Original Article

Intravenous dexmedetomidine as an adjunct to subarachnoid block: A simple effective method of better perioperative efficacy

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Abstract

Background and Aim: Dexmedetomidine (D) is a α2 agonist, has anesthetic and analgesic-sparing property. The objective of this study was to evaluate the effect of intravenous (I.V.) dexmedetomidine on the duration of sensory and motor block, postoperative analgesia, the level of sedation and side effect.

Material and Methods: Sixty patients were randomly divided into two groups of thirty each. Group D received dexmedetomidine infusion @1 mcg/kg over 10 min and then @ 0.6 mcg/kg/h for rest of duration during surgery, Group C (control) received a similar volume of normal saline infusion before spinal anesthesia with 3 ml of bupivacaine 0.5%. Time of onset and regression time for sensory and motor blockade, the maximum upper level of sensory blockade, duration of postoperative analgesia, Ramsay sedation score and hemodynamic parameters were recorded. Intraoperative bradycardia and atropine requirement along with other side effect were also recorded.

Results: The duration of sensorimotor block was significantly longer in D Group (341.7 ± 20.8 min for sensory block and 278.0 ± 11.0 min for motor block) as compared to control group (329.5 ± 22.1 min for sensory block and 250.0 ± 14.8 min for motor block), which was statistically significant ($P < 0.05$). The mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group (115.5 ± 8.7 min) compared to control group (95.8 ± 11.4) ($P < 0.001$). Intraoperative Ramsay sedation scores were significantly higher in D Group (mean - 3.4 ± 0.7, range – 2–4) as compared to C Group (mean - 2.9 ± 0.3, range – 2–4) ($P < 0.001$). 26.7% (8/30) cases had bradycardia that required atropine as compared to control group (2/30), and none of the patients in the dexmedetomidine group had postoperative shivering as compared to 10% in control group ($P = 0.056$). Statistical analysis was performed with statistical package for the social science version-20 using analysis of variance/Chi-square test/unpaired t-test, and $P < 0.05$ was considered statistically significant.

Conclusion: I.V. dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine spinal anesthesia. Dexmedetomidine provides an excellent sedation during surgery.

Key words: Dexmedetomidine, intravenous, motor and sensory block, spinal anesthesia, subarachnoid block

Introduction

In a bid to improve regional anesthesia techniques, many drugs have been tried as sedative agents in patients undergoing lower abdominal surgeries under subarachnoid block.[1-4] All these agents have their own integral merits and demerits, and none of them can be considered as an ideal agent for sedation during spinal anesthesia. Therefore, the search for supplementing regional anesthesia with sedative agents seems to be unending.

Studies have compared propofol and midazolam for achieving faster onset and longer duration.[5] However, patients receiving propofol were three times more likely to have hypotensive

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episodes which limited the role of propofol as a sedative agent, especially in cardiac patients.

Newer alpha-2 agonist dexmedetomidine has emerged as a wonderful drug in anesthesia practice since last one and a half decade.[6] Very few studies have been done with dexmedetomidine as a sedative agent to supplement subarachnoid block. As such there is a paucity of literature on the effect of dexmedetomidine on overall block characteristics of regional anesthesia. This limited literary evidence encouraged us to design a double-blinded randomized prospective to assess the effect of intravenous (I.V.) dexmedetomidine on spinal anesthesia with regard to duration of sensory and motor block, quality of sedation as well as for any observed side effect.

Material and Methods

The Hospital Ethical Committee approved the prospective, double-blinded randomized study and a written informed consent was taken from sixty patients of physical status American Society of Anaesthesiologist (ASA) Grades I and II, of age lesser than 60 years, scheduled for lower abdominal surgeries amenable under spinal anesthesia. Patients allergic to drugs used in regional anesthesia, ASA Grades III–V, patients on β-blocker and Ca^{2+} channel blocker, pregnant patient, obese patient, and patients for cesarean section were excluded from the study.

The study was conducted during 2012–2015 at our tertiary care center. The sample size for the study was evaluated to be sixty, which was generated using a sample size calculator. Considering a difference of 30 min in postoperative analgesia, a sample of 28 was considered adequate for the study keeping α-error at 0.05 and power of the study at 80%. However, we took thirty patients in each group for better validation of results. The study participants were randomly divided into two groups of thirty patients each ($n = 30$) using sealed envelope technique. In this technique, anyone envelope was picked up by the patient from a box which contains sixty envelopes in which thirty D Group and thirty C Group were mentioned. According to picked up the envelope, the drugs was given to the patients by a senior resident of our unit without disclosing the fact neither to patients nor researcher. Group D ($n = 30$) patients received a loading dose of 1 mcg/kg of I.V. dexmedetomidine by infusion pump over 10 min followed by a maintenance dose of 0.6 mcg/kg/h till the end of surgery whereas the Group C ($n = 30$) received an equivalent quantity of normal saline (NS) as loading and maintenance dose I.V. by infusion pump and served as control. After the arrival of the patient in the operation theater, I.V. line was secured with two 18-gauge cannula. Through one cannula ringer lactate infusion (10 ml/kg) infusion was started and baseline

vitals were recorded and through the other cannula infusion of respective study, drug solutions were given in respective groups. Baseline parameters were observed and recorded. Following this, spinal anesthesia was administered with a 25-gauge Quincke's needle at L3–L4/L2–L3 interspace using standard midline approach.

Vitals were recorded immediately after the subarachnoid block. Sensory blockade was checked by using pinprick technique at 1, 2, 5 min after giving spinal anesthesia and then at every 5 min till 30 min and then at every 15 min till recovery of block to S1 level. Motor blockade was assessed by modified Bromage scale at 1, 2, and 5 min after giving spinal anesthesia, then at every 5 min till 30 min and then every 15 min till full recovery of motor level by asking the patient to move and flex legs with prior information to operating surgeon during intraoperative period. The level of sedation was evaluated both intra- and post-operatively on the basis of sedation scale used in one of the previous studies.[2] Intraoperatively, sedation scale was evaluated at 1, 2, and 5 min after giving spinal anesthesia, then at every 5 min till 30 min and then every 15 min till discharge from postanesthesia care unit. Side effects during intra- and post-operative were also observed and recorded and treated accordingly. Intraoperative side effect such as hypotension and bradycardia were detected by the continuous monitoring of blood pressure (BP) and heart rate (HR). The systolic BP (SBP) <90 mmHg was the cut off point to consider Hypotension and HR < 60 beat/min was the cut off point for bradycardia. Postoperative pain intensity was assessed using a 10 point visual analog scale (VAS) on which 0 indicated no pain and 10 indicated the worst pain imaginable. Postoperative nausea, vomiting, and shivering were also observed till the discharge of the patients. Hypotension (SBP <90 min), bradycardia (HR <60/min), and postoperative complications like nausea and vomiting were managed appropriately. Any hypotension with SBP <90 mmHg was managed with a fluid bolus of 300–500 ml NS. If such hypotension did not respond to this fluid administration, then injection mephentermine 5 mg I.V. was administered. If hypotension did not respond to two repeat doses of mephentermine, then dopamine infusion was started to maintain the BP. Any incidence of bradycardia with HR <50/min was treated with atropine 0.6 mg I.V. For postoperative pain, tramadol 100 mg intravenously was given if VAS >3 and ondansetron 4 mg intravenously was used to treat Postoperative nausea and vomiting (PONV).Statistical analysis was done using Statistical Package for the Social Sciences Version 20 for windows (IBM Corp, Armonk, New York). All continuous variables were analyzed using Student's *t*-test. Categorical variables were analyzed using Chi-square test and ordinal variable like Ramsay sedation scale was analyzed using Mann–Whitney U-test. $P < 0.05$

was considered statistically significant and $P < 0.001$ was considered highly significant.

Results

All patients ($n = 60$) completed the study. There was no statistically significant difference in two groups with regards to demographic profile including patient's age, gender, weight, ASA physical status I and II, and the duration of surgery [Table 1]. The onset of sensorimotor block was earlier in dexmedetomidine group (9.6 ± 5.2 min for sensory block and 2.3 ± 0.9 min for motor block ($P < 0.001$) as compared to control group (9.8 ± 2.8 min for sensory block and 5.1± 2.0 min for motor block), which was statistically significant ($P < 0.05$). The duration of sensory blockade was significantly prolonged in dexmedetomidine group (341.7 ± 20.8 min) as compared to control group (329.6 ± 22.1 min) ($P < 0.001$). The mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group (115.5 ± 8.7 min) compared to control group (95.8 ± 11.4 min) ($P < 0.001$). The regression time to reach the modified Bromage scale to "0" was significantly prolonged in dexmedetomidine group (278.0 ± 11.0 min) as compared to control group (250.0 ± 14.8 min) ($P = 0.001$) [Table 2]. Intraoperative Ramsay sedation scores were significantly higher in dexmedetomidine group (mean - 3.4 ± 0.7, range – 2–4) as compared to control group (mean - 2.9 ± 0.3, range - 2–4] ($P < 0.001$). More than 30% of patients in the dexmedetomidine group had sedation score of 4 whereas more than 90% of patients in the control group had sedation score of 2–3 [Table 3]. There was significant statistical difference noted in

the hemodynamic parameters (BP and HR) in two groups. The lowest mean HR after subarachnoid block was significantly lower in dexmedetomidine group (51.2 ± 7.3) as compared to control group (68.2 ± 7.4) ($P < 0.001$).

In this study, in 26.7% (8/30) cases had bradycardia that required atropine as compared to control group (2/30) [Table 4]. The lowest intraoperative SBP after spinal block was significantly lower in dexmedetomidine group (97.6 ± 9.3) as compared to control group (103.9 ± 10.9) ($P = 0.001$) and there was significant difference in the number of patients requiring mephentermine for management of hypotension in both groups (33.3% vs. 10% in dexmedetomidine and control groups, respectively [$P = 0.001$]). Total I.V. fluids administered in dexmedetomidine group (2922 ± 516.2 ml) was significantly more as compared to control group (2240 ± 280 ml) ($P = 0.012$) [Table 5].

The time of first request for postoperative analgesic was significantly prolonged in dexmedetomidine group (5.3 ± 1.8 h) as compared to control group (3.8 + 0.6 h) ($P < 0.001$) [Table 6]. There was no significant difference in the incidence of postoperative nausea, vomiting, and shivering between both groups [Table 7]. However, none of the patients in the dexmedetomidine group had postoperative shivering as compared to 10% in control group ($P = 0.056$).

Discussion

Different drugs such as epinephrine, phenylephrine, adenosine, magnesium sulfate, sodium bicarbonate, and neostigmine and alpha2 agonists have been used as adjuvants to local anesthetics to prolong the duration of spinal anesthesia. Among them clonidine, a α_2 agonist is widely used by oral, intrathecal, and I.V. routes as an adjuvant to prolong spinal anesthesia.[7] Dexmedetomidine is a more suitable adjuvant to spinal anesthesia compared to clonidine as it has more sedative and analgesic effects due to its more selective α-2A receptor agonist activity.[6]

In this study, there is statistically difference in the onset as well as in the duration of sensory block in dexmedetomidine

Table 1: Demographic profile of patients

Demographic Profile	Group D	Group C
Age (years)	42.6±5.6	39.4±8.3
Sex (male/female)	6/24	18/12
Weight (kg)	50.1±6.4	53.1±6.8
ASA physical status (I and II), %	33.3/66.7	46.7/53.3
Duration of surgery (min)	83.3±20.0	81.5±16.1

Data are presented as mean±SD. There are no significant statistical differences in two groups. SD = Standard deviation, ASA = American Society of Anaesthesiologist

Table 2: The comparison of sensory and motor block characteristics in two groups

Characteristics	Group D	Group C	*P*
Highest level of sensory block	T4.0±0.4	T4.5±0.5	0.000*
Time for attaining highest level of sensory block (min)	9.6±5.2	9.8±2.8	0.439*
Duration for two dermatomal regression of sensory blockade (min)	115.5±8.7	95.8±11.4	0.000*
Duration of sensory blockade (min)	341.7±20.8	329.5±22.1	0.000*
Time duration of motor blockade to reach modified Bromage score 3 (min)	2.3±0.9	5.1±2.0	0.000*
Time duration of motor blockade regression to modified Bromage score 0 (min)	278.0±11.0	250.0±14.8	0.001*

*P<0.05 so significant

and control group. The onset of sensory block was earlier in dexmedetomidine group (9.7 ± 5.2 min) as compared to control group (9.8 ± 2.8 min). The duration of sensory blockade was significantly prolonged in the dexmedetomidine group (341.7 ± 20.8) as compared to control group (329.5 ± 22.1) ($P < 0.001$). The time for attaining the highest level of sensory block was comparable in dexmedetomidine (9.6 ± 5.2 min) and control groups (9.8 ± 2.8 min). The median highest cephalad level of sensory block T4 (T3–T8) was attained in 15 min in the dexmedetomidine and control groups which is almost similar to the observations by Whizar-Lugo et al.[8] In the present study, mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group (115.5 ± 8.8 min) as compared to control group (95.8 ± 11.4) ($P < 0.001$). These findings are in synchronization with observations of other similar studies in which significant prolongation in mean duration of sensory blockade in dexmedetomidine group was reported.[5,6]

These effects can be explained on the basis of site of action of dexmedetomidine which is locus coeruleus and is mediated by hyperpolarization of noradrenergic neurons thus inhibiting noradrenaline release and inhibiting activity in descending medullospinal noradrenergic pathways.[6] Analgesic effects are mainly meted by α-2C and α-2A receptors present on the neurons of the superficial dorsal horn in lamina II, by inhibiting the release of pronociceptive transmitters namely substance P and glutamate and by hyperpolarization of spinal interneurons.

These similar mechanisms also possibly explain the motor blockade augmentation effects. In this study, there was a significant difference in time taken for motor blockade to reach modified Bromage scale 3 in dexmedetomidine group as compared to control group. 2.3 ± 0.9 min in dexmedetomidine versus 5.1 ± 2.0 min in control group ($P < 0.001$). The regression time to reach the modified Bromage scale 0 was significantly prolonged in dexmedetomidine group (278.0 ± 11.0 min) as compared to control group (250.0 ± 14.8 min) ($P = 0.001$). Elcıcek et al.[9] and Hong et al.[10] also found that complete resolution of motor blockade was significantly prolonged in dexmedetomidine group, and the findings of present study corroborate these facts. Mean arterial BP shows biphasic variations with an initial transient rise with a reflex fall in HR brought about by stimulation of α-2B subtypes of receptors present in vascular smooth muscles. This is followed by fall in BP and HR due to inhibition of central sympathetic outflow and stimulation of presynaptic α-2 receptors cause decreased release of noradrenaline leading to further fall in the BP.[6] The mean intraoperative HR was significantly lower in dexmedetomidine group as compared to control group ($P < 0.001$). These findings are on expected lines as dexmedetomidine is known to cause bradycardia and hypotension. The results obtained in the present study with regards to HR almost matches those with other research studies.[9,11] However, in the present study, bradycardia owing to dexmedetomidine was very much treatable with I.V. bolus doses of atropine which can be considered as safety feature with this adjuvant. These hemodynamic effects; however, may be deleterious in patients with fixed stroke volume, on

Table 3: Ramsay sedation score in both groups during intraoperative period

Ramsay sedation score	Group D (%)	Group C (%)
6	0	0
5	0	0
4	28.1	8.9
3	38.6	46.4
2	33.3	44.7
1	0	0

Table 4: Comparison of intraoperative bradycardia and atropine requirement in two groups

Parameter	Group D (%)	Group C (%)	P
n (%) of patients with HR <50 beat/min	9 (30)	3 (10)	0.000[†]
n (%) of patients requiring atropine due to persistent bradycardia	8 (26.6)	2 (6.7)	0.003[†]
Atropine requirement (mg)	0.2	0.0	0.000[†]

[†]$P<0.05$ so significant. HR = Heart rate

Table 5: Intraoperative fall in systolic blood pressure and intravenous mephentermine and intravenous fluid requirement in two groups

Parameters	Group D	Group C	P
n (%) of patients with systolic BP <90 mmHg	4 (13.3)	3 (10)	0.001[†]
n (%) of patients requiring mephentermine for management of hypotension	10 (33.3)	3 (10)	0.001[†]
Mephentermine requirement	2.3 mg Range (0-15 mg)	1 mg Range (0-15 mg)	0.382
Total I.V. fluid requirement (ml)	2922±516	2240±280	0.012[†]

[†]$P<0.05$ so significant. I.V. = Intravenous, BP = Blood pressure

Table 6: Duration of first rescue analgesic in two groups

Rescue Analgesia	Group D	Group C	P
Duration of the first rescue analgesic (h)	5.3±1.8	3.8±0.6	<0.001

Table 7: Adverse effect such as hypotension, bradycardia, shivering, nausea, and vomiting in two groups

Adverse effect	Group D (%)	Group C (%)	P
Hypotension	14 (46.6)	6 (20)	<0.001*
Bradycardia	24 (80)	6 (20)	0.000*
Shivering	0	3 (10)	0.046*
Nausea and vomiting	2 (6.6)	0	0.495

*P<0.05 so significant

rate reducing drugs such as beta blockers and digitalis, and in hypovolemic patients.

The consumption of atropine dosage can be considered as a normal entity as the incidence and management of the bradycardia almost coincides with the results of earlier studies.[8] However, few earlier studies did not find any significant difference in the incidence and management of bradycardia, both in dexmedetomidine and control group.[10] Similarly, the average intra- and post-operative mean arterial and diastolic BPs were significantly lower in the dexmedetomidine group as compared to control group. Elcıcek *et al.*[9] reported a significant decrease in mean arterial pressure after 20, 25, and 30 min after dexmedetomidine infusion as compared to control group. Contrary to above studies and the present study, Al-Mustafa *et al.*[11] reported no significant difference in mean arterial pressures in dexmedetomidine and control groups. In this study, there was a significant difference in the number of patients requiring mephentermine for the management of hypotension in both groups (33.3% vs. 10% in dexmedetomidine and control groups, respectively [P = 0.001]). This finding is in contrast to the study of Tekin *et al.*[12] who reported no significant difference between groups in the number of patients who received ephedrine to treat hypotension.

In the present study, intraoperative Ramsay sedation scores were significantly higher in dexmedetomidine group as compared to control group. Ramsay sedation score was 2 in all patients in the control group and ranged from 2 to 5 in dexmedetomidine group in the study done by Al-Mustafa *et al.*[11] Hong *et al.*[10] noted that the median sedation scores during surgery were 4 in the dexmedetomidine group and 2 in the control group (P < 0.001), respectively. Ramsay sedation score significantly favorable (P < 0.0001) along with minimum hemodynamic responses to intubation (P < 0.05) and less oxygenation desaturation (P < 0.0001) in dexmedetomidine group than control group reported by Mondal.[13] Recovery and discharge times were 15 min

longer in the dexmedetomidine group noted by Ahmed *et al.*[14] A significantly higher average sedation score in dexmedetomidine group was also reported by others.[13,15,16] Sedation characteristics of dexmedetomidine include a normal sleep pattern and calming effect on the patients who remain quiet but arousable and cooperative. Sedation is a desirable feature in regional anesthesia as it diminishes the anxiety associated with surgical thoughts to a large extent.

Dexmedetomidine was found to be effective in providing postoperative analgesia in the present study. The time to first request for postoperative analgesic was significantly prolonged in the dexmedetomidine group (5.3 ± 1.8 h) as compared to control group (3.8 + 0.6 h) (P < 0.001). Similarly, Hong *et al.*[10] and Whizar-Lugo *et al.*[8] noticed that postoperative pain intensity was lower and the mean time to first request for postoperative analgesia was longer in the dexmedetomidine group compared to the control group (6.6 h vs. 2.1 h). Kaya *et al.*[17] in their study observed that dexmedetomidine increased the time to the first request for postoperative analgesia (P < 0.01) compared to midazolam and saline, and decreased analgesic requirements (P < 0.05). The use of dexmedetomidine as an adjuvant to local anesthetics, when used in conjunction with general anesthesia, have shown to lower intraoperative esthetic requirements, improved oxygenation, and prolonged postoperative analgesia. In this study, none of the patients in dexmedetomidine group had postoperative shivering as compared to 10% in control group (P = 0.056). Similar results were reported by other researchers in which they used dexmedetomidine by various routes.[15] The incidence of other adverse effects including PONV as well as other side effects did not show any significant difference as compared to observation reported by other studies Mittal *et al.*[18] and other.[19,20]

Conclusion

I.V. dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine spinal anesthesia. Dexmedetomidine-induced hemodynamic changes are transient but are responsive to pharmacological agents and I.V. fluid administration. Dexmedetomidine provides excellent sedation during surgery, and sedation scores reach normal within 15 min after stopping the drug. Dexmedetomidine is effective in providing significant intraoperative sedation, postoperative analgesia, and minimization of postoperative shivering.

Conflicts of interest
There are no conflicts of interest.

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