecal administration of dexmedetomidine, clonidine, and fentanyl in conjunction with hyperbaric 0.5% bupivacaine for spinal anaesthesia.

Material and Methods: In a recent study, two hundred patients set to undergo elective lower extremity surgery with a subarachnoid block were randomly divided into four distinct groups. The participants were randomly assigned to four distinct groups, with each group consisting of 50 patients. In this study, participants in Group A were administered 12.5 mg of hyperbaric bupivacaine combined with normal saline. Meanwhile, Group B received the same dosage of bupivacaine, but with an added 25 µg of fentanyl. Group C's regimen included 12.5 mg of bupivacaine along with 30 µg of clonidine, while Group D was given 12.5 mg of bupivacaine paired with 5 µg of dexmedetomidine. The timing for achieving peak sensory and motor levels, the duration of sensory and motor block regression, haemodynamic variations, and any side effects were meticulously documented.

Results: The comparison of the onset times for both sensory and motor block revealed no statistically significant differences across all four groups ($P > 0.05$) [Table 2]. The peak sensory block level reached was T6, recorded at 10.09±3.4, 09.72±2.4, 09.68±3.9, and 10.35±2.9 minutes post-injection. The data did not reach statistical significance. ($p>0.05$) In group D, the duration of sensor y and motor block was notably extended when compared to the other groups, with a statistical significance of $P < 0.05$. Intrathecal dexmedetomidine emerges as a compelling alternative to fentanyl and clonidine for extended surgical procedures. Its significant anaesthetic and analgesic effects, coupled with a favourable side effect profile, make it an appealing option for clinicians seeking effective pain management strategies.

Conclusion: Incorporating dexmedetomidine as an adjunct to hyperbaric bupivacaine administered intrathecally results in a notable extension of both sensory and motor block duration. This combination also provides enhanced perioperative analgesia while maintaining optimal haemodynamic stability and minimising side effects.

Keywords: Bupivacaine, Clonidine, Dexmedetomidine, Lower Limb Surgery.

Introduction

Various anaesthetic methods can be employed for surgeries involving the lower limbs, such as local infiltration, neuraxial blocks, and general anaesthesia. The neuraxial block emerges as the preferred technique among the various options presented. Spinal anaesthesia presents a range of advantages, such as rapid onset and a robust block. This approach effectively reduces stress responses, minimises the risk of postoperative pulmonary complications, and lowers the chances of deep vein thrombosis, all while remaining a cost-efficient choice. The transient nature of intrathecal local anaesthetics presents notable challenges, underscoring the importance of implementing effective post-operative analgesic strategies. [1,2]

The use of different types of analgesics alongside local anaesthetics has been adopted to prolong pain relief and reduce side effects.[3] Several medications have been utilised as supplementary options in spinal anaesthesia to prolong pain relief during and after surgery. These include opioids, α2 agonists, neostigmine, and vasoconstrictors, among others. Clonidine and dexmedetomidine are both α2 agonists that function by interacting with pre- and post-synaptic α2 receptors.[4.5]

The Food and Drug Administration (FDA) has approved dexmedetomidine as a short-term sedative for patients in the intensive care unit (ICU) requiring mechanical ventilation. Based on earlier human studies, the use of intrathecal 5 µg dexmedetomidine appears to improve postoperative pain relief when paired with hyperbaric bupivacaine in spinal anaesthesia, potentially reducing side effects as well.[6-8]

Fentanyl is a synthetic opioid that acts centrally in the body to produce its effects. Intrathecal fentanyl effectively lowers the required dosage of local anaesthetics, simultaneously improving their analgesic properties, and does so with minimal or negligible side effects.[9]

Given the limited evidence regarding dexmedetomidine's effectiveness as an adjunct to hyperbaric bupivacaine in spinal anaesthesia, we aimed to investigate its potential benefits. Additionally, we sought to compare this novel alpha-2 adrenergic agonist with the well-established adjuncts clonidine and fentanyl, focussing on their impact on spinal block characteristics in patients undergoing lower limb surgery.

Material and Methods

This research, structured as a prospective double-blind randomised trial, was conducted over a year at the Department of Anaesthesia in a Tertiary Care Teaching Institute in India. During the preanaesthetic evaluation, patients were provided with detailed information about the study procedure, encompassing both its advantages and disadvantages, along with their right to decline participation. Afterward, consent was secured, and those who opted out of participation were removed from the study.

The study comprised 200 patients, ranging in age from 18 to 60 years, all of whom were categorised as class I or II according to the American Society of Anaesthesiologists (ASA) classification. Patients were set to receive elective surgeries on their lower limbs, utilising a subarachnoid block for anaesthesia. Individuals suffering from severe anaemia, those with compromised cardiopulmonary status, haemodynamic instability, mental instability, and any apparent drug allergies were not included in the study. The study similarly excluded patients who were either unwilling or noncooperative, along with those requiring emergency surgical interventions.

All participants who met the inclusion criteria were enrolled in the study and then divided into four equal groups. The group assignment was carried out using a random selection method, employing a computer-generated list to ensure impartiality. An anaesthesiologist carefully opened the opaque sealed envelope, having meticulously prepared the necessary drug solution in accordance with the randomisation, while remaining an observer in the study process. The anaesthesiologist responsible for performing the block procedure and overseeing the study outcomes was not informed of the group treatment assignments. The anaesthesiologist responsible for data collection was not made aware of the group allocation.

Participants in the study were randomly assigned to one of four groups, with each group consisting of 50 patients. In the study, Group A was administered 12.5 mg of hyperbaric bupivacaine combined with normal saline. Group B received the same dosage of bupivacaine, but with the addition of 25 µg of fentanyl. Meanwhile, Group C was given 12.5 mg of bupivacaine along with 30 µg of clonidine. Lastly, Group D was treated with 12.5 mg of bupivacaine paired with 5 µg of dexmedetomidine.

Prior to their surgical procedures, each patient received a thorough evaluation. Patients were prescribed oral alprazolam at a dosage of 0.5 mg to be taken the night before their surgical procedures. On the day of the procedure, standard monitoring protocols were followed, incorporating the attachment of five leads for echocardiography, non-invasive blood pressure measurement, and pulse oximetry to evaluate oxygen saturation levels. The initial vital parameters were documented as per standard protocol. An 18 G cannula was inserted into the back of the limb that was not involved in the surgical procedure to establish venous access. In a meticulous process that prioritised aseptic techniques, the patient was strategically placed in the left lateral position. A subarachnoid block was effectively delivered through a lumbar puncture at the L3−L4 interspace, utilising a 25G standard spinal needle.

The study solutions were meticulously prepared in a 5 ml syringe by an anaesthesiologist. These solutions were then provided in a coded format to the attending anaesthesiologist, who remained unaware of the specific drug administered. A subarachnoid block was performed at the L2–3 or L3–4 vertebral level utilising a 26-gauge Quincke spinal needle, with patients positioned in a sitting stance and adhering to strict aseptic protocols. Patients were positioned supine after the block was administered. The anaesthesiologist responsible for the block meticulously documented the intraoperative data.

Patients were assessed at designated intervals throughout a 3-hour timeframe after receiving spinal injections of the experimental medications, facilitating an in-depth evaluation of various outcome measures. The initiation and length of sensory block, peak level of sensory block achieved, time taken to attain the highest dermatomal level of sensory block, onset of motor block, duration until complete recovery from motor block, and the overall duration of spinal anaesthesia were meticulously documented.

Vital signs were monitored at 5 minutes prior to the intrathecal injection, followed by assessments at 5, 10-, 15-, 20-, and 25-minutes post-injection, and then every 15 minutes thereafter. The assessment of haemodynamic stability was conducted by examining pulse rate, systolic blood pressure, and diastolic blood pressure.

Pain scores were measured using the Visual Analogue Scale (VAS) at several key intervals: five minutes prior to the intrathecal injection, immediately following the commencement of surgery, and then every 15 minutes until the procedure concluded. Postoperatively, VAS assessments continued to monitor pain levels. Intravenous fluids were administered to sustain blood pressure levels. Instances of pruritus, nausea, vomiting, and sedation were documented.

Statistical analysis

The gathered information was systematically arranged and entered into a spreadsheet program (Microsoft Excel 2019) prior to being transferred to the data editing interface of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described using means and standard deviations or medians and interquartile ranges, based on their distribution patterns. Qualitative variables were presented as counts and percentages. The confidence level for all tests was determined to be 95%, with a significance level established at 5%.

Results

A total of 200 patients participated in our study. The research evaluated a range of factors for each patient, encompassing demographic information, haemodynamic metrics, the onset time for sensory and motor block, the duration for two-segmental sensory regression, average block duration, analgesic duration, and the incidence of perioperative complications, both during and after surgery. The demographic characteristics were comparable in both groups. Table 1

The comparison of the onset times for both sensory and motor block revealed no statistically significant differences across all four groups (P > 0.05). (Table 2)

The comparison of the onset times for both sensory and motor block revealed no statistically significant differences across all four groups (P > 0.05). Table 2. The peak sensory block level reached T6, recorded at 10.09±3.4, 09.72±2.4, 09.68±3.9, and 10.35±2.9 minutes post-injection. The data did not reach statistical significance. (p>0.05)

Group D exhibited a notable extension in the duration of sensor y and motor block when compared to the other groups, with a statistically significant difference (P < 0.05). Group A exhibited a notably shorter duration of both sensory and motor block in comparison to Groups B, C, and D, with a statistically significant result (P < 0.05). Group C and B showed comparable results, with no statistical differences observed between the two groups [Table 2].

Table 1: Distribution of demographic data among the studied group

Variables	**Group A (n=50)**	**Group B (n=50)**	**Group C (n=50)**	**Group D (n=50)**	**P value**
Age (years)	30.05±11.4	28.90±12.5	31.14±09.45	30.90±10.48	0.17
Gender					
Male	54	52	53	52	0.10
Female	6	8	7	8	
Duration of surgery (min)	131.24±8.2	133.45±9.6	130.22±9.5	129.36±08.48	0.32
ASA grade (%)					
I	45	43	42	44	0.32
II	15	17	8	6	

Statistically significance at p≤0.05

Table 2: Comparison of block outcomes in between the groups

Variables	**Group A Mean±SD**	**Group B Mean±SD**	**Group C Mean±SD**	**Group D Mean±SD**	**P value**
Onset of sensory block	7.78±1.95	8.88±0.98	8.41±1.2	8.39±0.75	0.47
Onset of motor block	09.19±2.48	09.10±0.56	09.88±1.50	09.74±1.45	0.30
Time to reach maximum sensory level	10.09±3.4	09.72±2.4	09.68±3.9	10.35±2.9	0.48
Duration of sensory block	103.5±16.5	120.4±16.6	116.4±20.5	145.4±21.6	0.02*
Duration of motor block	160.25±18.48	195.47±25.10	199.1±24.2	270.5±23.56	0.003*

*** Indicate statistically significance at p≤0.05**

Discussion

The exact way in which intrathecal α 2 -adrenoceptor agonists prolong the effects of motor and sensory block from local anaesthetics is still not fully understood. Their mechanism operates by attaching to presynaptic C-fibers and postsynaptic dorsal horn neurones. The pain-relieving effects are linked to the inhibition of C-fiber transmitter release and the hyperpolarisation of postsynaptic dorsal horn neurones.10 Local anaesthetic agents work by blocking sodium channels. The prolonged effect may be linked to the combined action of local anaesthetics and α 2 -adrenoceptor agonists. Furthermore, the prolonged motor block seen with spinal anaesthetics could be attributed to the interaction of α 2 -adrenoceptor agonists with motor neurones situated in the dorsal horn.[11] Studies show that intrathecal α2-receptor agonists provide pain-relieving effects for both somatic and visceral pain. Fentanyl is an opioid that functions as a lipophilic μ-receptor agonist. When fentanyl is administered intrathecally, it engages with opioid receptors found in the dorsal horn of the spinal cord, which may result in effects that reach beyond the immediate spinal area.[12]

The findings from our research indicate that the addition of 5 µg dexmedetomidine to spinal bupivacaine notably extended both sensory and motor block when compared to intrathecal 25 µg fentanyl and 30 µg clonidine. The use of dexmedetomidine as an adjuvant has led to a notable enhancement in the quality of analgesia, particularly when compared to groups that included fentanyl and clonidine or solely bupivacaine.

The onset times documented in the study conducted by Al Ghanem et al. were significantly shorter compared to those observed in our research. This variation could be associated with the administration of isobaric bupivacaine, differing interpretations of onset time, and the positioning of patients during the procedure. The exact way in which dexmedetomidine improves sensory and motor block is still not fully understood. The targeted action of dexmedetomidine as an α2 agonist provides extra pain relief by blocking the release of C fibre transmitters and promoting hyperpolarisation in postsynaptic neurones.10 Throughout the intraoperative period, none of the patients required analgesics.

The understanding of how intrathecal 2 adrenoreceptor agonists extend the duration of motor and sensory block provided by local anaesthetics remains largely theoretical. The observed outcomes could result from an additive or synergistic effect, stemming from the distinct mechanisms of action associated with local anaesthetics and intrathecal 2 adrenoreceptor agonists. Local anaesthetics function by inhibiting sodium channels.

Two adrenoreceptor agonists function by attaching to the presynaptic C-fibers and the postsynaptic dorsal horn neurones. Their mechanism of action involves the suppression of C-fiber transmitter release and the hyperpolarisation of postsynaptic dorsal horn neurones, leading to analgesic effects. The synergistic effect of local anaesthetics combined with 2 adrenoreceptor agonists plays a significant role in their powerful pain-relieving capabilities. The extended duration of motor block associated with spinal anaesthetics could be attributed to the interaction of 2 adrenoreceptor agonists with motor neurones located in the dorsal horn. Dexmedetomidine demonstrates an impressive eightfold increase in specificity and selectivity as a 2 adrenoreceptor agonist when compared to clonidine. This characteristic positions it as a valuable and safe adjunct in a variety of clinical settings.[13-15]

The majority of clinical experience with intrathecal 2 adrenoreceptor agonists has primarily focused on clonidine. However, there is a pressing need for clinical studies investigating intrathecal dexmedetomidine to establish its efficacy, safety, and appropriate dosing for use alongside spinal local anaesthetics. The intrathecal dose of dexmedetomidine chosen for this study was informed by prior human research, which indicated an absence of neurotoxic effects.[16-18]

The onset time of sensory block was found to be relatively consistent across all groups studied. The results align with those reported by Al Ghanem et al, who found no significant difference in the onset time among patients administered dexmedetomidine and fentanyl as adjuncts to isobaric bupivacaine ($P > 0.05$). The study by Al Ghanem et al. reported shorter onset times compared to our findings. This discrepancy may be linked to their use of isobaric bupivacaine, variations in the definition of onset time, and differences in patient positioning. In a similar vein, Kanazi et al. observed a comparable time of onset for sensory block among the study groups when they compared 3 µg of dexmedetomidine with 30 µg of clonidine.

The use of 5 µg dexmedetomidine intrathecally in our study demonstrated a comparable onset of motor block, accompanied by a significantly extended duration of motor block. These findings align with those reported by other researchers who have compared various adjuvants, including clonidine, fentanyl, and sufentanil, in their investigations.[6-8]

Although side effects may occur with any anaesthesia medication, the most effective choices are distinguished by their strong efficacy and low incidence of adverse effects. Among the notable side effects associated with the administration of intrathecal 2 adrenoreceptor agonists, bradycardia and hypotension stand out as particularly significant concerns.[19] The current investigation found that the side effects were not significant, likely due to the administration of a small dose of intrathecal dexmedetomidine, clonidine, and fentanyl alongside a high dose of local anaesthetics. Gupta et al.19 reported that elevating the dose of dexmedetomidine from 2.5 mcg to 10 mcg leads to improved quality of sensory and motor block, while exhibiting minimal or no related side effects.

This study does not include an active control to assess the systemic effects of dexmedetomidine. Therefore, additional research comparing the effects of intrathecal and IV dexmedetomidine on spinal bupivacaine could be beneficial. As interest in regional anaesthesia techniques continues to rise, particularly for enhancing the quality of intraoperative and postoperative analgesia while minimizing side effects, the use of intrathecal dexmedetomidine as an adjunct to local anaesthetics is gradually evolving. Ongoing clinical studies are demonstrating its efficacy and safety, while also determining the appropriate dosages of dexmedetomidine needed to supplement spinal local anaesthetics.

Conclusion

The use of intrathecal dexmedetomidine as an adjuvant to bupivacaine seems it to be an attractive alternative to fentanyl and clonidine for long duration surgical procedures due to its profound intrathecal anesthetic and analgesic properties combined with minimal side effects.

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