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A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND MIDAZOLAM TO INTRATHECAL BUPIVACAINE ON POSTOPERATIVE ANALGESIA.

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ABSTRACT **Background:** Although midazolam and Dexmedetomidine regulate spinal analgesia through distinct mechanisms, no human studies assess their effects on postoperative analgesia following neuraxial administration. **Aim:** We looked at the clinical safety profile and length of time that effective analgesia lasted when intrathecal bupivacaine was combined with either Dexmedetomidine or Midazolam. **Materials & Methods:** It is a prospective study carried out in the Department of Anaesthesiology at Malla Reddy Medical College for Women, Hyderabad. A total of 60 patients were taken and were divided into 3 groups, Control (n=20), Dexmedetomidine (n=20), and Midazolam (n=20) groups, respectively. Ethics approval was taken before the initiation of the study. **Results:** The Dexmedetomidine group experienced a considerably longer duration of effective analgesia (time to first analgesic request) (286 ± 65 minutes). At the end of the first 15 minutes following intrathecal injection, patients from the Dexmedetomidine group had a mean rank sedation score of 35.47 for Dexmedetomidine, 25.01 for Midazolam, and 30.80 for control, indicating that they were more sedated than patients from the Midazolam and control groups. There were no discernible variations in the side effects during the trial period. The duration of the two-segment sensory regression and the time to initially request analgesia were not prolonged by Midazolam. **Conclusion:** The duration of effective analgesia is greatly extended when Dexmedetomidine (5 mcg) is added to 3 mL of intrathecal hyperbaric Bupivacaine (0.5%), as compared to 1 mg of Midazolam or a placebo (0.9% normal saline), with similar occurrences of adverse effects.

KEYWORDS : Spinal anaesthesia, Subarachnoid block, Dexmedetomidine, Midazolam.

INTRODUCTION

The main reason for adding neuraxial support to intrathecal (IT) or spinal bupivacaine is to delay postoperative pain relief by prolonging the duration of sensory deprivation. Patients undergoing short-term neuromedical procedures experience mild to moderate pain in the postoperative period. This type of pain is usually not localized, or visceral and adds more pain than pain to the patient. Since most of these endoscopic procedures are performed under anaesthesia, the addition of neuraxial supplements not only prolongs postoperative analgesia but is also effective in relieving nonlocal visceral pain. Dexmedetomidine and Midazolam are effective for this purpose.[1,2]

Dexmedetomidine is an α2-adrenergic receptor agonist that modulates nociception by inhibiting the peripheral release of norepinephrine, thereby inhibiting the production of pain signals. At the same time, postsynaptic activation of α2-adrenergic receptors in the central nervous system can prevent sympathetic activity depression and bradycardia. Midazolam, a benzodiazepine derivative, modulates nociception through gamma-aminobutyric acid (GABA) receptors located in the dorsal horn of the spinal cord and activation of δ-opioid receptors. Unlike the conservative action of Dexmedetomidine, IT midazolam maintains sympathetic nervous system function.[3,4]

A literature review found no human trials comparing the addition of Dexmedetomidine or Midazolam to hyperbaric bupivacaine. However, several studies have been conducted using these drugs individually as an adjunct to hyperbaric spinal bupivacaine and have concluded that both drugs prolong survival. This study investigated the analgesic efficacy in terms of hemodynamic stability and sedation when IT Dexmedetomidine (5 mcg) and Midazolam (1 mg) were used together as an adjunct to hyperbaric Bupivacaine in patients undergoing endoscopic procedures under programmed anaesthesia.

MATERIALS & METHODS

It is a prospective study carried out in the Department of Anaesthesiology at Malla Reddy Medical College for Women, Hyderabad. A total of 60 patients were taken and were divided into 3 study groups. Ethics approval was taken before the initiation of the study.

Group Allocation

1. Control group (n=20)- received 3ml of 0.5% hyperbaric Bupivacaine + 0.5ml of 0.9% saline
2. Dexmedetomidine (n=20)- received 3ml of 0.5% hyperbaric Bupivacaine + 5mcg Dexmedetomidine
3. Midazolam (n=20)- received 3ml of 0.5% hyperbaric Bupivacaine + 1mg Midazolam

Methodology

Characteristics of spinal cord block were assessed, such as time to onset of consciousness (time from the end of IT drug infusion to onset of complete loss of pinprick sensation at T8), the highest level of block dermatome sensory, and the time to reach this level in the spinal cord. Blocks are evaluated parametrically. Injection time (peak of sensory impedance) and duration of sensory impedance (defined as the time from completion of IT drug injection and step 2 reduction of sensory impedance using the pinprick technique). The motor level was assessed according to the Bromage score (5): (0: no motor loss, 1: inability to move the tail joint, 2: inability to move the knee joint, 3: inability to move the leg joint). The onset time of the motor block was defined as the time interval from the end of the IT injection to the onset of the Bromage 1 score.

Pain severity was assessed by NRS, (scale of 0 = no pain to 10 = worse pain possible).

The level of sedation of the patients was assessed by the Ramsay sedation score (1: anxious, agitated, and restlessness; 2: oriented and cooperative; 3: responds to command only; 4: brisk response to loud voice and light glabellar tap; 5: sluggish to no response to light glabellar tap or loud auditory stimulus; 6: no response even to pain).

Statistical Analysis

Data was analysed using SPSS (version 20) software. Data was expressed as Mean±SD, and p value ≤0.05* is considered as significant.

RESULTS

The demographic data revealed that the mean age of the study population was 43.1 years (Control grp), 40.5 (Dexmedetomidine grp) & 46.7 (Midazolam grp), respectively. Female gender was found to be predominant in all the study groups. The average weight in the study population was 61.4kgs (Control grp), 63.3kgs (Dexmedetomidine grp) & 62.2kgs (Midazolam grp), respectively. The duration of surgery in the study population was 61mins (Control grp), 64mins (Dexmedetomidine grp) & 62mins (Midazolam grp), respectively. (Table 1)

The effect of Saline, Dexmedetomidine, and Midazolam as adjuvant to hyperbaric Bupivacaine on spinal blockade and duration of postoperative analgesia was observed. The Onset of Sensory Block was 2.3 (Control grp), 2.2 (Dexmedetomidine grp) & 2.7 (Midazolam

grp), respectively. The time to peak Sensory Block found was 8 (Control grp), 8.5 (Dexmedetomidine grp) & 8.7 (Midazolam grp), respectively. The Time to 2 Segment Regression was 73.5 (Control grp), 130.9 (Dexmedetomidine grp) & 99.2 (Midazolam grp), respectively, and the p value for significant (p=0.001*). The Time to 1st Analgesic Request was 167 (Control grp), 286 (Dexmedetomidine grp) & 171 (Midazolam grp), respectively, and the p value for significant (p=0.001*). The Number of Analgesic requests in 24 hours was 0.54 (Control grp), 0.44 (Dexmedetomidine grp) & 0.50 (Midazolam grp), respectively. (Table 2)

The comparison of the Sedation Score among Control, Dexmedetomidine, and Midazolam groups was done, in which the score for 15 mins was, 30.80 (Control grp), 35.47* (Dexmedetomidine grp) & 25.01 (Midazolam grp), respectively, and the p value for significant (p=0.03*). For 30 minutes the score was 29.10 (Control grp), 34.72 (Dexmedetomidine grp) & 27.54 (Midazolam grp), respectively, and the p value for significant (p=0.03*). At the end of the surgery, the score was 29.40 (Control grp), 32.51 (Dexmedetomidine grp) & 29.48 (Midazolam grp), respectively. (Table 3)

The adverse effects among Control, Dexmedetomidine, and Midazolam groups reveal that Control grp) had 7, Dexmedetomidine grp had 12 & Midazolam grp had 9, adverse effects in total. (Table 4)

Table 1: Sociodemographic Characteristics

Study Variables	Control (n=20)	Dexmedetomidine (n=20)	Midazolam (n=20)	p value
Age (Years)	43.1±8.9	40.5±11.9	46.7±14.1	0.27
Gender (Male/Female)	2/18	5/15	3/17	0.25
Weight (Kgs)	61.4±8.5	63.3±13.9	62.2±11.4	0.72
Duration of surgery (minutes)	61±8.5	64±12.6	62±11.0	0.60

Table 2: Effect Of Saline, Dexmedetomidine, And Midazolam As An Adjuvant To Hyperbaric Bupivacaine On Spinal Blockade, Duration Of Postoperative Analgesia, And Analgesic Requirement.

Study variables	Control (n=20)	Dexmedetomidine (n=20)	Midazolam (n=20)	p value
Block Heights	T6 (T4-T6)	T6 (T6-T8)	T6 (T6-T8)	0.12
Onset of Sensory Block (Minutes)	2.3±0.9	2.2±1.3	2.7±1.9	0.31
Time to peak Sensory Block (Minutes)	8.0±1.9	8.5±2.9	8.7±5.5	0.74
Onset of Motor Block (Minutes)	3.4±1.9	3.3±2.6	5.0±3.7	0.22
Time to 2 Segment Regression (Minutes)	73.5±34.7	130.9±36.0	99.2±39.2	0.001*
Time to 1st Analgesic Request (Minutes)	167±73	286±65	171±77	0.001*
Number of Analgesic requests in 24 hours	0.54±0.6	0.44±0.6	0.50±0.6	0.73

Table 3: Comparison Of Sedation Score Among Control, Dexmedetomidine, And Midazolam Groups.

Study variables	Control (n=20)	Dexmedetomidine (n=20)	Midazolam (n=20)	p value
15 minutes	30.80	35.47*	25.01	0.03*
30 minutes	29.10	34.72	27.54	0.03*
At the end of surgery	29.40	32.51	29.48	0.41

Table 4: Adverse Effects Among Control, Dexmedetomidine, And Midazolam Groups.

Adverse effects	Control (n=20)	Dexmedetomidine (n=20)	Midazolam (n=20)	p value
Nausea or vomiting	1	0	0	0.46
Shivering	1	2	0	0.34
Hypotension	3	6	7	0.33
Bradycardia	2	4	2	0.34
Total	7	12	9	

DISCUSSION

Both midazolam and dexmedetomidine are relatively newer additions to the list of adjuvants used in IT anaesthesia and may act synergistically with IT bupivacaine to prolong the duration of postoperative analgesia. When administered intrathecally, the mechanisms by which the two medications mediate antinociception are different. According to the current study's findings, compared to bupivacaine alone, the addition of 1 mg midazolam or 5 mcg dexmedetomidine as an adjuvant to 3 mL of 0.5% hyperbaric bupivacaine extended the duration of effective analgesia during the postoperative period. Additionally, it seems that dexmedetomidine is more analgesic efficient than midazolam, as indicated by the length of time that analgesia lasts when effective or by the time that analgesia is first requested or administered.

IT midazolam (10–15) and dexmedetomidine (16–21) affect the properties of spinal block in a dose-dependent manner with similar hemodynamic stability, extending the duration of sensory analgesia, time to 2-segment regressions, and time to first postoperative analgesic request. Their impact on the onset of motor and sensory block, however, varies. According to a study by Sanwal et al,[5] the amount of bupivacaine, not the amount of midazolam, controls when sensory or motor block starts. We used the same dose of hyperbaric bupivacaine (15 mg) in our study, and the duration of sensory and motor block, the height of the block, and the time to peak sensory block were similar in all three groups.

Higher doses of IT dexmedetomidine (15 mcg) prolong the duration of effective analgesia and lower Ramsay sedation scores (median score of 2-4), according to Hala et al.[6] Within the first half-hour following the IT injection, patients in the dexmedetomidine group in our study tended to be more sedated. After the procedure, though, every patient was alert, compliant, and quick to obey verbal commands.

The adverse effects among Control, Dexmedetomidine, and Midazolam groups reveal that Control grp) had 7, Dexmedetomidine grp had 12 & Midazolam grp had 9, adverse effects in total.[7,8,9,10]

CONCLUSION

Dexmedetomidine (5 mcg) enhances analgesia efficiency when combined with 0.5% hyperbaric bupivacaine, prolonging postoperative analgesia without significant hemodynamic instability, and may be beneficial in short-term endourological procedures.

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