Indian Journal of Basic and Applied Medical Research; December 2019: Vol.-9, Issue- 1, P. 285 - 292

Original article:

To analyse and compare between the effects of administration of intravenous dexmedetomidine versus intravenous midazolam on quality of bupivacaine subarachnoid block

Dr Anil Kumar Sharma, Dr Mamta Chadha# , Dr Prasoon Pathak, , Dr Sushil Krishnan, Dr Rakesh Kumar, Dr Ashok Bansal

Department of Anaesthesiology, Northern Railway Central Hospital, New Delhi-55

Corresponding author: Dr Mamta Chadha, ACHD, Department of Anaesthesiology, Northern Railway Central Hospital, New Delhi-55

ABSTRACT

INTRODUCTION: Spinal anaesthesia is a common technique and when it is used with adjuvants it helps in prolongation of duration, onset of sensory and motor blockade and postoperative analgesia. Dexmedetomidine, alpha-2 agonist and Midazolam, a benzodiazepine are short acting drugs commonly used in practice.

AIMS & OBJECTIVE : To compare the effects of intravenous Dexmedetomidine infusion versus intravenous Midazolam used as an adjuvant to subarachnoid block using 0.5% bupivacaine heavy on parameters like Onset and duration of sensory block, Onset and duration of motor block, Hemodynamic profile and Level of sedation.

METHODOLOGY: After obtaining the approval from IEC and SRC committee approval, 60 patients were allocated to two groups, Group D (N=30) – Patients received injection dexmedetomidine infusion 0.5 µg / kg/ hr over 10 minutes after spinal anaesthesia using bupivacaine 0.5% heavy 0.3 mg/kg.

Group M (N=30) – Patients received injection midazolam 0.04mg/kg after spinal anaesthesia using bupivacaine 0.5% heavy 0.3 mg/kg.

RESULTS : The observations were statistically analysed and to assess the quality of spinal anaesthesia. Calculations and results regarding two segment regression of sensory block(min), Duration of sensory block regression to S-1, Visual analogue scale >3 (time in min), Sedation score respectively.

CONCLUSION : It was found that in both groups, Group-D (Dexmedetomidine) as well as Group-M (Midazolam), there was an improvement in the quality of anaesthesia administered for the surgical procedures. In both study groups, the patients remained hemodynamically stable throughout the study period.

KEY WORDS: Dexmedetomidine, Midazolam, subarachnoid block

INTRODUCTION

Spinal anaesthesia is a common technique used extensively to provide a fast and profound nerve block by means of single injection of local anaesthetic solution into the subarachnoid space. It allows the production of ideal operating condition in lower part of the body through the relatively simple injection. When this technique of spinal block is used with adjuvants this gives us new means of prolongation of duration, onset of sensory and motor blockade and postoperative analgesia. Different agents, like epinephrine, phenylephrine, adenosine, magnesium sulphate, fentanyl, clonidine, and dexmedetomidine etc. have been used as adjuncts to local anaesthetics for prolonging the duration of

spinal analgesia via the intrathecal route. Dexmedetomidine is a commonly available alpha-2 agonist, which received FDA approval in 1999, for use as a short term (less than 24 h) sedative analgesic in the intensive care unit. Dexmedetomidine compared to Clonidine is a more selective alpha -2 adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha-1 receptors. In addition, Dexmedetomidine is short-acting drug than clonidine and has an antagonist, atipamezole for reversal of its sedative effect. These properties render dexmedetomidine suitable for sedation and analgesia during the entire perioperative period: as premedication, as an anaesthetic adjunct for general and regional anaesthesia, and as postoperative sedative and analgesic. Intravenous dexmedetomidine has been used for pre-medication and is found to attenuate the intubation response. It also decrease the requirement of inhalation agents and opioids during general anaesthesia and minor procedures. It has also proved to be useful to blunt the extubation response and also reduced the emergence reaction and analgesic requirement after extubation of trachea. Dexmedetomidine has also been used in brachial plexus block and also proved to prolong spinal anaesthesia when given intrathecally and also when given intravenously . It also hastens the onset of spinal block when used as a supplement to bupivacaine. It has also been proved that intravenous dexmedetomidine also reduces the requirement of opioid supplementation when used with thoracic epidural in post-thoracotomy patients.

There are several studies related to use of oral, intrathecal and intravenous clonidine in prolongation of spinal anaesthesia but very few studies are available regarding the effects of intravenous use of dexmedetomidine on spinal anaesthesia. So we decided to study and compare the effects of intravenous dexmedetomidine and intravenous clonidine when given in a patient who has been administered spinal block using bopivacaine, so that a search for ideal intravenous agent to be used along with spinal anaesthesia can be proposed for better outcome in patients.

AIMS & OBJECTIVE

Primary Aim: To assess the effects of intravenous dexmedetomidine infusion used as an adjuvant to subarachnoid block using 0.5% bupivacaine heavy.

Secondary Aim: To compare the effects of intravenous dexmedetomidine infusion versus intravenous Midazolam used as an adjuvant to subarachnoid block using 0.5% bupivacaine heavy on following parameters

1. Onset and duration of sensory block
2. Onset and duration of motor block
3. Hemodynamic profile
4. Level of sedation and

METHODOLOGY

This study was conducted after obtaining the approval from institutional ethical committee and Scientific committee. A written & informed consent from patients scheduled to undergo surgical procedures under subarachnoid block using 0.5% bupivacaine heavy at our hospital were considered to be included in our study. 60 patients were allocated to two groups by randomization method which was done by using a computer-derived random number sequence and sealed opaque envelopes. The two study groups were as follows

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Group D (N=30) – Patients who received injection dexmedetomidine infusion 0.5 µg / kg/ hr over 10 minutes (through infusion pump) after spinal anaesthesia using bupivacaine 0.5% heavy 0.3 mg/kg.

Group M (N=30) – Patients who received injection midazolam 0.04mg/kg after spinal anaesthesia using bupivacaine 0.5% heavy 0.3 mg/kg.

TECHNIQUE

After obtaining written informed consent from the patient who meets the inclusion criteria for our study was taken up on operation theatre table. They were connected to standard monitoring including NIBP, ECG, SpO_2. All patients were pre-loaded with 10ml/kg of Ringer's Lactate solution. Subarachnoid block with 0.3 mg/kg body weight of 0.5 % bupivacaine was given in the L3 – L4 interspace using a 26-gauge Quincke spinal needle with patient in sitting position.

After performing the spinal block, vital signs were recorded every 5 minutes or earlier if required. After 15 minutes of institution of the subarachnoid block if all hemodynamic parameters of the patient remains stable then following drug was administered according to the group assigned to that patient i.e. Group-D or Group-M. The patients were assigned respective groups by using lottery method with closed envelope technique.

To avoid any bias, 2 syringes were prepared, one 5 ml and second 20 ml with following drugs.

Group- D- 5 of ml Normal saline through 5 ml syringe given intravenously followed by Injection Dexmedetomidine 0.5 µg / kg prepared in 20 ml syringe will be administered as infusion using syringe pump at the rate 0.5 µg / kg/ hr over a period of 10 minutes in order to avoid any bias

Group- M 5 ml of 0.04 mg/kg Midazolam diluted with Normal Saline through 5 ml syringe given intravenously followed by Injection Normal Saline prepared in 20 ml syringe administered as infusion using syringe pump over a period of 10 minutes in order to avoid any bias

Also the observer will be blinded to the group to which patient belongs

The following parameters are noted.

Onset of sensory blockade and motor blockade.

Maximum level of sensory blockade attained and the time taken for the same was noted.

Total duration of analgesia was noted.

Total duration of sensory blockade and motor blockade was noted.

Sensory blockade was tested using pinprick method at every 5 minutes for next 15 minutes after giving spinal anesthesia and every 15 minutes for next 60 minutes and every 30 minutes till the end of surgery and there after every 30 minutes till 6 hours

Quality of motor blockade was assessed by modified Bromage scale.

Level of sedation by using modified Ramsay Sedation Score.

Total duration of surgery and any side effects was noted.

Patients were monitored during the post operative period for analgesia, and any side effects like sedation, post operative nausea and vomiting

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

RESULTS

The study was conducted to compare and evaluate the effects of intravenous dexmedetomidine infusion & intravenous midazolam as adjuvant to subarachnoid block using 0.5% bupivacaine heavy in assessing the quality of spinal anaesthesia.

Tables 1 and 2 show types of surgeries performed on patients included in our study and their group distribution respectively. Table no. 3 to 6 (Annexure) shows statistical observations, calculations and results regarding two segment regression of sensory block(min), Duration of sensory block regression to S-1, Visual analogue scale >3 (time in min), Sedation score respectively.

Maximum upper levels of sensory block were higher with dexmedetomidine (T 9.47 ± 1.04) than with midazolam (T 9.37 ± 1.0) (P=0.353). Time for sensory regression of two dermatomes was 184 ± 35.87 min in the dexmedetomidine group, longer than in the midazolam group (134 ± 18.86 min; P< 0.001). Duration of motor block was 230.00± 22.74 min in the dexmedetomidine group, longer than in the midazolam group (177 ± 14.42 min); P < .001 . The overall 6-hr VAS pain scores were similar for the two groups . The VAS pain scores did not change over time (each 30 min) in the two groups, and were similar among groups at any observation period for up to 6 hr after surgery.

Time to first request for postoperative analgesia was later in the dexmedetomidine group groups (238.97 ± 20.41) than in the midazolam group (170.69± 22.74) .

The median (range) of the highest Ramsay sedation score was 3 (2–4) in the each group. Excessive sedation (Ramsay sedation score of 5) was not observed in patients of the dexmedetomidine group neither in patients of the midazolam group . The lowest HR and MAP during spinal anaesthesia were approximately 20% lower than baseline values and there were no differences among groups. No patient in both group had bradycardia or hypotension needing treatment, No other complications attributable to the drugs, and procedure were noted .

The total amount of fluids administered following spinal anaesthesia was similar in the two groups. There were no differences among groups regarding SpO2, Respiratory parameter (SpO2) remained within normal limits throughout the procedure after surgery.

TABLE NO. 1 (TYPE OF SURGERY)

	Group D	**Group M**
Total Knee replacement	12	9
Total Hip replacement	5	5
Dynamic Hip Screw	3	3
Bipolar Hemiarthoplasty	2	4
Int fixation of ankle fracture	6	3
Tibia plating	2	6
Total (N)	30	30

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

TABLE NO. 2 (FREQUENCY OF DISTRIBUTION OF PATIENTS)

	N	**%**
Group D (Dexmed)	30	50%
Group M (Midazolam)	30	50%
Total	60	100%

TABLE NO. 3 (TWO SEGMENT REGRESION OF SENSORY BLOCK(min))

	Group D	Group C
Duration (Mins)	184.00	134.00
Std. Deviation	± 35.87	± 18.86
Total (N)	30	30

TABLE NO. 4 (DURATION OF SENSORY BLOCK REGRESSION TO S-1)

	Group D	Group M
Duration (Mins)	220.00	170
Std. Deviation	± 26.52	± 16.4
Total (N)	30	30

TABLE No. 5 (VAS >3 (TIME IN MIN))

	Group D	Group M
VAS achieved(Min)	238.97	170.69
Std. Deviation	± 20.41	24.19
Total (N)	30	30

TABLE NO.6 (SEDATION SCORE)

Median	Group D	Group C
Sedation score	3	2
Total (N)	30	30

DISCUSSION

The present study was conducted to compare and evaluate the effects of intravenous dexmedetomidine infusion & intravenous midazolam as adjuvant to subarachnoid block using 0.5% bupivacaine heavy in assessing the quality of spinal anaesthesia **.** The onset and duration of sensory and motor blockade, maximum level of sensory blockade, total duration of analgesia, changes in blood pressure, pulse rate, side effects (if any) and sedation score were noted for both the groups. Pain score was assessed using 10 point visual analog scale (VAS). Rescue analgesic was given when VAS >3. All vital parameters were monitored intraoperatively and postoperatively. In available literature, It is recommended to administer dexmedetomidine over 10 min, as rapid administration might produce tachycardia,

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

bradycardia, and hypertension[13] Furthermore, an evaluation of the analgesic effect of different doses of intravenous dexmedetomidine (0.25, 0.5, and, 1 μg/kg) on ischemic pain in healthy volunteers demonstrated moderate analgesia with a ceiling effect at 0.5 μg/kg.[14] With this in mind, dexmedetomidine, 0.5 μg/kg was given over 10 min in this study. Bolus administration of midazolam 0.05 mg/kg was reported to give enough sedation and amnesia without any adverse effects on hemodynamics and respiration in patients aged 30–70 yr under spinal anesthesia.[15] Therefore, midazolam 0.05 mg/kgwas administered to the patients in this study.

In our study Dexmedetomidine 0.5μg/kg was given over 10 min after administering spinal anesthesia. It does not appear to have direct effects on the heart. In the coronary circulation, dexmedetomidine causes a dose dependent increase in coronary vascular resistance and oxygen extraction, but the supply/demand ratio is unaltered [13]. A biphasic cardiovascular response has been described after the administration of dexmedetomidine. A bolus of 1μg/kg results in a transient increase in blood pressure (BP) and a reflex decrease in heart rate (HR). This initial response is attributed to the direct effects of β-adrenoceptor stimulation of vascular smooth muscle. This response can be attenuated by a slow infusion over 10min, as given in our study, 0.5μg/kg over 10 min. The decrease in the heart rate was more evident in group D but not statistically significant when compared with group M, and no patients required atropine for bradycardia. The lower HR observed in group D could be explained by the decreased sympathetic outflow and circulating levels of catecholamines that are caused by dexmedetomidine. Other studies support the finding that the bradycardia caused by dexmedetomidine is long lasting when used as a premedication drug.

Previous studies have shown that the hypotension caused by dexmedetomidine persists in the intraoperative as well as in the postoperative period. In our patients there was a fall in mean arterial pressure in group D as well as in group M and clinically was not significant. The mean duration of two segment regression in group D and group M was 184±35.87 and 134±18.86min respectively. The difference in the duration between the groups is statistically significant. This is consistent with the findings reported by Fatma Nur Kaya et al [1] who concluded that Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anaesthesia. Our study also correlates with the study of Mahmoud M Al-Mustafa et. Al [3] who concluded that intravenous dexmedetomidine prolongs bupivacaine spinal analgesia.

The mean duration of analgesia in group D and group M was 238.97±20.41 and 170.69± 24.19 min ($p<0.001$) respectively which correlates with the findings reported by Fatma Nur Kaya et al [1] with the findings of Mahmoud M Al-Mustafa et. Al [3] also with Víctor Whizar-Lugo et. Al [2] who studied, Intravenous Dexmedetomidine vs. Intravenous Clonidine to prolong Bupivacaine Spinal Anaesthesia.

The mean duration of motor blockade in group D was 230±22.74 which was significantly higher than that of group M(177±14.42). The prolongation of motor blockade with dexmedetomidine has been reported in several studies.

The highest level of sensory blockade achieved was T 9.47±1.04 in group D and T 9.37±1 in group M, which are comparable. This is in discordance with the results of Fatima et al.[1] who observed a significantly higher sensory level with dexmedetomidine as compared to midazolam. This could be due to the fact that they had administered fix dosage of bupivacaine whereas we have used weight based dosage for the same.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Pain was assessed by VAS score and injection diaclofenac sodium 75 mg (rescue analgesic) was given when VAS > 3. The time of first dose of analgesic in group D was 238.97±20.41 min and was 170.69± 24.19 min in group M. Our results are consistent with the results of Fatima et al.[1] concluded that intravenous dexmedetomidine delays the onset of postoperative pain and reduces the requirement of analgesic. Our study is also in concordance with Víctor Whizar-Lugo e. al.[2] Sedation score in both groups D and M was 3. Sedation produced by dexmedetomidine is different from other sedatives as patient is easily arousable and remains cooperative. The participation of non rapid eye movement sleep pathways seems to explain why patients who appear to be “deeply asleep” from dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep[36]. This type of sedation is branded “cooperative” or “arousable”, to distinguish it from the sedation induced by drugs acting on the GABA system, In previous studies, it has been shown that dexmedetomidine caused no or minimal respiratory depression.23However, midazolam is known to cause apnea and arterial desaturation in sedative doses.24 There was no respiratory depression in any patients and respiratory parameters (respiratory rate, and SpO2) remained with in normal limits throughout our procedure. such as midazolam which produce a clouding of consciousness[37]

CONCLUSION

On the basis of our study, it is concluded that when surgical procedures are performed under subarachnoid block, it is better to administer some agent to provide sedation or sedation with analgesia also. In our study group, it was found that in both groups, Group-D (Dexmedetomidine) as well as Group-M (Midazolam), there was an improvement in the quality of anaesthesia administered for the surgical procedures. In both study groups, the patients remained hemodynamically stable throughout the study period.

In addition the patients in our study group remained sedated due to administration of injection Dexmedetomidine in Group-D and injection Midazolam in Group-M. This helped to allay the anxiety and fear during the surgical procedure and all the patients tolerated the surgical procedures comfortably.

None of the patient belonging to either of the two study groups showed any other complication like nausea, vomiting, hemodynamic instability during post operative period. So it is concluded that administration of either of our study drugs Midazolam as well as``` Dexmedetomidine to patients undergoing surgical procedures in subarachnoid block improves the quality of anaesthesia as it adds to patient comfort, provide good surgical conditions and may result in improved surgical outcomes.

REFERENCES

1. Fatma Nur Kaya, Belgin Yavascaoglu, Gurkan Turker, Arzu Yildirim,Alp Gurbet, Elif Basagan Mogol and Berin Ozcan Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anaesthesia. Canadian Journal Of Anaesthesia; 2010; 57:39-45.
2. Víctor Whizar-Lugo, Irma A. Gómez-Ramírez, Roberto Cisneros-Corral , Nora Martínez Gallegos Intravenous Dexmedetomidine vs. Intravenous Clonidine to prolong Bupivacaine Spinal Anaesthesia. A Double Blind Study.2007; 19:143-146.

3. Mahmoud M Al-Mustafa, Izdiad Z Badran, Hamdi M Abu-Ali, Bassam A Al-Barazangi, Isalm M Massad and Subhi M. Al-Ghanem: Intravenous Dexmedetomidine Prolongs Bupivacaine Spinal Analgesia. M.E.J. Anesth; 2009; 20: 225-31.
4. Racle JP, Benkhadra A, Poy JY, Gleizal B. Prolongation of isobaric bupivacaine spinal anaesthesia with epinephrine and clonidine for hip surgery in the elderly. AnesthAnalg. 1987; 66:442-6.
5. Khalili G, Janghorbani M, Sajedi P, Ahmadi G J. Effects of adjunct intrathecal magnesium sulfate to bupivacaine for spinal anaesthesia: a randomized, double-blind trial in patients undergoing lower extremity surgery. Anesthesiology. 2011 Dec; 25:892-7.
6. Deepika Shukla, Anil Verma, Apurva Agarwal, H D Pandey, Chitra Tyagi. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol. 2011 Oct-Dec; 27: 495–499.
7. A Gurbet, G Turker, N K Girgin, H Aksu, N H Bahtiyar. Combination of ultra-low dose bupivacaine and fentanyl for spinal anaesthesia in out-patients anorectal surgery. J Int Med Res. 2008 Sep-Oct; 36:964-70.
8. Kamibayashi T, Maze M. Clinical uses of alpha2-adrenergic agonists. Anesthesiology; 2000;93:1345-9.
9. Dobrydnjov I, Axelsson K, Samarutel J, Holmstrom B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine. Acta Anaesthesiol Scand; 2002; 46:806-14.
10. Fogarty DJ, Carabine UA, Milligan KR. Comparison of the analgesic effects of intrathecal clonidine and intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacement. Br J Anaesth; 1993; 71:661-4.
11. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamics, and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaesthesiol Scand; 1994; 38:724-8.
12. Tamsen A, Gordh T. Epidural clonidine produces analgesia. Lancet; 1984; 2:231-232.
13. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous Dexmedetomidine in humans, II: Hemodynamic changes. Anesthesiol. 1992; 77:1134–42.
14. Corning J.L.N.Y. Med. J. 1885; 42, 483 (reprinted in 'Classical File', Survey of Anesthesiology 1960; 4, 332)
15. Bier A. Versucheüber, Cocainisirung des Rückenmarkes. Deutsch ZeitschriftfürChirurgie 1899; 51:361. (translated and reprinted in 'Classical File', Survey of Anesthesiology 1962; 6, 352)
16. Ralph Gertler, H. Cleighton Brown, Donald H. Mitchell, and Erin N. Silvius. Dexmedetomidine: a novel sedative-analgesic agent. BUMC Proceedings 2001; 14:13-21