Original article

CONSCIOUS SEDATION WITH DEXMEDETOMIDIINE/ MIDAZOLAM INFUSION IN PATIENTS WITH INYRATHECAL BUPIVACAINE FOR INFRAUMBILICAL SURGERIES.

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Key words: CONSCIOUS SEDATION ,DEXMEDETOMIDIINE/ MIDAZOLAM INFUSION ,INFRAUMBILICAL SURGERIES.

ABSTRACT

Background: *spinal anesthesia is very much common regional anesthesia. Assurance and conscious sedation is required to make patients calm and co-operative. We have also assessed effect of dexmedetomidine/ midazolam infusion on sensorimotor characteristics of spinal bupivacaine.*

Material and methods *:*

We selected 50patients for the study, 25 in each group.

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.* ***Observation*** *The pulse rate & SBP in group D was significantly lower as compared to group M from 10 minutes to 120 minutes after subarachnoid block. Significant difference was seen between group D and group M. There was no statistically significant change in pulse rate between 120mins to 24 hrs postoperatively between the groups.*

There was no statistically significant difference up to 24 hrs post operatively.

There was no significant change in RR and SPO_2 in any group.

Highest sensory level and duration of sensory and motor blockade and duration of analgesia and No. Of analgesic requests in 24 hrs were compared.

Intraoperative and postoperative adverse effects were noted.

Higher sensory level (T_5 28% and T_6 72%) is achieved in Group D as compared to Group M (T_6 44% and T_8 56%).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 ($p < 0.001$).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. ***Conclusion:*** *DEXMEDETOMIDIINE is more effective supplementation then Midazolam in terms of sedation as well as prolonged sensorimotor charestristics of inyrathecal bupivacaine.*

Key words: concious Sedation,dexmedetomidine infusion, midazolam infusion, intrathecal bupivacaine.

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.

Bupivacaine is the most commonly used local anaesthetic agent having satisfactory sensory and motor blockade with limited duration of action. Various intrathecal adjuvant have been tried with local anaesthetic agents

"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.

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

CONSCIOUS SEDATION only some of the centers in the medullary reticular formation and thalamus are depressed in a dose dependent manner. Thus this level of sedation additionally provides the benefit of preservation of protective airway reflexes, especially in monitored anesthesia care.[19]

Dexmedetomidine a parenteral selective α_2 agonist[39] with sedative anxiolytic and analgesic properties without causing respiratory depression. The sedative and analgesic effects are mediated by α_2 adrenergic receptors in the brain(Locus ceruleus)[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] Dexmeditomedine has unique pharmacodynamic properties it is suitable for peri-operative care during general and regional anesthesia. It is used as adjuvant to regional anesthesia.[14]

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 infusion 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

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 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 intraoperative and postoperative hemodynamic stability in both the groups,To observe intraoperative and postoperative sedation,Duration of effective analgesia,To observe any perioperative adverse effect,Duration of postoperative analgesia.

MATERIAL AND METHODS

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 score 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 blockHistory 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 pumpover 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.

On arrival 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 ivand inj. Glycopyrolate 0.004mg/kg I.M 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 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 and group M patients received 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.

Sensory block was assessed by the loss of sensation to pinprick. Time

to 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 T_5 - T_8 was achieved. Time from subarachnoid injection to second sacral dermatome (S_2) was assessed by pinprick and recorded in minutes.

Motor block was assessed by Modified Bromage score.

Time for onset of grade-3 motor blockade was noted.

Total duration of grade-3 motor blockade was noted.

DATA COLLECTION

Pulse, BP, SPO_2 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,shiveringDryness of mouth,Involuntary (paradoxical) movements[40].Sedation levels were assessed using Ramsay's sedation score.

Hypotension (defined as 30% fall in systolic BP from the baseline systolic BP) was treated with intravenous fluids and inj. Mephentermine 6 mg i.v. Bradycardia (defined as pulse rate < 60 beats per minute) was treated with inj. Atropine 0.6 mg i.v. Shivering was treated with 100%, O_2 warm fluids and adequate patient covering.[7] No other sedative or analgesic drug was given to the patients intraoperatively. Respiratory depression (defined as RR <12 / min or SPO_2< 90%) was treated with 100% O_2 . 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 'Time to first rescue analgesic' recorded in minutesPatients were inquired about neurological deficit 7 days post-operatively.

STATISTICAL ANALYSIS

Statistical analysis done using the SPSS software. Inter-group comparison was done, using paired 't' test as well as comparing mean and standard deviation. A 'p' value < 0.05 was taken as significant an 'p' value < 0.001 was taken as highly significant.

OBSERVATIONSAND RESULTS

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. We have evaluated 50 patients randomly divided in two groups of 25 each.

Table 1.

DEMOGRAPHIC CHARACTERISTICS			
	Group D	Group M	Inference
Sex(M/F)	15/10	13/12	NS

Age(Years)	46.08±5.90	43.48±5.77	NS
Height(cm)	164.6±6.034	164.04±5.74	NS
Weight(kg)	66.84±4.50	65.72±4.83	NS
ASA I/II	13/12	12/13	NS
Duration of surgery (min)	95.4± 12.83	98.0 ± 10.21	NS

Demographically both groups are comparable. There was no significant difference between them

Haemodynamics;

There was significant difference in HR 5 min after administration of the study drugs.In group D ,HR and SBP remain 20% less than baseline from 10 to 120 min in comparison to Group M($P<0.001$)There was no change in haemodynamics in Postoperative period

RSS score:

Mean RSS of the D group was 3.4 whereas of M group was5.4 after 15 mins.($p<0.001$)

Table 2

CHARETERISTICS OF SPINAL BLOCK				
	Group D	Group M	P-Value	Inference
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	246 ± 16.5	236 ± 16.6	0.03	S

Bromage 1(min)				
Analgesic requests in 24 hrs (no.)	1.96 ± 0.35	3.4 ± 0.50	< 0.001	HS

Table 2 shows characteristics of spinal block in the two groups. Statistically highly significant difference was present between the two groups for time to regression by 2 dermatome, time of 1st rescue analgesic and analgesic requests in 24 hrs (no.).

Highest sensory level:

Significantly higher sensory level is achieved in Group D72% patients haveT6 level,In group M 44% patients have T6 level.

Adverse effects:

In groupD 6 patients have bradycardia & 2 have Hypotension,In group M 4 patients have Respiratory depression,2 patients have shivering.like various adverse effects .

Postoperative Monitoring :

We have monitored all patients in post-operative period till 24 hrs for HR, B.P, SpO_2 , RR, RSS and VAS every 30 mins till 2 hrs then at 4 hrs, 6 hrs, 12 hrs abd 24 hrPost operative Vital parameters of All patients were in normal limits.

Analgesics were repeated after VAS was more than 3.

All patients were conscious and co-operative.

No adverse effect noted during post-operative monitori

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.Duration of analgesic

action of local anaesthetics can be prolonged by mixing them with certain pharmocologic agents called additives or adjuvants. A wide variety of centraly active drugs are used to provide sedation, anxiolysis and amnesia. Dexmedetomidine is an attractive alternative to anesthetic adjuvant used at present due to its anesthetic sparing and hemodynamic stabilizing effects. Used along with regional anesthesia, dexmedetomidine prolongs the action of local anesthetics along with providing analgesia and sedation without causing respiratory depression. Dexmedetomidine is also used as a sedative for monitored anesthesia care due to its analgesic properties, co-operative sedation and lack of respiratory depression.[36]

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.

DEMOGRAPHIC CHARACTERISTICS :

Table 1 shows demographic characteristics of both the groups. The two groups were comparable ($p>0.05$).

In 2015 **Surjya Prasad Upadyay et al[37] ,** study shows same comparable demographics

Heamodynamic characteristics :

Heart rate :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 ($p < 0.001$).

Lower heart rate in Group D can be explained due to decreased sympathetic outflow by activation of post-synaptic □□□□receptors in CNS and decresed circulatory levels of catecholamines caused by dexmedetomidine.

In 2014 **Swati Bist et al[38],** observed that the reduction in heart rate was more in group D than in group M, 5 mins afterwards starting demedetomidine infusion.

In 2011 **Yongxin et al[41],** observed 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.

In **2014 Chilkunda et al[8],** observed significantly higher proportion of patients in the dexmedetomidine group (33%) had bradycardia compared to the control group (4%).

Systolic Blood Pressure :

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 al 38 observed that Group D recorded a significant fall in systolic blood pressure (SBP) after 40 minutes ($p < 0.006$). **Chilkunda et al[8],** conducted a study in which. They observed significantly higher proportion of patients in group D had bradycardia and fall in systolic blood pressure more than 20% of baseline value. Systolic, diastolic, and mean arterial blood pressures were relatively lower in group D.

In 2011 **Yongxin et al[4]** ovserved that MAP was significantly reduced during the intraoperative period in two groups, and the reduction did not show significant differences between the two groups.

Ramssay's sedation score 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 al[20], ovserved 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 ($P < 0.001$). Excessive

sedation (Ramsay sedation score of 5) was observed in two patients of the dexmedetomidine group and in five patients of the midazolam group.

Sang Hi Park et al[35], observed that there was no patient who showed excessive sedation in the control group. To show excessive sedation means Ramsay sedation score = 5 or 6). In the dexmedetomidine 0.5 Group and 1.0 group RSS was significantly higher than control group . In both Dexmedetomidine groups, sedation score was the deepest around the 20-minute period and it decreased thereafter .

Chilkunda et al[8], observed that intraoperative Ramsay sedation scores were significantly higher in group D (mean 4.4 ± 0.7, range 3-6) as compared to group C (mean 2 ± 0.1, range 2-3) (P < 0.001)

CHARACTERISTICS OF SPINAL BLOCK :

Table 4shows effect of the study drugs on different charecteresticsof spinablock. 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 ($p < 0.001$).

Swati Bist et al[38], show that better sensorimotor charestristics with Dexmedetomidiine group than Midazolam group P value <0.001.

In **2015 Kiran Kumar S et al** (22)0bserved that the Duration for 2 dermatomal Regression of sensory blockade (137.4±10.9 mins), duration of sensory blockade (269.8±20.7min) and duration for motor block regression to Modified Bromage scale 0 (220.7±16.5 mins) prolonged significantly than clonidine and control groups.

In **2014 Ahmed et al[2],** observed that dexmedetomidine intravenously or intrathecally extended the duration of bupivacaine motor block and it was significantly longer in the IT group compared with the IV group.

Kaya.F.N et al[20], obeserved that the time for sensory regression of two dermatomes was 145 ± 26 min in the dexmedetomidine group, than in the midazolam ($P < 0.05$) and saline ($P < 0.05$) groups. Reddy **et al[32,]** Conducted a study and observed better spinal charestristics in Dexmedetomidiine group than clonidine and placebo groups.

Highest sensory level acheived : Table 6 shows highest sensory level acheived in the both study groups. Higher sensory level (T_5 28% and T_6 72%) is achieved in Group D as compared to Group M (T_6 44% and T_8 56%).our results correlate with results of Swati **Bist et al[38], Kaya.F.N et al (20), Reddy et al** ($p < 0.001$).

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.

In 2011 **Yongxin et al[41]**, 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.

In **2014 Chilkunda et al[8],** conducted a study in which there was no shivering in groupD but present in controle 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.

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