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Comparison of Intravenous Dexmedetomidine vs Intravenous Midazolam in Spinal Anaesthesia with Bupivacaine

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KEYWORDS :

INTRODUCTION

Multimodal anesthesia techniques are available for infraumblical and lower limb surgeries e.g- regional anesthesia(spinal,epidural),local anesthesia,periferal block,general anesthesia. Subarachnoid block is popular among them. Regional anaesthesia is generally well tolerated by all patients, producing less post-operative complications like confusion, delirium and post-operative thromboembolism than general anaesthesia. However, subarachnoid block has got its own inherent complications, especially related to cardiovascular stability.

"Pain" is an unpleasant sensory and emotional experience associated with actual / potential tissue damage or described in terms of such tissue damage.11 Many factors modify pain. Goal of pain management is to eliminate pain with minimum side effects. One of the modality is neuraxial anaesthesia. Pain persists as unpleasant sensation and produce over all delay in recovery of patient.

Concept of post operative analgesia is gaining importance now-a-days. So the aim of anesthesia technique should be;- minimum invasive, causes minimum adverse effect, provide prolonged analgesia and economically acceptable.

During spinal anesthesia sedative and tranquilizing drugs are required to counteract stress and anxiety which may trigger stress response and related haemodynamic complications. Various drugs as I.V supplementation like benzodiazepines , propofol, narcotics are used for sedative and analgesic purpose. But they all causes RS and CVS depression.

Dexmedetomidine a parenteral selective alpha 2 agonist39 with sedative anxiolytic and analgesic properties without causing respiratory depression. It also have sympatholytic effects that blunt many of the cardiovascular responses seen during the peri-operative period. The sedative and analgesic effects are mediated by a2 adrenergic receptors in the brain(Locus coeruleus)15 and spinal cord. So it provides adequate sedation after spinal anesthesia,reduces anxiety level, physiological and psychological stress and patient and surgeon satisfaction. It also alleviates position related discomfort. Most importantly it has an opioid sparing effect so does not significantly depresses respiratory drive. Few studies suggest that I.V Dexmedetomidine supplementation prolongs the effect of spinal anesthesia.18

Midazolam is a water soluble short acting benzodiazepine which is used for pre-operative medication and conscious sedation. The amnestic effect of midazolam is more potent than its analgesic effect. Thus patients may be awake fallowing administration of midazolam but remains amnestic for events and conversations for several hours.27,28,29

The present study was undertaken to evaluate efficacy and potency of midazolam and dexmeditomedine administered intra-venously just after induction with intra-thecal bupivacaine for effect on sensory and motor blockade,sedation hemodynamic stability, duration of effective analgesia, post-operative pain relief,post-operative analgesic requierment and adverse effect of drugs used.

AIMS OF STUDY

The present study was designed to compare the effect of intravenous dexmedetomidine (Group-D),intravenous midazolam (Group-M) administered just after giving spinal anesthesia with 3.0 ml bupivacaine heavy (15 mg) in various infraumblical and lower limb surgeries for the following points:-

- To evaluate the efficacy of I.V dexmeditomedine and I.V midazolam on subarachnoid block by intrathecal bupivacaine.
- To evaluate the effect of both I.V drugs on sensory and motor blockage.
- To observe intra-operative and post-operative hemodynamic stability in both the groups.
- To observe intra-operative and post-operative sedation.
- Duration of effective analgesia.
- To observe any peri-operative adverse effect.
- Duration of postoperative analgesia.

MATERIAL AND METHOD

A randomized controlled study was conducted on 50 patients (ASA grade I or II) aged 20-60 years scheduled for infra-umblical surgeries after taking informed consent.

Study Protocol:-

Detailed preoperative history and physical examination of patient done. Patients having h/o allergy to any study drug and contraindications for spinal anesthesia are excluded from study. All the patients were evaluated pre-operatively and laboratory investigations complete blood count, blood sugar, renal function tests, serum bilirubin, serum electrolytes and chest x-ray, ECG were reviewed.

Procedure was explained to patient. Patient was informed about perception of pain and perception of any discomfort during surgery. VAS was

explained to the patient on 1-10 scale. Written informed concent of patient and their relative taken.

EXCLUSION CRITERIA :

- Patient's age less than 20 years and above 60 years.
- Pregnant patients.
- Infection at site of block.
- History of allergy to local anaesthesia drug.
- Patient with severe cardiac or respiratory disease.
- Patient with coagulation disorder.

Patients who were selected and posted for surgeries were randomly allocated in two groups.

Group-D : Received a loading dose of I.V dexmedetomidine 0.5mcg/kg by infusion pump over 10 min + 0.5mcg/kg/hr infusion till the end of surgery.
Group-M : Recieved a loading dose of I.V midazolam 0.02mg/kg by infusion pump over 10 min + 0.04mg/kg/hr infusion till the end of surgery.

PREPARATION

All the patients were fasted for minimum 6 hours prior to scheduled time of surgery. Psychological preparation was done and the procedure explained to all the patients in advance. In operation theatre anaesthesia machine was checked and emergency drugs were kept ready.

In the operating room an I.V. access was secured using an 18G cannula. Each patient preloaded with infusion of 10 to 15 ml/kg of lactated Ringer's solution. Standard monitoring included continuous electro-cardiogram, pulse-oximetry, non-invasive blood pressure measurements and visual assessment of respiration. Inj. Ondansatrone 0.08 mg/kg and inj. Glycopyrolate 0.004mg/kg I.V given as premedication 30 min before dura puncture.

PROCEDURE

In all the patients, under strict aseptic and antiseptic precautions, lumber puncture was performed (after giving local anaesthesia with a 26G hypodermic needle) using a 25-gauge Quincke's needle positioned midline at the L3-L4 interspace in lateral position.

Patients of both the group received 3 ml (15 mg) hyperbaric bupivacaine 0.5% in subarachnoid block. After completion of injections the patients were immediately returned to the supine position, pillow was placed under head of the patient and time of injection was noted. Then afterwards no change in patient's position done.9,25 Just after giving supine position patients of group D and group M patients received drugs as described above in group allocation.

Sensory block was assessed by the loss of sensation to pinprick. Time for onset of sensory block, maximum level of sensory block achieved and time to achieve maximum sensory block were noted in minutes. Sensory level in between T5 - T8 was achieved. Time from subarachnoid injection to second sacral dermatome (S2) was assessed by pinprick and recorded in minutes. Motor block was assessed by Modified Bromage score.

DATA COLLECTION

Pulse, BP, SPO2 and RR were recorded on 1, 5, 10, 20, 30, 45, 60 , 90 and 120 minutes after giving spinal anaesthesia.

INTRA OPERATIVE ADVERSE EFFECTS:-

Patients of both the group are observed for adverse effects like,

- Sedation
- Hypotension
- Bradycardia
- Respiratory depression
- Nausea, Vomiting
- shivering
- Dryness of mouth
- Involuntary (paradoxical) movements40.
  Sedation levels were assessed using Ramsay's sedation score.

Hypotension (20% fall in SBP) was treated with intravenous fluids and inj. Mephentermine 6 mg i.v. Bradycardia (HR < 60 bpm) was treated with inj. Atropine 0.6 mg i.v. Shivering was treated with 100%, O2 warm fluids and adequate patient covering.7 No other sedative or analgesic drug was given to the patients intraoperatively. Respiratory depression (RR <12 / min or SPO2< 90%) was treated with 100% O2 . In addition to the loading dose of intravenous fluids, patients received a maintenance infusion of lactated ringer's solution as calculated according to the conventional formula.Shivering, nausea, vomiting if present treated accordingly. Duration of surgery for each case was noted.

After completion of surgery patients are monitored every 30 min upto 2 hrs then at 4 hrs, 6 hrs, 12hrs and 24hrs.

Pain measurement was done using VAS scale.When VAS score was >3 cm, the patients were given inj. Tramadol 1 mg/kg I.V + inj. Ondansatrone 0.08 mg/kg I.V and this time was noted.

Time from subarachnoid injection to administration of first rescue analgesic was taken on 'Time to first rescue analgesic' and recorded in minutes. Patients were inquired about neurological deficit 7 days post-operatively.

DISCUSSION

Spinal anaesthesia is the preferred anaesthesia technique for lower abdominal and lower limb surgeries. Bupivacaine is the most commonly used local anaesthetic in spinal anaesthesia. The use of adjuvants with local anaesthetics provides prolonged and superior quality of anaesthesia and postoperative analgesia with relatively small doses of individual drugs with less requirement of postoperative analgesia.

Dexmedetomidine is an attractive alternative to anesthetic adjuvant used at present due to its anesthetic sparing and hemodynamic stabilizing effects.

Current literatures suggest a ceiling effect on prolonging post-spinal analgesia after 0.5 mg /kg boluses. With increasing the dose beyond 0.5 mg /kg resulted in unwanted side effects notably bradycardia and excessive sedation. Dexmedetomidine has linear pharmacokinetics and dose dependent sedative action, when a loading dose of dexmedetomidine 1 mcg/kg administered over 10 min, the average peak concentration was reached in 17 min with terminal half-life of 2 hr 10 min. So a single bolus dose might be sufficient for procedure lasting less than 60 min whereas continuous infusion is needed for longer procedure.

Intravenous bolus dose technique has been shown to be associated with peaks and troughts in plasma concentrations producing significant side effects and delayed recovery. Continuous infusions have been proved to produce lesser side effects, faster recovery, easy control over desired depth of sedation.

Heamodynamic characteristics :

Heart rate :

Table 1 shows HR (bpm) variation in two study group. Base line (grp. D 99.3±6.52, grp M 99.3± 6.92) and 1 min (grp D 99.0±4.68, grp M 98.6±6.88) values in both the group are comparable and statisticaly not significant ($p > 0.05$). After 5 mins in Group D and as compared to Group M fall in HR is statisticaly highlly significant ($p < 0.001$). Swati Bist et al38,observed that the reduction in heart rate was more in group D than in group M, 5 mins afterwards starting demedetomidine infusion. Yongxin et al41,ovserved that the Dexmedetomidine patients in this study had a significant reduction in HR which occurred most commonly during a bolus or within 10 minutes of the start of an infusion.Chilkunda et al8,observed significantly higher proportion of patients in the dexmedetomidine group (33%) had bradycardia compared to the control group (4%).

Systolic Blood Pressure :

Table 2 shows variation in systolic blood pressure amongst the two groups. There is no statisticaly significant difference in SBP of the two groups at base-line,one min and at 5 min.10 min onwards there is a highly significant difference in SBP in the two groups. Swati Bist et al38,observed that Group D recorded a significant fall in systolic blood pressure (SBP) after 40 minutes ($p < 0.006$). Our study was in corellation with Chilkunda et al8 and Yongxin et al41.

Ramssay's sedation score :

Table 3 shows intra-operative RSS in the two study groups. The highest level of sedation acheived in the two groups are significantly different. Intraoperative Ramsay sedation scores were significantly higher in group D (range 2-4) as compared to group M (range 2-6); (P < 0.001). Maximum scores in group D ranged from 3 to 4. In group D, the maximum sedation score was 4 whereas in group M maximum sedation score was 6. RSS of Post-operative period in both groups were comparable with no significant difference.Kaya.F.N et al20, observed that the median (range) of the highest Ramsay sedation score was 2 (2–5) in the dexmedetomidine group, 3 (2–5) in the midazolam group (P < 0.001).Chilkunda et al8, observed similar result in their study.

Highest sensory level acheived :

Table 4 shows highest sensory level acheived in the both study groups. Higher sensory level (T5 28% and T6 72%) is achieved in Group D as compared to Group M (T6 44% and T8 56%).Swati Bist et al38, conducted study and observed that Group D has recorded a higher level of sensory block. T6 was the highest sensory level in 72% patients in group D while only 28 % had the same in group M (p<0.001).Kaya.F.N et al20, conducted a study and observed that maximum upper levels of sensory block were higher with dexmedetomidine (T 4.6 ± 0.6) than with midazolam (T 6.4 ± 0.9) (P<0.001) or with saline (T 6.4 ± 0.8) (P<0.001).Reddy et al32 and Chilkunda et al8, observed that the level of sensory blockade was significantly higher in group D.

CHARACTERISTICS OF SPINAL BLOCK :

Table 5 shows effect of the study drugs on different charecteresticsof spinablock. Time for sensory onset, time for grade 3 motor blockade and time for highest sensory level are comparable in both the groups (p>0.05). Time to regression by two dermatome (min) in group D is 211 ±11.4 where as in group M is 162±11.3 which is highly significant (p < 0.001).Time of 1st rescue analgesic (min) in group D is 325 ± 23.7 where as in group M is 218 ± 15.3 which is highly significant (p < 0.001).Time of motor block to Bromage 1 (min) in group D is 246 ± 16.5where as in group M is 236 ± 16.6 which is statistically significant (p < 0.05).Analgesic requests in 24 hrs (no.) in group D is1.96 ± 0.35 where as in group M is 3.4 ± 0.50 which is highly significant (p < 0.001). Our findings were corellated with study of Swati Bist et al38, and Kiran Kumar S et al22 . Kaya.F.N et al20, also observed that in dexmeditomidine group time of first rescue analgesia was significantely prolonged and total analgesic requirment during 24 hours is also reduced.

Adverse effects :

Table 6 shows Adverse effects (in no. of patients) in the two different groups. In group D hypotension occured in 2 (8%) patients and bradycardia in 5 (20%) patients. No other adverse effect noticed in group D. In group M respiratory depression occured in 4 (16%) patients and shivering in 2 (8%) patients. Adverse effect profile in different groups are related to pharmacological properties of the study drugs. Yongxin et al41, and they ovserved that the patients who had received dexmedetomidine for sedation during the surgical procedure had no respiratory depression but in midazolam group total 8 patients had respiratory depression. The number of patients who suffered bradycardia was significantly larger in the dexmedetomidine group.Chilkunda et al8, conducted a study in which there was no shivering in group D but present in control group (10%).

CONCLUSION

DEXMEDETOMIDINE markedly prolongs duration of sensory blockage, arrousable sedation and provides excellent quality of post-operative analgesia with decreases no. of analgesic requests in 24 hrs. But it should be used cautiously due to its heamodynamic effects.MIDAZOLAM provides stable heamodynamics with higher level of sedation but comparatively less effect on quality of spinal blockage and post-operative analgesia.

Table 1.

HR(bpm)				
	Group D	Group M	P-Value	Inference
Base Line	99.3 ± 6.52	99.3 ± 6.92	0.98	NS
1 min	99.0 ± 4.68	98.6 ± 6.88	0.79	NS
5 min	82.8 ± 5.80	97.8 ± 6.76	< 0.001	HS
10 min	61.1 ± 2.49	95.5 ± 5.46	< 0.001	HS
15 min	61.5 ± 2.34	95.3 ± 5.92	< 0.001	HS
20 min	61.6 ± 1.97	95.2 ± 5.53	< 0.001	HS
25 min	62.2 ± 2.43	95.8 ± 5.68	< 0.001	HS
30 min	61.5 ± 1.96	94.9 ± 5.16	< 0.001	HS
45 min	67.7 ± 2.81	95.2 ± 5.14	< 0.001	HS
60 Minute	74.5 ± 2.10	95.1 ± 5.09	< 0.001	HS
75 Minute	78.5 ± 3.07	95.5 ± 5.40	< 0.001	HS
90 Minute	80.7 ± 2.71	95.3 ± 6.03	< 0.001	HS
120 Minute	82.6 ± 1.67	95.6 ± 5.15	< 0.001	HS

Table 2.

SYSTOLIC BLOOD PRESSURE (mm of Hg)				
	Group D	Group M	P-Value	Inference
Base Line	130.6 ± 4.38	130.5 ± 4.43	0.98	NS
1 Minute	124.5 ± 4.55	125.4 ± 4.14	0.50	NS
5 Minute	119.1 ± 3.48	121.6 ± 3.87	0.09	NS
10 Minute	107.1 ± 2.76	121.9 ± 3.18	< 0.001	HS
15 Minute	106.3 ± 3.77	121.6 ± 3.24	< 0.001	HS
20 Minute	106.3 ± 3.30	121.8 ± 3.05	< 0.001	HS
25 Minute	108.2 ± 2.32	122.3 ± 2.86	< 0.001	HS
30 Minute	108.7 ± 2.89	121.9 ± 2.80	< 0.001	HS
45 Minute	109.6 ± 3.14	121.8 ± 3.05	< 0.001	HS
60 Minute	111.7 ± 3.48	121.9 ± 2.98	< 0.001	HS
75 Minute	114.4 ±3.21	121.9 ± 2.91	< 0.001	HS
90 Minute	119.05 ± 3.20	121.4 ± 3.28	< 0.001	HS
120 Minute	122.4 ± 2.19	122.0 ± 2.97	< 0.001	HS

Table 3.

Ramssay's sedation score				
	Group D	Group M	P-Value	Inference
Base Line	1.8 ± 0.33	1.8 ± 0.41	0.98	NS
1 Minute	1.8 ± 0.37	1.8 ± 0.41	0.98	NS
5 Minute	1.8 ± 0.40	1.9 ± 0.28	>0.05	NS
10 Minute	2.2 ± 0.40	2.16 ± 0.37	>0.05	NS
15 Minute	3 ± 0.29	2.5 ± 0.49	< 0.001	HS
20 Minute	3.3 ± 0.48	3.0 ± 0	< 0.001	HS
25 Minute	3.5 ± 0.51	3.9 ± 0.28	< 0.001	HS
30 Minute	3.5 ± 0.51	4.5 ± 0.51	< 0.001	HS
45 Minute	3.6 ± 0.44	5.0 ± 0.00	< 0.001	HS
60 Minute	3.5 ± 0.51	5.3 ± 0.46	< 0.001	HS
75 Minute	3.6 ± 0.50	5.4 ± 0.51	< 0.001	HS
90 Minute	3.4 ± 0.60	5.5 ± 0.51	< 0.001	HS
120 Minute	3.4 ± 0.55	5.4 ± 0.51	< 0.001	HS

Table 4.

Highest sensory level achieved (no. of patients)		
Group D	T_5	7 (28%)
	T_6	18(72%)
Group M	T_6	11(44%)
	T_8	14(56%)

Table 5.

CHARETERISTICS OF SPINAL BLOCK				
	Group D	Group M	P-Value	Inference
Time for sensory onset(min)	6.8 ± 0.87	6.9 ± 0.73	>0.05	NS
Time for grade 3 motor blockade(min)	8.7 ± 0.83	8.4 ± 0.77	>0.05	NS
Time for highest sensory level(min)	11.6 ± 1.04	11.5 ± 0.82	>0.05	NS
Time to regression by 2 dermatome (min)	211 ± 11.4	162 ± 11.3	< 0.001	HS
Time of 1st rescue analgesic (min)	325 ± 23.7	218 ± 15.3	< 0.001	HS
Time of motor block to Bromage 1(min)	246 ± 16.5	236 ± 16.6	0.03	S

Analgesic requests in 24 hrs (no.)	1.96 ± 0.35	3.4 ± 0.50	< 0.001	HS

Table 6.

	Group D	Group M
Bradycardia	5	nil
Hypotension	2	nil
Respiratory depression	nil	4
Shivering	nil	2
Dryness of mouth	nil	nil
Nausea Vomiting	nil	nil

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