Original Research Article

Intravenous Dexmedetomidine Premedication on Spinal Anaesthesia with Hyperbaric Bupivacaine in Patients Undergoing Total Abdominal Hysterectomies

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ABSTRACT

Background: Dexmedetomidine has both analgesic and sedative properties that may prolong the duration of sensory and motor block obtained with spinal anaesthesia. This study was designed to assess the effect of single dose intravenous dexmedetomidine on duration and analgesia of subarachnoid block using 0.5% bupivacaine and sedation in patients undergoing total abdominal hysterectomies.

Methods: In a randomized controlled study, 70 patients belonging to ASA physical status 1 and 2 received dexmedetomidine 0.5 µg/kg or normal saline intravenously before spinal anaesthesia with 15mg of hyperbaric bupivacaine (35 patients per group). The maximum upper level of sensory block and sensory regression time was recorded. Sedation scores and post- operative analgesic requirements with VAS scores were also recorded.

Results: Onset of sensory blockade (151.14 seconds Vs 274.29 seconds in normal saline group) and motor blockade was shorter in dexmedetomidine group (P<0.001). The mean time for two segment regression in sensory blockade was prolonged in dexmedetomidine group compared to control group (147±14.96 minutes Vs 102±11.71 minutes). Time for first rescue analgesia was also longer in dexmedetomidine group with 240.71 minutes compared to 129.29 minutes in normal saline group (P<0.001). The median sedation scores (Ramsay sedation score 3 vs. score 1) were higher in dexmedetomidine group in comparison to normal saline group.

Conclusion: Single dose intravenous infusion of dexmedetomidine prior to subarachnoid block shortens the onset of sensory and motor blockade and prolongs the sensory blockade. It also provided sedation and additional post-operative analgesia.

Key words: Intravenous dexmedetomidine, hyperbaric bupivacaine, spinal anaesthesia, premedication, sedation.

INTRODUCTION

Providing comfort and alleviating anxiety during and after performing regional anaesthesia is important in patient care posted for any surgery. This requires administration of hypnotic, sedative or amnesic drugs during regional anaesthesia, [1,2] which may have adverse effects depending on type and dosage of the drugs. Adjuvants like opioids, epinephrine,

clonidine etc, have been used to prolong spinal anaesthesia, with the possible advantages of delayed-onset of postoperative pain and reduced analgesic requirements. [3] Dexmedetomidine, a highly selective α_2-adrenoreceptor agonist with α_2/α_1 selectivity ratio eight to ten times more than clonidine, has been used for premedication and as an adjunct to general anaesthesia. Intravenous dexmedetomidine premedication before general anaesthesia provides preoperative sedation, analgesia, and hemodynamic stability and reduces requirements for intraoperative inhalational agents and postoperative analgesics. [4,5] Also, it has been used safely as premedication or as a sedative agent in patients undergoing surgical procedures under regional anaesthesia. [4,5] Although a synergistic interaction between intrathecal dexmedetomidine and local anaesthetics has been observed in previous studies, [6] there is insufficient clinical data regarding the effect of intravenous dexmedetomidine premedication on the duration of sensory and motor block during spinal anaesthesia. In this randomized controlled clinical study, we assessed the effects of intravenous dexmedetomidine premedication on spinal block duration as well as on sedation and postoperative analgesia in patients undergoing total abdominal hysterectomy.

MATERIALS AND METHODS

After institutional approval and written informed consent from all 70 female patients, aged between 20 to 65 years, belonging to American Society of Anaesthesiologists Physical Status 1 and 2, undergoing total abdominal hysterectomy under subarachnoid block (SAB) were included in our study.

Those patients with a history of alcohol or drug abuse, diabetes mellitus, cardiac disease, hypertension, chronic obstructive respiratory disease, psychological disease, hepatic and/or renal disease, spinal deformities or any contraindication to spinal anaesthesia (for e.g., coagulation defects, infection at the puncture site, pre-existing neurological deficits in the body, etc.) and patients allergic to amide type of local anaesthetics were excluded from the study.

All patients' age, weight, height, and body mass index (BMI) were noted. Patients were kept nil per orally for overnight before anaesthesia and were premedicated with tablet Ranitidine 150 mg and tablet Alprazolam 0.5 mg orally, the night before surgery. In the preoperative room, patients were randomly allocated to receive 0.5 µg/kg dexmedetomidine intravenous infusion in 100 ml normal saline (Group- D) or normal saline infusion (Group- N), given over a period of 10 minutes, 15 minutes before SAB.

On arrival in the operation theatre, continuous ECG, non-invasive blood pressure, and pulse-oximeter were attached, and baseline values of heart rate, blood pressure, and SpO_2 were recorded.

All patients were preloaded with Ringers lactate (10 ml/kg). Heart rate with continuous electrocardiogram, non-invasive blood pressure, pulse oximetry (SpO_2) were monitored throughout the surgery. All patients received oxygen at the rate of 3-5 L/min using nasal prongs/face mask. Under all aseptic precautions, SAB was performed in lateral position (left/right) using 25 G Quinke's spinal needle, at L_2-L_3 or L_3 –L_4 interspace with 3.0 ml of 0.5 % hyperbaric bupivacaine injected intrathecally. The level of sensory blockade was assessed using sterile pin prick method in the mid-axillary line on both sides of chest and the surgery was allowed to start only when a sensory level of T_8 was achieved. Immediately after sensory block assessment, motor block was assessed using a modified Bromage scale [7]

Grade 0: No paralysis;
Grade 1: Unable to raise extended leg;
Grade 2: Unable to flex knee;
Grade 3: Unable to flex ankle.

In the intra operative period, hypotension (Systolic BP <30% of the baseline value or Systolic BP <90mm of Hg) was treated with intravenous fluids and boluses of inj. Mephentermine 3 mg, and bradycardia (heart Rate <60/minute with hypotension or <50/minute without hypotension) was treated with inj. Atropine 0.6 mg intravenously.

Sensory and motor block was assessed every 15 to 20 seconds for the first 10 minutes and thereafter every 10 mins during surgery and every 10 minutes postoperatively. Onset times of both sensory and motor blockade were assessed and recorded. Recovery time for the sensory blockade was defined as two-dermatome regression of anaesthesia from the maximum level and was recorded. Postoperative pain was assessed by using the visual analogue scale, [8] (with score 0: No pain; to score 10: Worst possible pain) at 4, 8, 12 and 24 hr. Patients with a VAS score of 3 or more received injection Diclofenac sodium 75 mg intramuscularly. The time of first request for postoperative analgesia after surgery was recorded as duration of postoperative analgesia.

The Ramsay sedation score, [9] was used to assess sedation
1. Anxious or agitated;
2. Co-operative and tranquil;
3. Drowsy but responsive to command;
4. Asleep but responsive to glabellar tap;
5. Asleep with a sluggish response totactile stimulation; and
6. Asleep and no response.

The score was re-evaluated every 10 min after administration of drug for up to 180 min and every 15 min thereafter. Excessive sedation was defined as sedation score greater than four (score 5 or 6).

Statistical analysis: The both parametric and non-parametric data were tabulated and was presented as mean ± SD and median values as per category. The non-parametric data was statistically analysed using Chi-square test and Fischer exact test as appropriate and parametric data was analyse using Student`s *t*-test. The Mann-Whitney U-test was used to analyze differences between the groups. Statistical significance was considered when p Value was <0.05.

RESULTS

Subarachnoid block was successful in all patients included in the study. Demographic profile given in table 1; patient characteristics like age, height, weight and body mass index (BMI) were similar between the two groups and there was no statistical differences in these patient characteristics between the groups. Baseline patient parameters like heart rate, blood pressure, and respiratory rate were clinically similar and statistically not significant between the two groups.

Table 1: Demographic profile

Characteristics	Group D		Group N		p-value
	Mean	Standard Deviation	Mean	Standard Deviation	
Age (years)	42.91	5.12	41	6.097	0.159
Weight (kg)	53.49	3.11	53.14	3.41	0.662
Height (cms)	149.51	4.02	150.51	3.12	0.249
BMI (kg/m^2)	24.17	1.47	23.71	1.79	0.247
Baseline HR (bpm)	79.09	6.26	79.97	6.22	0.555
Baseline MAP (mmHg)	99.74	5.75	98.03	5.42	0.204
Duration of surgery (minutes)	90.86	10.396	90.43	9.50	0.858

Table 2: Comparison of onset of sensory blockade and motor blockade, two segment sensory regression and first rescue analgesic times between the groups.

Characteristics	Group D		Group N		p-value
	Mean	Standard Deviation	Mean	Standard Deviation	
Onset Sensory Blockade (seconds)	151.14	38.90	274.29	51.94	P<0.001
Onset Motor Blockade (seconds)	202.57	35.61	297	41.199	P<0.001
Time for 2 segment regression (minutes)	147	14.96	102	11.71	P<0.001
Time of first rescue Analgesic (minutes)	240.71	41.13	129.29	17.70	P<0.001

Onset of sensory blockade was shorter in group D with 151.14 seconds compared to 274.29 seconds in group N which was both clinically and statistically significant (p-Value<0.001). Similarly onset of motor blockade was also shorter in group D with 202.57 seconds compared to 297 seconds in group N which was clinically and statistically significant (p-Value<0.001). Time for two segment regression in sensory anaesthesia was longer in dexmedetomidine group compared to saline group which was significant.

The mean duration of analgesia was prolonged in dexmedetomidine group in comparison to control group. In our study, the time for first rescue analgesia was longer in dexmedetomidine group with 240.71 minutes compared to 129.29 minutes in normal saline group which was statistically significant with p-Value <0.001.The incidences of haemodynamic side effects (bradycardia and hypotension) were similar between the two groups and incidence of nausea and vomiting were also similar between the groups.

The median sedation scores (Ramsay sedation score 3) were higher in dexmedetomidine group compared to median score (Ramsay sedation score 1) in normal saline group, which was significant with p value<0.001. The VAS pain scores did not change over time (postoperative 4, 8, and 12 hours) in the two groups, and was significant between the groups at 24 hour post operatively.

Table 3: Showing sedation scores and VAS scores (using Mann-Whitney U-test).

Variable	Group	Median	Interquartile range	p-value	Significance
Sedation Score	D	3	2	p<0.001	Significant
	N	1	0		
VAS-0	D	1	2	0.362	Not significant
	N	1	3		
VAS-2	D	1	3	0.456	Not significant
	N	1	2		
VAS-6	D	2	2	0.310	Not significant
	N	2	3		
VAS-12	D	2	3	0.243	Not significant
	N	1	2		
VAS-24	D	0	1	P<0.001	Significant
	N	2	2		

DISCUSSION

As subarachnoid block is the major form of anaesthesia used in gynaecological surgeries, these patients often need a medication to provide anxiolysis and some sedation during the procedure. Dexmedetomidine, a highly selective alpha 2 adrenergic receptor agonist, acts at both central (supra-spinal and spinal) and peripheral receptors, produces both sedation and analgesia via systemic route and prolongation of sensory blockade on its use as an adjuvant to local anaesthetics during regional anaesthesia. According to Jaakola et al [10] dose of inj dexmedetomidine required to provide moderate analgesia with a ceiling affect at dose 0.5 µg/kg body weight. Similarly, Aantaa et al [11] found that single dose of dexmedetomidine in range 0.33 µg/kg to 0.67µg/kg was optimal for

intravenous premedication for minor surgeries. Rapid intravenous administration of dexmedetomidine may cause tachycardia, bradycardia and hypertension. [12] So, we chose single intravenous infusion of dexmedetomidine at dose 0.5 μg/kg over 10 minutes in our study.

In our study, we observed a significantly short onset of sensory blockade after spinal anaesthesia similar to a study by Fatma Nur Kaya et al. [13] Kanazi et al [6] also observed shorter onset of sensory and motor blockade time in their study. Similar to results observed by Hong et al [14] (61 min Vs 41 min for pin prick method), Kaya et al [13] 145 ± 26 min vs. 97 ± 27 min ($P < 0.001$), Tekin et al [15] 148.3 min vs. 122.8 min ($P < 0.001$) in the dexmedetomidine and control groups respectively, the mean time for two segment regression in sensory blockade was prolonged in our study in dexmedetomidine group compared to control group (147±14.96 minutes Vs 102±11.71 minutes). Onset of motor blockade was shorter in dexmedetomidine group compared to control group in our study. Study by Lugo et al, [16] found no significant effect on motor blockade but Al-Mustafa et al [17] found prolongation of motor blockade.

The time for first rescue analgesic was significantly prolonged in our study in dexmedetomidine group (240.71±41.13 minutes) compared to control group (129.29±17.70 minutes). Similar results were observed by Whizar-Lugo et al, [16] in their study time to first rescue analgesic in the dexmedetomidine group was (220 ± 30 min) as compared to the control group (150 ± 20 min). Hong et al, [14] noticed a decreased intensity of post operative pain in the dexmedetomidine group and longer time for first rescue analgesic requirement in these patients. Apart from prolonged time for first rescue analgesic in their study, Kaya et al, [13] also noticed a decreased

requirement of rescue analgesic in the dexmedetomidine group.

The sedation scores were higher during intra-operative period in dexmedetomidine group compared to saline group, with median sedation score of 3 on Ramsay sedation scale, similar results were observed by Al Mustafa et al [17] who observed scores ranging between 2 to 5 and Hong et al [14] observed that the median sedation score was 4 during the intra-operative period. In our study, none of the patient in dexmedetomine group didn`t had respiratory depression, which was assessed by fall in SpO_2 level during the intra-operative and post operative periods, similar to study results of Al Mustafa et al. [17]

Many studies have reported significant incidences of bradycardia in their patients varying upto 30% to 40% and requirement of atropine to treat in some instances during the study. In our study, the incidence of bradycardia was low and also transient, which may be explained by the fact that, we used a single dose dexmedetomidine infusion at slower rate. Kaya et al, [14] had similar observations on incidence of bradycardia in their study. Both intraoperative and post operative systolic, diastolic and mean arterial blood pressures were similar between dexmedetomidine group and control group, with group D showing slightly lower pressures. Al Mustafa et al, [17] and Tekin et al, [15] reported no significant difference between the dexmedetomidine and control groups in mean arterial pressures in intraoperative and post operative period , Tekin et al [15] also reported that no difference in requirement of ephedrine to treat hypotension in their study groups in contrary to study by Eliceek et al. [18]

In our study, VAS scores were statistically not significant between the dexmedetomidine group and saline group in most of the post operative period except the

scores at 24 hour after surgery. Annamalai A et al, [19] had similar observations in regard to VAS scores between the groups in their study, as they used requirement of rescue analgesic for calculating prolongation of analgesia, in their opinion, using requirement of rescue analgesic was a limitation to assess secondary variable VAS and its differences between groups in their study.

We conclude that, use of single dose intravenous infusion of dexmedetomidine prior to sub arachnoid block using hyperbaric bupivacaine, causes early onset of sensory and motor blockade and prolongs the duration of sensory blockade. In addition to prolonged post operative analgesia, it also provides easily arousable sedation without haemodynamic side effects.

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