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COMPARISION BETWEEN THE EFFECTS OF INTRATHECAL MIDAZOLAM AND FENTANYL FOR ENDOSCOPIC UROLOGICAL SURGERIES: A RANDOMISED CLINICAL TRIAL

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ABSTRACT

INTRODUCTION : Spinal anaesthesia is a form of regional anaesthesia involving injection of a local anaesthetic into the cerebrospinal fluid of the patient's subarachnoid space to anaesthetize the spinal nerve roots running through it. The local anaesthetic deposited in the subarachnoid space act on the spinal nerve roots and not on the substance of the cord. The aim of the study is to compare intrathecal fentanyl along with bupivacaine and midazolam combined with bupivacaine for the duration and the quality of spinal anaesthesia in patients undergoing endoscopic urological surgeries.

MATERIALS & METHODS :A prospective randomized double blind clinical study undertaken to compare the effects of intrathecal midazolam and fentanyl as additives to intrathecal bupivacaine 0.5 % for spinal anaesthesia on 120 adult patients of SA physical status 1 & 2 in the age group of 18 to 60 years, posted for elective endoscopic urological surgeries at Government General Hospital, Kurnool from the period December 2015 to August 2017. Pulse rate, respiratory rate, arterial blood pressure and oxygen saturation were recorded every 5mins for first 30mins, and for every 15mins for next 90 mins with help of standard monitors like pulse oximetry, ECG and NIBP. The following parameters were observed - onset and duration of sensory block, onset and duration of Motor block, Two segement regression time, time for first request analgesia and any side effects associated with these drugs.

CONCLUSION : The present study concludes that there were no differences in the onset and duration of sensory blockade when fentanyl 25 micrograms or midazolam 2mg was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia.
There were no differences in the durations of onset and duration of motor blockade and effective(time for first request) analgesia when fentanyl 25 micrograms or midazolam 2mg was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia.

KEYWORDS : Fentanyl, Midazolam, Bupivacaine, endoscopic urological surgeries

INTRODUCTION:

Spinal anaesthesia is a form of regional anaesthesia involving injection of a local anaesthetic into the cerebrospinal fluid of the patient's subarachnoid space to anaesthetize the spinal nerve roots running through it. The local anaesthetic deposited in the subarachnoid space act on the spinal nerve roots and not on the substance of the cord. The aim of the study is to compare intrathecal fentanyl along with bupivacaine and midazolam combined with bupivacaine for the duration and the quality of spinal anaesthesia in patients undergoing endoscopic urological surgeries.

PATIENTS AND METHODS:

This clinical study was conducted on 120 adult patients of ASA physical status 1 & 2 in the age group of 18 years to 60 years, of either sex, posted for elective lower endoscopic urological surgeries under spinal anaesthesia at Kurnool Medical College, Kurnool , Andhra pradesh from the period December 2015 – August 2017.

Patients were selected randomly by lottery method, where 'B' group received intrathecal bupivacaine only and group 'BM' received intrathecal bupivacaine with preservative free midazolam and group 'BF' received intrathecal Bupivacaine with fentanyl Patients who were allocated to group 'B' received 3.5 ml of hyperbaric bupivacaine 0.5% + 0.5 ml of saline 0.9% intrathecally.

Patients who were allocated to Group 'BM' received 3.5 ml hyperbaric bupivacaine 0.5% + 0.4ml preservative free midazolam(2mg) + 0.1ml of saline 0.9% intrathecally.

Patients who were allocated to Group 'BF' received 3.5 ml hyperbaric bupivacaine 0.5% + 0.5ml fentanyl(25µg) intrathecally.

The patients were kept nil per orally 8 hours before surgery. The anaesthetic procedure was briefly explained to the patients. All patients were explained about the visual Analogue scale of pain assessment. An informed written consent was obtained from the patient or his/her relatives.

Once the patient was shifted to the operation theatre, the patient was connected to the routine monitors which included pulse oximetry, noninvasive blood pressure monitoring and electrocardiogram. All resuscitation equipments like intubation trolley with airways, laryngoscope, appropriate size endotracheal tubes along with drugs like atropine, mephentermine were kept ready. The anaesthesia machine was also checked along with oxygen delivery system.Baseline pulse rate, blood pressure, SPO2. were recorded. A wide bore intravenous access with 18G Cannula was obtained and secured. All patients were preloaded with 500ml of Ringer's lactate prior to spinal anaesthesia. The patients were premedicated with injection ondensetron 4mg IV and injection ranitidine 50mg intravenously. The patient was placed in left lateral position. The skin over the back prepared with antiseptic solution and draped with sterile towel. The L3-L4 inter space was identified and 25G Quincke Babcock spinal needle was introduced in this space through midline approach. After confirming the free flow of CSF, the study drug was injected intrathecally and the patient was immediately made to lie in supine position. The time of intrathecal injection of drug was noted. All patients were supplemented with 4L of O2/min throughout the procedure.

Statistical Analysis of data:

Collected data was analyzed by means of various statistical software such as SPSS Graph pad prism and appropriate tests.

ANOVA test has been used to find the significance of study parameters on continuous scale between the groups and Student's T-test (single tailed) has been used whenever necessary to compare between two groups. Chi-square test and fischer exact test has been used to find the significance of study parameters on categorical scale between the two groups. Significance was assessed at 5% level of significance.

OBSERVATION AND RESULTS

Data collection:

Data collection was done by filling the Pro forma containing the background information including age, gender, height, sensory analgesia, duration of effective analgesic time, degree of motor block and changes in heart rate and blood pressure. In addition, sedation score and adverse effect were noted for analysis of data. This randomized study was conducted to compare the effects with regards to the onset and duration of sensoryblock, motor block durations of complete and effective analgesia,and associated sideeffects.

Sensory block characteristics:

The onset of sensory block in GROUP- B was 187.98 seconds, and in GROUP- BM was 169.13 seconds, and in GROUP - BF was 168.65 seconds which is shown in table 1 below, inter group comparison is done to know the difference between groups by using student 't' test The group BM (169.13 sec) and Group BF (168.65 sec) has faster onset than group B (187.98 sec) in terms of sensory blockade and the values are also statistically significant (P-value<0.05) where as there is no difference among group BM (169.13 sec) and Group BF (168.65 sec) and the value is also statistically insignificant (P-value >0.05) which is shown in Table1.

Table -1: Onset of sensory blockade(seconds) among three groups:

	GROUPS Onset of sensory blockade (in secs)		P VALUE	T TEST VALUE	
STUDENT T tests	B (187.98 ± 8.21)	BM (169.13 ± 7.47)	0.0001	10.74	Significant
	B (187.98 ±8.21)	BF (168.65 ± 7.73)	0.0001	10.84	Significant
	BM(169.13 ± 7.47)	BF (168.65 ± 7.73)	0.78	0.28	NotSignificant

Maximum level of sensory block :

In Group B 24 patients achieved block upto T6 and 7 patients each upto T4 and T8 .In Group BM 25 patients achieved block upto T6 and 9 patients upto T4 and 6 patients upto T8 where as in Group BF 25 patients achieved block upto T6 and 10 patients upto T4 and 5 patients upto T8 which is shown in table 2.

Table-2: Maximum level of sensory block achieved among three groups

	LEVEL	Grou p - B	Group - BM	Group - BF
Maximum sensory level block	T4	7	9	10
	T6	24	25	25
	T8	7	6	5

Time to achieve maximum sensory level (seconds):

Time to achieve maximum sensory level in GROUP- B was 440.25 seconds, and in GROUP- BM was 397.75 seconds, and in GROUP - BF was 391.60 seconds which is shown in table 3 below to know the difference between groups by using student 't' test The group BM (397.75 sec) and Group BF (391.60 sec) has faster onset than group B (440.25 sec) in terms of maximum sensory blockade level and the values are also stastisfically significant (P-value<0.05) where as there is no difference among group BM (397.75 sec) and Group BF (391.60 sec) and the value is also stastisfically insignificant (P-value >0.05) which is shown in Table 3 .

Table-3: time to achieve maximum sensory level (seconds):

	GROUPS Onset of sensory blockade (in secs)		P VALUE	T TEST VALUE	
STUDENT T tests	B (440.25± 28.57)	BM (397.75 ±30.14)	0.0001	6.47	Significant
	B (440.25± 28.57)	BF (391.60± 34.86)	0.0001	6.82	Significant
	BM(397.75± 30.14)	BF (391.60± 34.86)	0.40	0.81	NotSignificant

Onset of motor blockade :

The time of onset of motor block in group-B was 231.3 secs as compared to 225.08 secs in group-BM and 224.7 secs in group-BF represented in table 4 below, inter group comparison is done to know the difference between groups by using student 't' test. The group BM (225.08 sec) and Group BF (224.7 sec) has faster onset than group B (231.3 sec) in terms onset of motor blockade and the values are also statistically significant (P-value<0.05) where as there is no difference among group BM (225.08 sec) and Group BF (224.7 sec) and the value is also stastisfically insignificant (P-value >0.05) which is shown in Table4.

Table-4: Onset of motor blockade (in seconds) among three groups

	GROUPS Onset of motor blockade (in secs)		P VALUE	T TEST VALUE	
STUDENT T tests	B (231.3± 6.51)	BM (225.08±5.41)	0.0001	4.64	Significant
	B (231.3± 6.51)	BF (224.7± 7.86)	0.0001	4.09	Significant
	BM(225.08± 5.41)	BF (224.7 ±7.86)	0.81	0.24	NotSignificant

Two dermatomal segments regression of sensory level:

Time to two segment regression in group-BM was 113.43 mins and in group –BF was 115.88 mins where as in group - B it was only 91.75 min which is shown in table 5 inter group comparison is done to know the difference between groups by using student 't' test The group BM (113.43 min) and Group BF (115.88 min) prolonged duration than group B (91.75 min) in terms of two dermatomal segment regression of sensory level and the values are also statistically significant (P-value<0.05) where as there is no difference among group BM (113.43 min) and Group BF (115.88 min) and the value is also statistically insignificant (P-value >0.05) which is shown in Table5.

Table-5: Two dermatomal segments regression of sensory level (minutes)

	GROUPS Two segment regression time (mins)		P VALUE	T TEST VALUE	
STUDENT T tests	B (91.75± 4.97)	BM (113.43 ± 5.43)	0.0001	18.62	Significant
	B (91.75 ±4.97)	BF (115.88 ± 7.58)	0.0001	16.83	Significant
	BM((113.43 ± 5.43)	BF (115.88± 7.58)	0.10	1.66	NotSignificant

Motor recovery:

The time taken by the patients for complete motor recovery (i.e. Regression of Bromage scale from 3 to 0) was 175.93 mins in group-BM, compared to 173.43 mins in group-BF and 146.5 mins only in group B patients in order to establish statistical difference student t test was done among groups . The group BM (175.93 mins) and Group BF (173.43 mins) has taken prolonged time than group B (146.5 mins) for complete motor recovery and the values are also statistically significant (P-value<0.05) where as there is no difference group BM (175.93 mins) and Group BF (173.43 mins) and the value is also statistically insignificant (P-value >0.05) which is shown in Table 6

Table-6:Time (in minutes) for complete motor recovery:

	GROUPS Motor recovery time (in mins)		P VALUE	T TEST VALUE	
STUDENT T tests	B (146.5 ± 14.92)	BM (175.93 ± 13.79)	0.0001	9.16	Significant
	B (146.5 ± 14.92)	BF (173.43 ± 16.35)	0.0001	7.69	Significant
	BM(175.93 ±13.79)	BF (173.43 ± 16.35)	0.46	0.73	NotSignificant

First request of analgesic :

The time for first request of analgesics by the patients in group-BM was 222.95 minutes, where as it was 220.45 minutes in group - BF and only 175.43 minutes in group-B patients and student t test was done to find out statistical significance of difference among the groups Group BM (222.95 mins) and Group BF (220.45 mins) has taken more time than group B (175.43 mins) for the first request of analgesic and the values are also statistically significant (P-value<0.05) where as there is no difference Group BM (222.95 mins) and Group BF (220.45 mins) and the value is also statistically insignificant (P-value >0.05) which is shown in Table7

Table-7: Time (in minutes) of first request of analgesic by the patients:

	GROUPS First request analgesia (In mins)		P VALUE	T TEST VALUE	
STUDENT T tests	B (175.43 ± 8.98)	BM (222.95 ± 10.09)	0.0001	22.25	Significant
	B (175.43 ±8.98)	BF (220.45 ±14.20)	0.0001	16.94	Significant
	BM(222.95 ±10.09)	BF (220.45 ±14.20)	0.36	0.91	NotSignificant

SUMMARY: A prospective randomized double blind clinical study undertaken to compare the effects of intrathecal midazolam and fentanyl as additives to intrathecal bupivacaine 0.5 % for spinal anaesthesia on 120 adult patients of SA physical status 1 & 2 in the age group of 18 to 60 years, posted for elective endoscopic urological surgeries at Government General Hospital, Kurnool from the period December 2015 to August 2017. Patients belonging to group B received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml of normal saline. Patients belonging to group BF received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 µgms) of fentanyl. Patients of group BM received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.4 ml (2 mg) of preservative free midazolam + 0.1 ml of normal saline. Subarachnoid block was administered in L3-L4 intervertebral space with 25G Quincke'sneedle.Pulse rate, respiratory rate, arterial blood pressure and oxygen saturation were recorded every 5mins for first 30mins, and for every 15mins for next 90 mins with help of standard monitors like pulse oximetry, ECG and NIBP. The following parameters were observed - onset and duration of sensory block, onset and duration of Motor block, Two segement regression time, time for first request analgesia and any side effects associated with thesedrugs.

CONCLUSION:

There were no differences in the onset and duration of sensory blockade when fentanyl 25 micrograms or midazolam 2mg was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia.

There were no differences in the durations of onset and duration of motor blockade and effective(time for first request) analgesia when fentanyl 25 micrograms or midazolam 2mg was used as additive to intrathecal hyperbaric bupivacaine for spinalanaesthesia.

Compared to fentanyl, intrathecal administration of midazolam as additive to intrathecal hyperbaric bupivacaine was associated with less side effects like pruritus, etc. and no significant difference in other adverse effects.No significant sedation was associated with intrathecal administration ofmidazolam in comparison to fentanyl.

REFERENCES

1. Srivastava U, Kumar A, Saxena S, Saxena R, Gandhi NK, Salar P. Spinal anaesthesia with lignocaine and fentanyl. Indian J. Anaesth. 2004; 48(2): 121- 123.
2. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine. I J.Anaesth. 2007;51(5):415–419.
3. Karthivel S, Sadasivam S, Saxena A, Kannan TR, Effects of intrathecal ketamine added to bupivacaine for spinal anaesthesia. 2001; 55(9): 899-904.
4. Tan PH, Chia YY, Lo Y, Liu K, Yang LC, Lee TH. Intrathecal bupivacaine with morphine or neostigmine for post operative analgesia after total knee replacement. Can J Anaesth. 2001; 48(6): 551-556.
5. Schug SA, Saunders D, Kurowski I, Paech MJ. Neuraxial drug administration: a review of treatment options for anaesthesia and analgesia. 2006; 20(11): 917-933.
6. Biswas BN, Rudra A, Bose BK, Chakrabarty S, Bhattacharjee S. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post operative period. Indian J. Anaesth. 2002; 46(6)
7. Singh V, Gupta LK, Singh GP. Comparison among intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries. J Anaesth Clin Pharmacol. 2006; 22(4): 371-375.
8. Ozkardesler S, Gurpinar T, Akan M, Koca U, Sarikaya H, Olmez T et. al. A possible perianaesthetic serotonin syndrome related to intrathecal fentanyl. J Clin Anaesth. 2008; 20(2): 143-145.
9. Karakan M, Tahtaci N, Goksu S. Synergistic effect of intrathecal bupivacaine and fentanyl in spinal anaesthesia. Gazi Medical Journal. 1999; 10: 100-105.
10. Agrawal N, Usmani A, Seghal R, Kumar R, Bhadoria P. Effect of intrathecal midazolam bupivacaine combination on post operative analgesia. IJA 2005; 49(1).
11. Goodchild CS, Guo Z, Musgreave A, Gent JP. Antinociception by intrathecal midazolam involves endogenous neurotransmitters acting at spinal cord delta opioid receptors. Br J Anaeth. 1996; 77(6): 758-763.
12. Larson MD. History of anaesthetic practice. In Miller's anaesthesia. Ed by Ronald D Miller. 6th edn. Churchill Livingstone. 2005: 3-52.
13. Brill S, Gurman M, Fisher A. A history of administration of local analgesics and opioids. Eur J Anaesth. 2003; 20: 682-689.
14. Maduska AL, Hajghassemali M. A double blind comparison of butorphanol and meperidine in labour: maternal pain relief and effect on the new born. Canadian Anaesthetists' society journal. 1978; 25: 398- 404.