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ORIGINAL ARTICLE

EFFECT OF INTRATHECAL HYPERBARIC BUPIVACAINE WITH MIDAZOLAM AND HYPERBARIC BUPIVACAINE ALONE IN LOWER LIMB AND LOWER ABDOMINAL SURGERIES FOR POST OPERATIVE ANAELGESIA

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ABSTRACT

Spinal anaesthesia is effective in the management of perioperative pain which extends into the initial post operative period. In order to maximize postoperative pain free period numerous techniques and newer drugs have been tried. In this study, the anaesthetic properties of 12.5 mg of 0.5% hyperbaric bupivacaine with 0.4 ml of normal saline and 12.5 mg of 0.5% hyperbaric bupivacaine with 2 mg of midazolam given intrathecally were compared.A hundred ASA physical status I and II patients, posted for various elective lower limb and lower abdominal surgeries were studied.The patients were divided into two groups of fifty each:Group A – Received 0.5% hyperbaric bupivacaine 12.5 mg + 0.4ml of Normal saline.Group B – Received 0.5% hyperbaric bupivacaine 12.5 mg + 2 mg of midazolam. Addition of 2mg of midazolam to hyperbaric bupivacaine does not alter the onset and level of sensory and motor block. The time taken for two segment regression was significantly prolonged in Group B (Group A – 78.9; Group B 87.2min).The duration of analgesia was also longer in group B (Group A –158.8min; Group B – 316.1min).The time taken for maximum sensory blockade was significantly prolonged in Group B(Group A –7.4min; Group B – 5.5min). More number of the mean arterial pressure changes from baseline values varied from 6.76% for patients in group B compared with 5.41% group A. there was 8% fall in the mean pulse rate from the baseline in group B compared to 9.7% in group A.With the above findings it is evident that the use of 2 mg of intrathecal midazolam as an adjuvant to hyperbaric bupivacaine in lower limb and lower abdominal surgeries is beneficial in several aspects and scored over the use of hyperbaric bupivacaine alone without side effects.

Keywords: Spinal anaesthesia, Intraoperative, Postoperative, Bupivacaine, Midazolam

1.INTRODUCTION

Regional anaesthesia is the preferred technique for most of lower abdomen and lower limb surgeries. It allows the patient to remain awake, minimizes or completely avoids the problem associated with airway management. With spinal anaesthesia, the technique is simple to perform, the onset of anaesthesia is more rapid, avoids poly pharmacy, allowing the surgical incision to be made sooner and also provides post operative analgesia.

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Spinal anaesthesia with cocaine was initially produced inadvertently by Leonard J Corning in 1885, and first used deliberately by August Bier in 1898(Brown,2005).

For decades lignocaine had been the local anaesthetic of choice for spinal anaesthesia. Its advantages are rapid onset of action and good motor block manifested as good muscle relaxation. Its use is limited by its short duration of action and has been implicated in transient neurologic symptoms and cauda equina syndrome following intrathecal injection(Corbey and Bach,1998; Henderson et al., 1998).

Bupivacaine is three to four times more potent than lignocaine(Colin,1993) and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block.

Hyperbaric bupivacaine 0.5% is extensively used in India for spinal anaesthesia. Though the duration of action of bupivacaine is prolonged, it will not produce prolonged post operative analgesia. Hence another adjuvant is required for producing prolonged post operative analgesia. The discovery of opioid receptors and endorphins in spinal and supraspinal regions soon led to the use of spinal opiates.

Morphine was the first opioid administered intrathecally to augment neuraxial blocks(.Saxena and Arava,2004). Opioid analgesic drugs produce intense, prolonged analgesic action without gross autonomic changes, loss of motor power or impairment of sensation other than pain when injected into subarachnoid or epidural space(Etches et al., 1989).

Morphine can produce serious side effects like late and unpredictable respiratory depression, post operative nausea and vomiting, pruritus and urinary retention(Morgan,1989; Crone et al., 1988).

Knowledge from extensive research on pain and spinal cord antinociceptive mechanisms let to the use of drug other than local anaesthetic agents to potentiate and prolong the duration of intrathecal anaesthetics(Senra et al., 1992).

Since the early 1980, intrathecal administration of midazolam has been reported to have antinociceptive action in humans(Good child,1987; Borg and Krijnen,1996; Kim and Lee,1998).

Discovery of benzodiazepine receptors in spinal cord in 1977 triggered the use of intrethecal midazolam for prolongation of spinal anaesthesia(Mohler and. Okada,1977). Invitro autoradiography has shown that there is a high density of benzodiazepine (GABAa) receptors in Lamina II of the dorsal horn in the human spinal cord, suggesting a possible role in pain modulation (Faull and Villager,1986).

2.METHODS

Hundred patients in the age group between 30 years and 45 years of either sex belonging to ASA GradeA-and Grade-B posted for elective lower limb and lower abdominal surgeries without any co-morbid diseases were grouped randomly into two groups (n=50).Group A (control group):received 12.5 mg of 0.5% hyperbaric bupivacaine with 0.4 ml normal saline. Group B (study group):received 12.5 mg of 0.5% hyperbaric bupivacaine with 2 mg of midazolam to keep the volume constant.Intraoperatively hemodynamic stability,the onset of sensory and motor block, duration of sensory and motor block,time taken for two segment regression of sensory block,and total duration of anaelgesia were studied.Patients were observed for 24 hours post operatively to look for any complication.

3.RESULTS

Addition of 2 mg of midazolam to hyperbaric bupivacaine does not alter the onset and level of sensory and motor block. The time taken for two segment regression was significantly prolonged in Group B (Group A – 78.9; Group B 87.2min). The duration of analgesia was also longer in group B (Group A – 158.80±13.61 ; Group B – 316.1±19.22).The time taken for maximum sensory blockade was significantly prolonged in Group B(Group A –7.4min; Group B – 5.5min) and the duration of regression to S1 segments (Group A – 210±23.1 : Group B – 302.6±17.4) More number of patients in the study group were sedated and responds to verbal commands. No patient had any respiratory depression, nausea, vomiting or shivering in either of the groups. Haemodynamics were preserved both intraoperatively and postoperatively. However there was a small percentage of patients who developed significant fall in blood pressure and bradycardia which were easily managed without any untowards effect.

4.DISCUSSION

The aim of good postoperative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Commonly use local anaesthetics for intrathecal anaesthesia are Lignocaine and Bupivacaine in India.

Bupivacaine 0.5% heavy has more prolonged action compared to Lignocaine,but the post operative analgesic duration is limited. Other method of prolonging analgesia is using a continuous epidural analgesia, which is technically more difficult and more costly.

Hence, an intrathecal additive to these local anaesthetics forms a reliable and reproducible method of prolonged post operative analgesia and to prolong the duration of anaesthesia. This technique being simple and less cumbersome has gained a wide acceptance.

A number of adjuvants to local anesthetics for spinal anaesthesia like opioids (fentanyl and buprenorphine), benzodiazepines (midazolam), ketamine and neostigmine have been used. The most common agents used are opioids and they have formed a cornerstone option for the treatment of post operative pain(Kanazi et al., 2005) .

Spinal opiates prolong the duration of analgesia, but they do have drawbacks of late and unpredictable respiratory depression, pruritus, nausea, vomiting and urinary retention which requires constant postoperative monitoring and urinary catheterisation. Hence opioids are not ideally suited for all patients and for ambulant

Hence there is a requirement of an adjuvant to be used along with local anesthetics which can produce prolonged analgesia without the above said side effects of opioids.

The present study entitled adding 2 mg midazolam to intrathecal 12.5 mg of 0.5% hyperbaric bupivacaine on spinal block characteristics in patients scheduled for elective lower limb and lower abdominal surgeries" was undertaken to evaluate the efficacy and the safety of midazolam as adjuvant to intrathecal hyperbaric 0.5% bupivacaine. Hundred patients were randomly divided into two groups, each group consisting of fifty patients (n=50):

Group A (control group):received 12.5 mg of 0.5% hyperbaric bupivacaine with
0.4 ml normal saline.

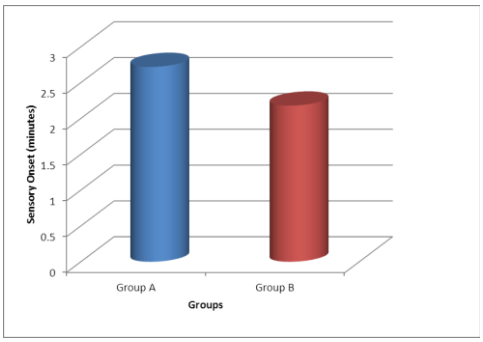
Group B (study group): received 12.5 mg of 0.5% hyperbaric bupivacaine with 2 mg of midazolam.

Table 1 :Results of the present study.

Spinal block characteristics	Group A	Group B
Time taken for onset of sensory blockade	2.72±0.72	2.18±0.69
Time taken for maximum sensory blockade	7.40±1.06	5.50±0.50
Time taken for regression of sensory block by two segments	78.90±10.11	87.20±22.27
Duration of sensory reg S1 in mins	210±23.18	302.6±17.41
Duration of analgesia	158.80 ± 13.61	316.10 ± 19.22
Onset of motor blockade	3.94±0.91	3.26±0.85
Time taken for maximum motor blockade	6.96±1.10	7.38±1.12
Duration of motor blockade	169.9±14.33	172.2±12.66

Table 2: Mean time taken for sensory onset in minutes

Time taken for sensory onset in mins	Group A	Group B	P Value A Vs B
Mean ±SD	2.7±0.72	2.18±0.69	
Minimum	2	1	0.314
Maximum	4	3	



Graph 2: Mean time taken for sensory onset in minutes

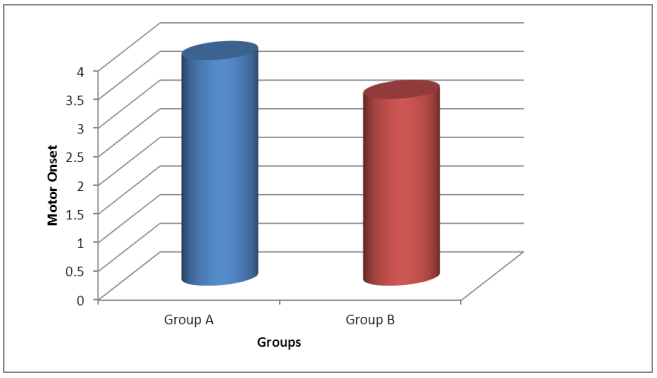
In our study the mean time taken for onset of sensory block is 2.72 mins in the control group, 2.18 mins in the study group. There is a no statistically significant decrease in the onset of sensory blocade in study group compared to conrol group.

In studies conducted by Yegin et al. who studied 44 patients using a bupivacaine midazolam combination and bupivacaine alone for anaelgesic effects.No statistical difference in onset of sensory block between the two groups was found(Yegin et al., 2004).

In studies conducted by Gupta et al.reported no significant difference between the two groups regarding time to onset of sensory block(Gupta et al., 2007).

Table 3: Time taken for motor onset in minutes.

Time taken for motor onset in mins	Group A	Group B	P Value A Vs B
Mean ±SD	3.9±0.91	3.2±0.85	
Minimum	2	2	0.653
Maximum	5	5	



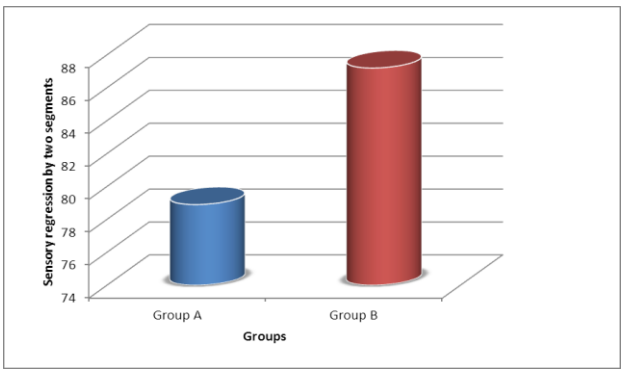
Graph 3: Time taken for motor onset in minutes.

In our study the mean time for onset of motor block is 3.94 mins in control group, and 3.26 mins in study group. There is statistically no significant decrease in the mean time for onset of motor blockade study group compared to the control group.

In studies conducted by Agrawal et al.reported no significant difference between the two groups regarding time to onset of motor block(Agrawal et al., 2005).

Table 4: Mean time taken for regression of sensory block by two segments

Duration of two segment sensory reg in mins	Group A	Group B	P Value A Vs B
Mean ±SD	78.9±10.1	87.2±22.2	
Minimum	60	115	0.000
Maximum	95	155	



Graph 4: Mean time taken for regression of sensory block by two segments

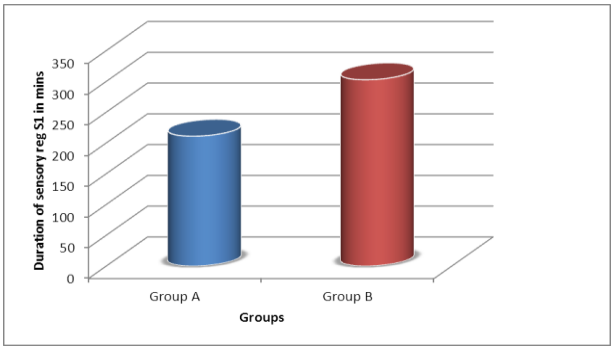
The time taken for regression of sensory block by two segments in the present study is 78.9mins in the control group, 87.20 mins in study group. There is a statistically significant increase in the mean time taken for regression of sensory block by two segments in study group compared to the control group.

In study conducted by Prakash et al.the time taken for two segment regression was prolonged in study group

In study conducted by Bharti et al.the time taken for two segment regression was prolonged in study group (Bharti et al., 2003).

Table 5: Duration of sensory reg S1 in mins.

Duration of sensory reg S1 in mins	Group A	Group B	P Value A Vs B
Mean ±SD	210±23.18	302.6±17.41	
Minimum	170	265	0.001
Maximum	240	355	



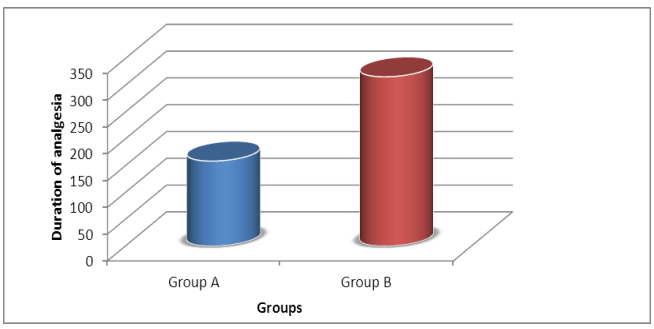
Graph 5: Duration of sensory reg S1 in mins.

The time taken for sensory block to regress to S1 in the present study 210.9 mins in the control group,302.6mins in the study group. There is a statistically significant increase in the mean time taken for regression of sensory block to S1 in study group compared to the control group.

In studies conducted by Batra et al.in 1999 reported a similar finding ,they concluded that intrathecal administration of midazolam along with bupivaine produces better postoperative anaelgesia and a prolonged sensory blockade(Batra et al., 1999.)

Table 6: Mean duration of analgesia

Duration of analgesia in mins	Group A	Group B	P Value A Vs B
Mean ±SD	158.80 ± 13.61	316.10 ± 19.22	0.029
Minimum	135	210	
Maximum	220	320	



Graph 6: Mean duration of analgesia

The mean duration of analgesia in our study is 158.8 mins in control group,316.1 mins in study group. There is a statistically highly significant increase in the duration of analgesia in midazolam group compared to the control group.

Kim M.H and Lee Y.M (2001) study of forty five patients found 1 mg midazolam and 2 mg midazolam administered intrathecally with bupivacaine provided a pain relief of 6.03±1.49 hours and 8.37±2.51 hours in comparison with 3.99±0.79 hours in control group bupivacaine(Kim and Lee,1998).

Bhattacharya D et al (2002) made the observation that intrathecal midazolam with bupivacaine provided pain free period of 300±11.82 minutes with that of 210±10.12 minutes in the control group[22].

Batra YK et al (1999) in a study of thirty patients found midazolam groups has a duration of analgesia 267.67±38 minutes as compared to control group of 229.8±41.4 minutes (Batra et al., 1999).

Valentine JM et al (1996) studies that the patients controlled analgesia systems (PCAS) usage was significantly greater in group with bupivacaine alone when compared to group which received midazolam(Valentine et al., 1996).

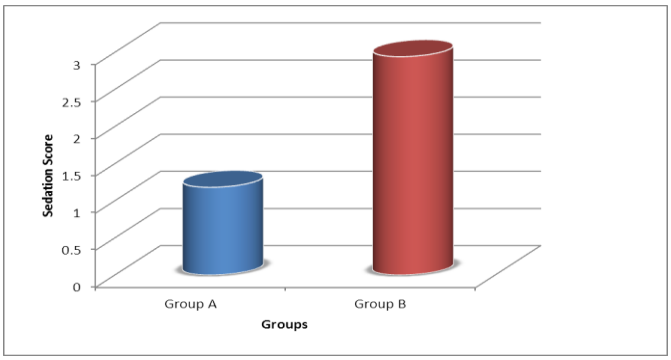
Bharti et al, however, found that the postoperative pain scores were lower in patients who received intrathecal midazolam (1 mg)along with bupivacaine(Bharti et al., 2003).

Prakash at aladministered intrathecal bupivacaine along with midazolam in either 1 mg or 2 mg doses. The latter observed that the duration of postoperative analgesia was significantly prolonged with the addition of intrathecal midazolam and that the effect was dose-dependent.

In an study of subarachnoid block with intrathecal bupivacaine (2 mL) with 2 mg midazolam for caesarean section, Prakash et al found that the mean duration of postoperative analgesia was 3.8 ± 0.5 hours in the group of patients administered bupivacaine alone as compared to 6.1 ± 1.0 hours in the midazolam group.

Table 7: Sedation score

Sedation score	Group A	Group B	P Value A Vs B
Mean ±SD	1.18 ± 0.43	2.94 ± 0.23	0.001



In studies conducted by Yegin et al. found that 2 mg of midazolam causes significant sedation(Yegin et al., 22004).

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