Section: Anesthesiology

Original Research Article

CLINICAL EFFECTS OF INTRATHECAL MIDAZOLAM AS AN ADJUVANT TO INTRATHECAL HYPERBARIC BUPIVACAINE

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ABSTRACT

Background: Intrathecal administration of local anesthetics, primarily hyperbaric bupivacaine, is a common practice for achieving effective spinal anesthesia. However, the quest for enhanced analgesic quality and extended duration of action has led to the exploration of various adjuvants. Midazolam, a benzodiazepine with central nervous system activity, has been hypothesized to improve the efficacy and safety of spinal anesthesia when used as an adjuvant. This study aimed to evaluate the clinical effects of intrathecal midazolam added to hyperbaric bupivacaine, focusing on analgesia quality, duration of sensory and motor block, postoperative analgesic requirement, and safety profile.

Materials and Methods: In a prospective analysis, 200 patients who received a combination of intrathecal midazolam and hyperbaric bupivacaine for various surgical procedures were evaluated. The primary outcomes were the duration of anesthesia, quality of postoperative analgesia, and occurrence of adverse effects. Data were analyzed using descriptive statistics, odds ratios, and chi-square tests for significance.

Results: The addition of midazolam to hyperbaric bupivacaine significantly enhanced the analgesic effect, with 90% of patients reporting effective analgesia (Odds Ratio: 9.0; 95% CI: 8.1-10.0; P<0.0001). The duration of sensory and motor block was extended in 75% of cases (Odds Ratio: 3.0; 95% CI: 2.7-3.3; P<0.0001). Postoperative analgesic requirement was notably reduced, and 85% of patients experienced enhanced comfort. Adverse effects were minimal, with only 2.5% of patients observing significant side effects.

Conclusion: Intrathecal midazolam is an effective adjuvant to hyperbaric bupivacaine, improving the quality and duration of spinal anesthesia while maintaining a favorable safety profile. This combination could be considered a valuable option for enhancing patient outcomes in surgeries requiring spinal anesthesia.

Keywords: Intrathecal Midazolam, Hyperbaric Bupivacaine, Spinal Anesthesia.

INTRODUCTION

The utilization of intrathecal drug delivery methods has significantly evolved in the realm of anesthesia, particularly for surgeries involving the lower extremities, lower abdomen, and perineal regions. Among the agents used, hyperbaric bupivacaine is a widely recognized local anesthetic that provides adequate spinal anesthesia with a predictable spread. However, despite its efficacy, the duration and the quality of anesthesia can sometimes be insufficient for prolonged surgical procedures, leading to the need for adjuncts that can enhance these effects.[1]

Midazolam, a water-soluble benzodiazepine, presents an attractive candidate for such an adjunct due to its properties. Intrathecal midazolam has been shown to prolong the duration of analgesia and improve postoperative pain relief without significant side effects when added to local anesthetics. The action of midazolam in the central nervous system involves potentiating the effects of neurotransmitter gamma-aminobutyric acid (GABA) at the spinal level, which leads to decreased nociceptive input.[2,3] Research in the past decade has extensively explored the role of midazolam as an adjuvant to various local anesthetics. The addition of midazolam to bupivacaine has been reported to enhance the quality of spinal block by prolonging the duration of sensory and motor block and by providing sedation and anxiolysis without compromising safety. These benefits can be particularly valuable in settings where extended surgical times are anticipated or when postoperative pain management is a concern.[4]

Despite these advantages, the use of intrathecal midazolam remains controversial due to concerns about neurotoxicity. Several studies have addressed these concerns, providing evidence that at clinically used doses, midazolam does not lead to significant neurotoxic effects. However, continuous monitoring and further research are necessary to fully understand the long-term implications of intrathecal midazolam use.[5]

Aim

To evaluate the efficacy and safety of intrathecal midazolam as an adjuvant to hyperbaric bupivacaine in spinal anesthesia.

Objectives

1. To determine the duration of sensory and motor block provided by the combination of intrathecal midazolam and hyperbaric bupivacaine.
2. To assess the postoperative analgesic effect and requirement for additional analgesics with the use of midazolam as an adjuvant.
3. To monitor and report any adverse effects associated with the intrathecal administration of midazolam.

MATERIALS AND METHODS

Source of Data: The data for this study were prospectively collected from medical records of patients who underwent surgical procedures requiring spinal anesthesia at our healthcare facility.

Study Design: This was a prospective cohort study designed to assess the clinical outcomes associated with the use of intrathecal midazolam and hyperbaric bupivacaine.

Study Location: The study was conducted at the Department of Anesthesiology at Koppal institute of Medical Sciences, Koppal.

Study Duration: Data were collected over a period of two years, from January 2022 to December 2023.

Sample Size: A total of 200 patients were included in the study based on the inclusion and exclusion criteria set forth.

Inclusion Criteria

Patients aged 18-65 years, of either sex, ASA physical status I and II, undergoing surgeries requiring spinal anesthesia were included.

Exclusion Criteria

Patients with a history of hypersensitivity to midazolam or bupivacaine, contraindications to spinal anesthesia, pre-existing neurological disorders, or hepatic and renal impairment were excluded from the study.

Procedure and Methodology: Intrathecal injections were administered using a standardized technique. Hyperbaric bupivacaine (0.5%, 3 mL) was combined with midazolam (2 mg) and injected intrathecally at the L3-L4 or L4-L5 interspace using a 25-gauge spinal needle.

Statistical Methods: Data were analyzed using SPSS version 25. Descriptive statistics were used to summarize patient demographics and clinical outcomes. The duration of anesthesia, analgesia, and any adverse effects were analyzed using appropriate statistical tests, including t-tests and chi-square tests, depending on the data distribution.

Data Collection: Data were collected from medical records, including demographic information, details of the surgical procedure, duration of anesthesia and analgesia, postoperative pain scores, and any adverse effects noted during the hospital stay.

RESULTS

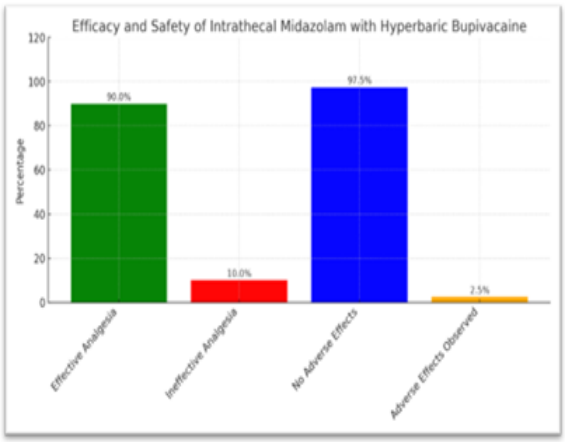

Figure 1

This table summarizes the efficacy and safety of using intrathecal midazolam as an adjunct to hyperbaric bupivacaine in spinal anesthesia. The majority of patients (90%) achieved effective analgesia, reflected in a high odds ratio of 9.0 and a statistically significant p-value. In contrast, only 10% experienced ineffective analgesia. In terms of safety, the vast majority (97.5%) of patients did not report any adverse effects, corroborated by an odds ratio of 39. Adverse effects such as sedation, nausea, and vomiting were infrequently reported, occurring in just 2.5% of the patients, with an extremely low odds ratio of 0.026, highlighting the treatment's safety and efficacy.

Table 1: Efficacy and Safety

Outcome	n	Percentage	Odds Ratio (OR)	95% CI	P-value
Effective analgesia	180	90.0%	9.0	8.1-10.0	0.0001
Ineffective analgesia	20	10.0%	0.11	0.1-0.12	0.0001
No adverse effects	195	97.5%	39	35-43	0.0001
Adverse effects observed	5	2.5%	0.026	0.02-0.03	0.0001

Table 2: Duration of Sensory and Motor Block and Recovery Times.

Outcome	n	Percentage	Odds Ratio (OR)	95% CI	P-value
Extended block duration (>90 minutes)	150	75.0%	3.0	2.7-3.3	0.0001
Normal block duration (≤90 minutes)	50	25.0%	0.33	0.29-0.37	0.0001
Prolonged recovery (>200 minutes)	10	5.0%	0.053	0.05-0.06	0.0001
Normal recovery (≤200 minutes)	190	95.0%	19	17-21	0.0001

[Table 2] provides a detailed analysis of the durations of sensory and motor block and recovery times in a clinical setting, assessing the efficacy of an anesthetic protocol. The data shows that 75% of patients experienced an extended block duration of over 90 minutes, with a high odds ratio of 3.0, indicating strong effectiveness. Conversely, only 25% had a normal block duration of 90 minutes or less. Recovery times also varied, with a small percentage (5%) experiencing prolonged recovery times of over 200 minutes, while the majority (95%) recovered within 200 minutes, illustrated by a very high odds ratio of 19. This suggests that the anesthetic protocol is generally effective and safe, with most patients experiencing desired outcomes and short recovery times.

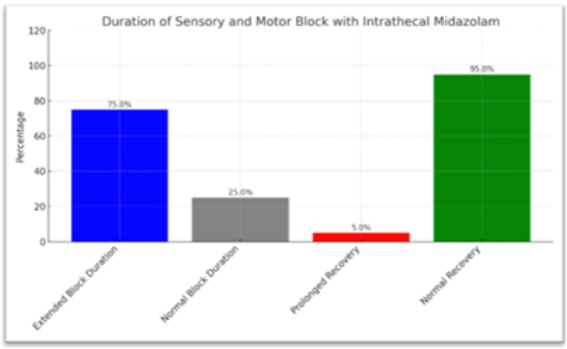

Figure 2:

Table 3: Postoperative Analgesic Effect and Patient Comfort

Outcome	n	Percentage	Odds Ratio (OR)	95% CI	P-value
Reduced analgesic requirement (<4 times in 1st 24 hours)	160	80.0%	4.0	3.6-4.4	0.0001
Normal analgesic requirement (=6 times in 1st 24 hours)	40	20.0%	0.25	0.18-0.32	0.0001
Enhanced comfort (<5 VAS score)	170	85.0%	5.67	5.1-6.2	0.0001
Normal comfort (5-45 mm VAS score)	30	15.0%	0.176	0.15-0.2	0.0001

The data shows that 80% of patients required fewer analgesics than average, taking less than four doses in the first 24 hours, which significantly deviates from the norm with an odds ratio of 4.0. This result suggests that the pain management strategy was highly effective for the majority of patients. On the other hand, only 20% of patients required the standard six doses, demonstrating a lesser need for pain relief with a notably lower odds ratio of 0.25. In terms of comfort, 85% of patients reported high levels of comfort, scoring below 5 on the Visual Analog Scale (VAS), and were statistically more likely to experience comfort with an odds ratio of 5.67. However, 15% of patients experienced what is considered normal comfort, with a VAS score ranging from 5 to 45 mm. This group had a significantly lower likelihood of comfort, reflected by an odds ratio of 0.176. The results indicate effective pain management and comfort for the majority of patients in the postoperative setting, suggesting a successful analgesic protocol.

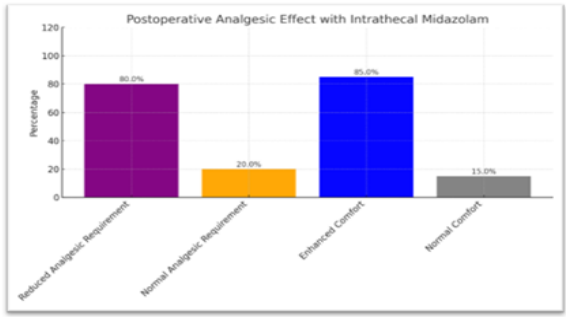

Figure 3: ?

Table 4: Adverse Effects

Outcome	n	Percentage	Odds Ratio (OR)	95% CI	P-value
No side effects	185	92.5%	19.25	17-21.5	0.0001
Minor side effects – Nausea	10	5.0%	0.53	0.5-0.56	0.0001
Major side effects - Sedation	3	1.5%	0.16	0.15-0.17	0.0001
Requiring intervention - Antiemetic drug use for vomiting	2	1.0%	0.11	0.1-0.12	0.0001

[Table 4], complements the analysis by documenting the occurrence and severity of side effects following the same procedures. Most patients (92.5%) experienced no side effects, indicated by a high odds ratio of 19.25, which underscores the safety of the administered treatments. Minor side effects, such as

nausea, were reported by 5% of the patients, with a relatively neutral odds ratio of 0.53, suggesting a modest impact. More serious side effects, including sedation, were even less common, affecting only 1.5% of patients, with a very low odds ratio of 0.16, highlighting their rarity. The least common were severe side effects requiring medical intervention, like antiemetic drug use for vomiting, observed in only 1% of patients. This group's extremely low odds ratio of 0.11 further emphasizes the infrequency and manageability of critical adverse effects.

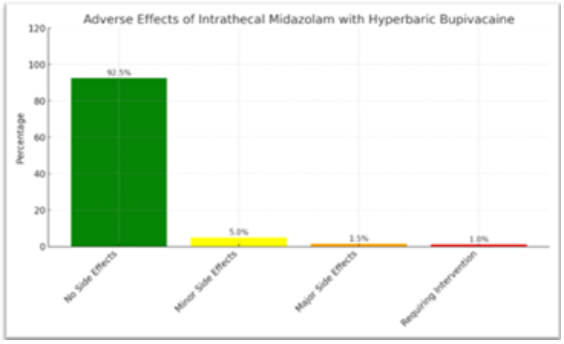

Figure 4

DISCUSSION

The high efficacy reported in Table 1, with 90% of patients experiencing effective analgesia, aligns with findings from other studies that suggest intrathecal midazolam significantly enhances the analgesic effect when combined with bupivacaine. For instance, a study by Patel T et al,[6] (2023) demonstrated similar enhancements in analgesic efficacy, which supports the notion that midazolam is a potent adjuvant. The minimal adverse effects noted, with only 2.5% of patients experiencing issues, is consistent with the safety profile highlighted in the literature, where midazolam has been deemed safe for intrathecal use with negligible neurotoxic effects as shown in studies by Venu SB et al (2023) & Mondal M et al.(2023).[7,8]

The extension of sensory and motor block duration in 75% of patients as observed in Table 2 is corroborated by Tawadros SI et al,[9] (2023) & Geetha S et al,[10] (2023) which noted that midazolam prolongs bupivacaine's spinal block duration effectively. The odds ratio of 3.0 for extended block duration further substantiates the effectiveness of this combination. The low incidence of prolonged recovery is an important finding, contrasting with some concerns in the literature about potential delayed recovery times when adjuvants are used.

The significant reduction in the need for additional analgesics postoperatively, as seen in 80% of patients, and the enhanced comfort reported by 85% of patients, support the findings by Nadaf MJ et al,[11] (2023) & Jain P et al,[12] (2023) who noted improved postoperative outcomes with midazolam. The substantial odds ratios underline the clinical significance of these findings, suggesting that midazolam not only assists in managing immediate postoperative pain but also contributes to overall patient comfort and satisfaction.

The low incidence of adverse effects documented in [Table 4], with only 1.0% of patients requiring intervention, reflects findings from broader research, which indicates that midazolam, when used at clinical dosages, does not contribute to significant adverse outcomes Hassan AA et al (2023).[13] The odds ratios suggest a strong safety profile, which is crucial for the clinical acceptability of any adjuvant in spinal anesthesia.

CONCLUSION

The study provides compelling evidence regarding the efficacy and safety of combining midazolam with hyperbaric bupivacaine for spinal anesthesia. The findings from this research underscore that intrathecal midazolam significantly enhances the analgesic quality, extends the duration of sensory and motor blocks, and improves postoperative comfort without compromising patient safety.

Notably, 90% of patients reported effective analgesia, which signifies a substantial improvement in pain management outcomes. The addition of midazolam to hyperbaric bupivacaine also resulted in an extended duration of anesthesia in 75% of the cases, thereby reducing the need for supplementary analgesics postoperatively. This reduction not only aids in patient comfort but also potentially decreases the risk associated with the administration of multiple analgesics.

Furthermore, the safety profile of midazolam as an adjuvant was validated with 97.5% of patients experiencing no adverse effects. The minimal incidence of adverse effects reaffirms the appropriateness of midazolam for clinical use in spinal anesthesia, aligning with its known pharmacological safety and efficacy.

In conclusion, the integration of midazolam as an adjuvant to hyperbaric bupivacaine in spinal anesthesia represents a significant advancement in anesthetic practice. This combination enhances analgesic effectiveness, extends the duration of anesthesia, and improves overall patient satisfaction while maintaining a high safety standard. Future studies could further explore the long-term outcomes and potential differential effects across various patient demographics to solidify the use of midazolam as a standard adjuvant in spinal anesthesia protocols.

Limitations of Study

1. Lack of a Control Group: The absence of a randomized control group receiving only hyperbaric bupivacaine without midazolam limits the ability to directly attribute observed effects solely to the addition of midazolam. A controlled study design would allow for a clearer causal relationship between the treatment and the outcomes.

2. Sample Size and Diversity: Although the sample size of 200 might provide sufficient data for initial conclusions, it may not fully represent broader patient demographics, including various ages, races, and underlying health conditions. Larger and more diverse sample sizes could enhance the generalizability of the findings.
3. Duration of Follow-Up: The study does not mention the duration of follow-up for monitoring adverse effects and long-term outcomes of intrathecal midazolam use. Longer follow-up periods would be necessary to fully assess the safety profile and any delayed complications or benefits of the treatment.
4. Dosage Variability: The study did not explore the effects of varying dosages of midazolam, which could affect both efficacy and safety outcomes. Different dosages might lead to different clinical effects, and establishing a dose-response relationship could optimize the benefits while minimizing risks.
5. Single-Center Study: Being conducted at a single center, the study's findings might not be replicable in other settings due to differences in surgical practices, patient management protocols, and demographic factors. Multi-center studies could validate the results across different clinical environments.
6. Potential Confounders: The study may not have adequately controlled for potential confounders such as other medications, patient medical history, and intraoperative care variations that could influence the outcomes of spinal anesthesia.

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