Original Article

Intravenous dexmedetomidine versus propofol for intraoperative moderate sedation during spinal anesthesia: A comparative study

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Abstract

Background and Aims: There has been a paradigm shift of focus toward quality of spinal anesthesia with sedation being an integral aspect of this regional anesthesia technique. Thus, this study was designed to compare efficacy of intravenous dexmedetomidine and propofol for moderate sedation during spinal anesthesia.

Material and Methods: A total of 120 patients of age group 18-60 years of American Society of Anesthesiologists grade I & II, posted for surgeries under spinal anesthesia were randomly divided in to three groups (n = 40 each); Group D received infusion of dexmedetomidine 1 μg/kg over 10 min followed by maintenance infusion of 0.5 μg/kg/h. Group P received infusion of propofol 6 mg/kg/h for 10 min followed by the infusion maintenance of 2.5 mg/kg/h. Group C (control group) received normal saline. Level of sedation (using observer's assessment of alertness/sedation score), pain intensity (by visual analogue scale), onset and recovery from sedation, hemodynamic changes, and overall patient's satisfaction were assessed.

Results: The onset and recovery from sedation were significantly earlier with propofol (15.57 ± 1.89 min vs. 27.06 ± 2.26 min; $P < 0.001$) however intraoperative sedation (level 4), and overall patient's satisfaction was significantly better with dexmedetomidine group ($p < 0.05$). Duration of postoperative analgesia was significantly prolonged with dexmedetomidine (225.53 ± 5.61 min vs. 139.60 ± 3.03 min; $P = 0.0013$). Mean heart rate and blood pressure were significantly lower in the propofol group ($P < 0.05$).

Conclusion: Dexmedetomidine with its stable cardio-respiratory profile, better sedation, overall patient's satisfaction, and analgesia could be a valuable adjunct for intraoperative sedation during spinal anesthesia.

Key words: Dexmedetomidine, moderate sedation, propofol

Introduction

Spinal anesthesia offers many advantages over general anesthesia, however, the fear of surgery, the unfamiliar environs of operation room, the sight and sounds of sophisticated instruments, and the masked faces makes the patient panic. The intense sensory and motor block, continuous supine position and the inability to move the body also brings a feeling of discomfort and phobia in many patients.[1,2]

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Access this article online

Quick Response Code:

Website: www.joacp.org

DOI: 10.4103/0970-9185.168172

Thus, sedation has been shown to increase patient satisfaction during regional anesthesia. Moderate sedation is defined as "A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by mild tactile stimulation. No intervention is required to maintain a patent airway and cardiovascular stability."[3] Earlier, this kind of sedation was popularly known as "conscious sedation" but Joint Commission on Accreditation of Healthcare Organization (JCAHO) in 2001 has coined the term moderate sedation.[3]

Many agents have been used for this purpose. Continuous infusion of propofol is a useful method for sedation because of the easy titratibility and rapid emergence. Intravenous (i.v.) dexmedetomidine prolongs the duration of spinal anesthesia, provides sufficient sedation, with fewer side effects.[4]

Hence we designed this study to evaluate the sedative, hemodynamic and side effects of i.v. dexmedetomidine and propofol when used for intraoperative moderate sedation alongwith spinal anesthesia.

Material and Methods

The present prospective, randomized, double-blinded clinical study was conducted after obtaining permission from institutional ethical committee on 120 American Society of Anesthesiologists grade I-II patients, between 18-60 years of age, of either sex posted for surgeries under spinal anesthesia. Patients using α_2-adrenergic receptor antagonists, calcium-channel blockers, angiotensin-converting enzyme inhibitors, having dysrhythmias, or a body weight more than 100 kg were excluded from the study.

Informed written consent was taken from all patients. The patients were allocated to either of the three groups using computer generated random numbers. Group D (dexmedetomidine group) received an initial dose of 1 μg/kg infused over 10 min, followed by maintenance of 0.5 μg/kg/h. Group P (propofol group) received an initial dose of 6 mg/kg/h infused over 10 min followed by maintenance of 2.5 mg/kg/h. Group C (control group) receiving normal saline infusion.

Standardized anesthetic protocol was followed in all the patients. No premedication was given to any patient. Patients were informed to communicate about the perception of any pain or discomfort during surgery. Preoperative sedation level was assessed using modified observer's assessment of alertness/sedation scale (OAA/S).[5]

Once the patients were shifted to the operating room, the patients were connected to multipara (IntelliView Phillips MP30) for monitoring noninvasive blood pressure monitor, pulse oximeter, and electrocardiogram. Baseline measurements were recorded. A large vein was chosen for intravenous i.v. access and 18G cannula was secured. All patients were preloaded with 15 ml/kg of ringer's lactate prior to spinal anaesthesia. Under aseptic precautions, lumbar puncture was performed at L3-L4 interspace with Polymed 25G Quincke type spinal needle. After free flow of CSF had been obtained, 3.5 ml of 0.5% Bupivacaine heavy was injected into the subarachnoid space. Patients were then made to lie in the supine position. Study drugs were started according to the group allocated, after assessment of maximum sensory blockade.

The onset of sedation was taken as time taken to reach OAA/S score of 4 as it most closely meets the condition of moderate sedation.[6] The infusion of propofol and dexmedetomidine was continued at a constant rate throughout the procedure and was not altered till a sedation score of 3. Level of sedation was assessed at every 5 min interval. The infusion was stopped 10 min before the completion of surgery. ECG, heart rate (HR), systolic blood pressure, diastolic blood pressure, mean blood pressure (MBP), respiratory rate (RR), oxygen saturation (SpO_2), and end-tidal carbon dioxide ($EtCO_2$) were recorded every 5 min intervals after baseline measurements till end of procedure.

Duration of effective analgesia (time interval between administration of spinal to first request for supplementary analgesics) and recovery time (time taken to return to sedation score 4 or more on modified OAA/S scale after stopping the infusion of study drugs) was recorded in all the patients studied. Overall satisfaction of patients was also assessed.[2]

The side effects such as nausea, vomiting, hypotension, respiratory depression, shivering, pruritus, motor weakness, and seizures were noted both intraoperatively and postoperatively. During the procedure, if bradypnea (RR <10) or SpO_2 92% or less were recorded, 4 L/min of supplemental oxygen was administered via a nasal cannula with reducing rate of infusion of the drug aiming to awaken the patient and to resume his normal breathing. Hypotension (MBP <50) was treated with fast 0.9% normal saline and i.v. bolus of mephenteramine 6 mg and bradycardia (HR <50) with 0.5 mg of i.v. atropine stat, with a reduction in the rate of infusion.

Statistical methods

Statistical analysis was done using Graph Pad InStat 3 software. Data were expressed as either mean and standard deviation or numbers and percentages. The means for the continuous variables were compared between the three groups using analysis of variance ANOVA. The $P < 0.05$ was considered statistically significant.

Results

All the 120 patients who were enrolled in the study completed the study protocol and included in the data analysis. No spinal analgesia failure was observed. Demographic data, was comparable among all three groups [Table 1]. Baseline mean sedation scores were statistically comparable in all three

Table 1: Demographic and recovery profile

Demographic and recovery profile	Group D	Group P	Group C
Number of patients	40	40	40
Age (years)	36.70±9.29	38.40±9.04	37.15±8.87
Sex (male/female)	28/12	29/11	26/14
Weight (kg)	55.53±5.31	55.05±6.05	55.85±6.24
Mean duration of surgery (min)	62.85±16.18	60.03±18.81	64.32±19.18
Mean duration of effective analgesia (min)	225.53±5.61	139.60±3.03	138.43±4.96
Recovery time to OAA/S* score 4 or more (min)	27.06±2.26	15.27±1.89	3.88±1.79

**OAA/S = Observer's Assessment of Alertness/Sedation*

groups. Significant difference in mean sedation score was observed at 5 min in Group P and at 10 min in Group D as compared to Group C, which remained till end of surgery. Group D when compared with group P showed significantly deeper level of sedation [Table 2].

Recovery time to OAA/S score 4 or more was significantly prolonged in group D and Group P as compared to Group C and was more prolonged in Group D as compared to Group P ($P < 0.001$) [Table 1]. Duration of effective analgesia was significantly prolonged in Group D as compared to Group P and Group C ($P = 0.0013$) [Table 1].

Though maximum number of patients in all the three groups had Grade 3 overall satisfaction grading but significantly higher number of patients in Group D had Grade 3 of overall satisfaction grading (77.50%) as compared to Group P (55.0%) and Group C (37.50%).

Baseline MBP was comparable in all the three groups. Significant fall in MBP was observed at 5 min in Group P as compared to Group D and Group C and this fall persisted throughout the study period. Group D and Group C were comparable in their MPB, and no significant change was observed from baseline [Table 3]. The baseline mean HR was comparable among three groups. Significant decrease in HR was observed in group D at 5 min that persisted throughout the procedure as compared to Group P and Group C. Mean HR in Group P and Group C was comparable, and no significant change occurred from baseline in both the groups [Table 4]. Ventilatory parameters ($EtCO_2$, SpO_2, and RR) were comparable in all three groups throughout surgery.

Table 2: Mean sedation scores (OAA/S) at various time intervals

Time interval (min)	Mean±SD			*P*-value		
	Group D	Group P	Group C	D vs. *P*	D vs. C	*P* vs. C
Baseline	4.96±0.29	4.93±0.41	4.88±0.11	0.2258	0.2313	0.3412
5	4.23±0.64	3.23±0.55	4.40±0.27	0.0123	0.2431	0.0034
10	3.80±0.40	3.33±0.30	4.86±0.14	0.0054	0.0013	0.0041
15	2.76±0.27	3.23±0.62	4.96±0.01	0.0013	0.0231	0.0023
20	2.66±0.20	3.13±0.22	4.90±0.09	0.0002	0.0152	0.0231
25	2.60±0.19	3.46±0.44	4.73±0.23	0.0057	0.0248	0.0341
30	2.80±0.83	3.13±0.31	4.62±0.36	0.0134	0.0012	0.0146
35	2.23±0.33	3.16±0.72	4.46±0.26	0.0278	0.0023	0.0214
40	2.30±0.20	3.23±0.40	4.90±0.08	0.0006	0.0002	0.0312
45	2.26±0.93	3.66±0.57	4.53±0.41	0.0016	0.0032	0.0015
50	2.24±0.36	3.36±0.35	4.87±0.03	0.0113	0.0013	0.0043
55	2.19±0.96	3.62±0.47	4.73±0.24	0.0015	0.0023	0.0023
60	2.64±0.61	3.28±0.61	4.56±0.42	0.0037	0.0014	0.0014
				<0.05	<0.0001	<0.001

OAA/S = Observer's Assessment of Alertness/Sedation, SD = Standard deviation

Table 3: Mean blood pressure at various time intervals (mmHg)

Time interval (min)	Mean±SD			*P*-value		
	Group D	Group P	Group C	D vs. *P*	D vs. C	*P* vs. C
Baseline	78.32±7.57	79.45±7.28	78.78±7.88	0.1879	0.2365	0.3145
5	76.65±7.13	62.43±7.04	75.54±7.52	0.0023	0.3417	0.0017
10	78.43±5.51	66.56±5.71	76.63±6.81	0.0145	0.2625	0.0034
15	77.43±5.27	61.45±3.07	74.12±7.86	0.0065	0.2155	0.0024
20	75.54±3.67	65.61±2.67	78.45±7.80	0.0012	0.3476	0.0012
25	77.98±3.00	63.32±2.54	76.69±8.74	0.0074	0.5276	0.0054
30	75.65±2.98	63.27±2.60	72.12±8.96	0.0249	0.3418	0.0026
35	74.34±3.28	66.96±5.63	78.23±8.58	0.0023	0.3524	0.0032
40	73.45±5.26	64.54±6.01	74.65±9.23	0.0037	0.2645	0.0043
45	79.56±6.65	63.67±5.56	75.87±8.78	0.0124	0.3216	0.0034
50	76.56±5.56	63.69±5.87	76.97±8.45	0.0345	0.4213	0.0023
55	77.36±4.79	64.58±8.11	77.16±8.26	0.0019	0.3623	0.0037
60	78.45±5.54	64.78±8.11	74.87±8.78	0.0040	0.2351	0.0054
				<0.001	>0.05	<0.001

SD = Standard deviation

Table 4: Mean HR at various time intervals (bpm)

Time interval (min)	Mean±SD			*P*-value		
	Group D	Group P	Group C	D vs. *P*	D vs. C	*P* vs. C
Baseline	79.20±8.29	81.16±6.41	77.60±8.93	0.2258	0.3243	0.3417
5	68.34±5.64	82.83±7.55	78.40±9.77	0.0023	0.0014	0.2625
10	64.32±6.40	80.43±6.30	76.36±8.34	0.0002	0.0034	0.2155
15	62.24±7.27	80.23±7.62	77.16±13.39	0.0032	0.0024	0.3476
20	65.35±5.20	77.13±5.22	73.90±11.16	0.0003	0.0012	0.5276
25	63.22±6.09	78.46±6.44	75.03±13.41	0.0012	0.0054	0.3418
30	62.67±5.83	76.81±5.31	74.62±8.36	0.0034	0.0026	0.3524
35	61.22±6.03	77.16±6.72	73.46±11.82	0.0023	0.0032	0.2645
40	62.23±6.10	78.23±7.10	73.90±11.84	0.0036	0.0043	0.3216
45	61.23±6.65	74.22±6.67	71.23±8.76	0.0021	0.0034	0.4213
50	62.34±6.34	73.27±6.78	70.34±7.45	0.0045	0.0023	0.3623
55	64.34±5.93	76.66±5.77	75.53±7.54	0.0003	0.0037	0.2351
60	63.22±5.96	76.66±4.37	74.83±7.54	0.0018	0.0054	0.3298
				<0.001	<0.001	>0.05

HR = Heart rate, SD = Standard deviation

Table 5: Incidence of side effects and complications among three groups

Complication	Number of patients (%)		
	Group D	Group P	Group C
Nausea/vomiting	5 (12.50)	01 (2.50)	03 (7.50)
Bradycardia	08 (20.0)	04 (10.0)	01 (2.50)
Shivering	01 (2.50)	02 (5.0)	05 (12.50)
Hypotension	03 (7.50)	09 (22.50)	04 (10.0)
Dry mouth	03 (7.50)	01 (2.50)	01 (2.50)
Pain at site of injection	02 (5.0)	10 (25)	02 (5.0)
Neurological	00 (0.0)	00 (0.0)	00 (0.0)

Higher incidence of bradycardia, nausea and vomiting were noted in Group D compared to hypotension and pain at the site of injection in Group P and shivering in Group C. None of patient required to stop or reduce the rate of infusion of propofol and dexmedetomidine for management of hypotension. Neurological complications were not noted among any of the groups [Table 5].

Discussion

The early onset time of sedation in the propofol group compared to dexmedetomidine group occurs because propofol is highly lipophilic and distributes rapidly into the central nervous system. Arain, *et al.*[7] noted that the targeted sedation was achieved within 10 min with propofol but took 25 min with dexmedetomidine. Similar results were obtained by Abdelkareim, *et al.*[8]

Both Groups D and P had significantly deeper level of sedation as compared to Group C. Group D when compared with Group P has significantly deeper level of sedation throughout the procedure. The finding of our study is well-supported with the results of Arain, *et al.*;[7] Kaya, *et al.*;[9] and Hoy and Keating.[10]

The mean recovery time was significantly prolonged in Group D and P as compared to Group C. Recovery time was shorter in Group P as compared to Group D possibly due to rapid metabolism and excretion of propofol. The finding of our study correlates well with the results of previous authors.[7,11]

Mean duration of effective analgesia was significantly prolonged in the dexmedetomidine group as compared to propofol group and control group. Our finding is comparable to the results of other authors.[10,12] Dexmedetomidine produces analgesia by binding to adrenoreceptors in the spinal cord. Jorm and Stamford, observed that dexmedetomidine has an inhibitory effect on the locus coeruleus (A6 group) which is located at the brain stem.[13] This supraspinal action could explain the prolongation of spinal analgesia after i.v. administration of dexmedetomidine.

In our study, a significant decrease in mean HR with dexmedetomidine was observed at 5 min of starting the infusion. This difference persisted throughout the procedure and could be attributed to sympatholytic properties and vagal mimetic effects of dexmedetomidine. The results of our study correlate well with Al-Mustafa, *et al.*[12] and Mahmoud, *et al.*[14]

MBP was significantly decreased in Group P at 5 min after starting infusion and persisted throughout the procedure as compared to Group D and Group C. There was no significant difference in MBP from baseline value in Group D and Group C throughout the whole duration of procedure. The fall in MBP in patients receiving propofol could be attributed to direct powerful inhibitory effect of propofol on

sympathetic outflow causing vasodilatation. Dexmedetomidine is also known to decrease sympathetic outflow and circulating catecholamine levels and would, therefore, be expected to cause a decrease in MBP similar to those of propofol. However, larger doses of dexmedetomidine have a direct effect at the postsynaptic vascular smooth muscle to cause vasoconstriction, and it is possible that the sympathoinhibitory effects of dexmedetomidine were slightly opposed by direct α-2 mediated vasoconstriction. Results similar to our study were observed by Arain, *et al.*;[7] Al-Mustafa, *et al.*[12] and Mahmoud, *et al.*[14]

Both propofol and dexmedetomidine are known to have minimal respiratory depression when used as sedative agents which is evident for our results wherein the $EtCO_2$ level, SpO_2, RR did not differ significantly from baseline among all the three groups. Ryu, *et al.*[15] observed that dexmedetomidine was associated with fewer incidents of oxygen desaturation and a reduced need for the oral cavity suction than Remifentanil during flexible bronchoscopy. Postoperative shivering was significantly reduced in the dexmedetomidine group as compared to the control group. Similar results were obtained by Jabbary, *et al.*[16] who observed no post anesthesia shivering in all the patients who received clonidine premedication irrespective of opium addiction ($P < 0.01$).

The above factors such as better sedation, stable cardio-respiratory profile and analgesic effect resulted in significantly better overall patient satisfaction in the dexmedetomidine group. Results of our study correlate well with those of Arain, *et al.*[7]

Conclusion

The present study shows that both dexmedetomidine and propofol produce adequate level of sedation but dexmedetomidine could be used as better alternative to propofol for intraoperative moderate sedation for surgeries under spinal anesthesia.

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How to cite this article: Shah PJ, Dubey KP, Sahare KK, Agrawal A. Intravenous dexmedetomidine versus propofol for intraoperative moderate sedation during spinal anesthesia: A comparative study. J Anaesthesiol Clin Pharmacol 2016;32:245-9.
Source of Support: Nil, **Conflicts of Interest:** None declared.