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Original Research Article

A comparative evaluation of epidural clonidine vs. dexmedetomidine as adjuvants in post-operative analgesia

Veeramachaneni Rajesh[1,*], Revathi Lokala[1], Harshavardhan Venkatayogi[1]

[1] *Dept. of Anesthesiology, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana, India*

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ABSTRACT

Background: Requirement of anesthetic agents is reduced due to addition of adjuvants in epidural anaesthesia as they augment the local anesthetic action and have analgesic properties as well. Effective epidural analgesia ensures stable hemodynamics and satisfactory perioperative period.
Objective: To evaluate efficacy of epidural clonidine compared to dexmedetomidine as adjuvants in post-operative analgesia
Materials and Methods: Comparative, randomized clinical study was carried out among 100 subjects undergoing abdominal and vaginal hysterectomies of age 44-65 years with ASA grade I and II. They were divided randomly into two group of 50 each. Group A received 17ml of 0.5% of bupivacaine with 2mcg per kg clonidine. Group B received 17ml of 0.5% of bupivacaine with 1.5mcg per kg dexmedetomidine. Various parameters related to sensory and motor blockade, Ramsay sedation scale for sedation score, Hemodynamic parameters were monitored continuously and recordings were made at regular intervals.
Results: Both groups were comparable in terms of age, weight, duration of surgery, ASA grades and type of surgery. Parameters pertaining to time for onset of sensory and motor block were significantly higher in clonidine group compared to the dexmedetomidine group ($p<0.05$). Postoperative block duration was significantly higher in dexmedetomidine group compared to clonidine group ($p<0.05$). The hemodynamic parameters and Ramsay sedation score at pre-operative and at 120min were comparable ($p>0.05$) between two groups except for heart rate which was significantly less in dexmedetomidine group at 120min compared to clonidine group ($p<0.05$).
Conclusion: Dexmedetomidine added to bupivacaine epidurally prolonged postoperative analgesia longer than clonidine.

1. Introduction

Regional anesthesia remains a commanding, safe & cost-effective approach during surgery. It is also the preferable choice for providing excellent post-operative analgesia. Epidural anesthesia enables titration of drugs to achieve surgical plane as well can be supplemented postoperatively for pain management. Though the regional anesthetic technique provides good operating conditions with excellent muscle relaxation, patients do have lot of apprehension and anxiety because of the fear about surgery, alien and dynamic environment of operation theatre and noise of sophisticated equipment. To combat this limitation, there has always been a search for drugs with sedative properties to be added as adjuvants to local anesthetics. Among which fentanyl, morphine, ketamine, $\alpha 2$ agonists like clonidine, dexmedetomidine have all been studied as additives to local anesthetics in different regional anesthetic techniques each having its own pharmacological profile and side effects. Prolonged analgesia and anesthesia are provided by all these drugs.[1–8]

Dexmedetomidine has more affinity compared to clonidine towards $\alpha 2$ adrenergic receptors. Hence clonidine has to be used in 1.5-2 times higher doses compared

* *Corresponding author*.
E-mail address: rajesh02veera@gmail.com (V. Rajesh).

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to dexmedetomidine.[9,10] Both these drugs have an added advantage of analgesia combined with sedation with lesser respiratory depressing potential.

Requirement of anesthetic agents is reduced due to adjuvants as they augment the local anesthetic action and they have analgesic properties. They are very useful agents as the hemodynamics of the patients remain stable and the demand for oxygen is decreased.[11,12]

With this background present study was carried out to compare epidural clonidine with dexmedetomidine as adjuvants in post-operative analgesia.

2. Materials and Methods

Source of data: The study was conducted at Department of Obstetrics and Gynecology, Mamata general hospital, Khammam, Telangana.

2.1. Study period

January 2015 – June 2016 [18 months]

2.2. Study design

Comparative, randomized clinical study

2.3. Ethical issues

Institutional ethical committee approval was obtained prior to the study. Written informed consent was obtained from all subjects

2.4. Sample size

Total 100 study subjects were studied and they were divided randomly into two group of 50 each.

2.5. Inclusion criteria

1. Patients undergoing abdominal and vaginal hysterectomies
2. Age between 44-65 years with ASA grade I and II

2.6. Exclusion criteria

1. Psychiatric Diseases
2. History of Drug abuse and allergy to local anesthetics of the amide type
3. ASA III and IV
4. Spine abnormalities
5. Hematological disease
6. Bleeding or coagulation test abnormalities
7. Local skin infection
8. Hemodynamically unstable patients such as bradycardia, orthostatic hypotension, atrioventricular block

2.7. Methodology

Pre-anesthetic checkup was done one day prior to the surgery. Patients were evaluated for systemic diseases and laboratory investigations recorded. The procedure of Epidural anesthesia was explained to the patients. Preparation of patients included period of overnight fasting. Patients were pre-medicated with Tab. Ranitidine 150 mg and Tab. alprazolam 0.5mg early on the day of surgery.

2.8. Preparation of operating theatre

Anesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure. Emergency drugs tray and warmed fluids were kept ready. Regional anesthesia kit and drugs were kept ready.

2.9. Procedure

18 g I.V. cannula was secured. Standard ASA monitors attached and baseline vitals noted. Patient's epidural space was penetrated with 18G tuohy needle in L2-L3 inter-spinous space by loss of resistance technique. Epidural catheter was inserted and secured 3-4cms into epidural space. Test dose of 3ml of 2% lignocaine hydrochloride solution containing adrenaline 1:2,00,000 was injected.

Patients were kept in supine position and drugs are diluted in following manner and injected in the epidural catheter.

1. Group A: Received 17 ml of 0.5% of bupivacaine with 2 mcg per kg clonidine.
2. Group B: Received 17 ml of 0.5% of bupivacaine with 1.5 mcg per kg dexmedetomidine.

After 15min patients who are undergoing vaginal hysterectomy were kept in lithotomy position.

2.10. Parameters recorded

Bilateral cold swab method was used to evaluate and check the sensory level & modified Bromage score was used for motor block. Time of attainment of sensory block level at T10, maximum sensory block level, motor block level, intensity of motor block, duration of analgesia was recorded. Ramsay sedation scale for sedation score was used. Heart rate (HR), blood pressure(BP), O_2 saturation (SPO_2) were monitored continuously and recordings were made at 1min, 5min, 10min, 20min and 30 min, thereafter at 15min intervals for 60 min and finally at 20min intervals up to 120 min. Comparison of postoperative block characteristics, mean time to 2 segment regression, mean time for regression to Bromage 1, mean time sensory regression at S1, time to first epidural top-up, any side effects like hypotension (defined as systolic arterial pressure

falling more than 20%) was noted and treated with inj. Ephedrine 6mg in bolus doses and bradycardia (heart rate <50 bpm) was noted and treated with 0.3mg inj. Atropine.

2.11. Statistical methods

The data was expressed as Mean±SD. Student t test (two tailed, independent) was used. $P < 0.05$ is significant was taken as statistically significant.

3. Results

The difference in baseline parameters of two groups were statistically not significant i.e. both groups were comparable to each other in terms of age, weight, duration of surgery, ASA grades and type of surgery undergone. (Table 1)

Parameters pertaining to time for onset of sensory and motor block like Time from injection to sensory level T10 (in minutes), Time for maximum sensory block (min) and Onset time for Bromage 3(min) were significantly higher in clonidine group compared to the dexmedetomidine group ($p < 0.05$). Mean SPO_2 was not significantly different in two groups. Postoperative block parameters like Time for 2 segment regression(min), Time for Bromage 1 (in min), Time for sensory regression to S1(min) and Time for epidural top-up (in min) were significantly higher in dexmedetomidine group compared to clonidine group ($p < 0.05$). (Table 2)

Highest sensory block achieved in two groups was comparable i.e. statistically no significant difference was found (> 0.05). (Table 3)

Incidence of Side effects like nausea, shivering, dry mouth, hypotension and bradycardia was comparable in two groups i.e. there was not statistically significant difference in two groups ($p > 0.05$) (Table 4)

The hemodynamic parameters like SBP, DBP, MAP, HR and Ramsay sedation score at pre-operative and at 120 min were comparable ($p > 0.05$) between two groups except for heart rate which was significantly less in dexmedetomidine group at 120 min compared to clonidine group ($p < 0.05$). (Table 5)

4. Discussion

The mean age of patients was 49.6 years and 50 years in group BC and BD respectively ($p > 0.05$) which is comparable to the study findings of Bajwa SJ et al.[11] The mean weight was 64.8kg and 66.4kg in group BC and BD respectively in the present study which is comparable to the study findings of Bajwa SJ et al.[11] The mean duration of surgery was 113 min and 113.2 min in group BC and BD respectively which is comparable to the study findings of Bajwa SJ et al.[11]The ASA grades in the present study was also similar in two groups which is comparable to the study findings of Bajwa SJ et al.[11]The two group in the present study were also similar in number undergoing total abdominal and vaginal hysterectomies which is comparable to the study findings of Bajwa SJ et al.[11] In the study by Shaikh SI et al[12] they have selected patients undergoing lower limb orthopedic surgeries.

In the present study, time for onset of sensory block was significantly higher in clonidine group compared to the dexmedetomidine group ($p < 0.05$). Similar findings were reported by Shaikh SI et al[12] (8.7 vs. 11.23 min) for dexmedetomidine vs. clonidine. Saravana Babu MS et al[13] also noted similar findings (7.33 vs. 8.40 min). Kaur S et al[14] noted that dexmedetomidine significantly reduced the time for onset of analgesia 12.53 min compared to 14.18 min for ropivacaine.

Time for mean maximum sensory block was significantly more in clonidine group compared to dexmedetomidine group in the present study ($p < 0.05$). Similar findings were reported by Shaikh SI et al [12] (12.87 vs. 17.13 min) for dexmedetomidine vs. clonidine. Saravana Babu MS et al[13] also noted similar findings (11.66 vs. 13.20 min). Bajwa SJ et al[11]also reported that mean time was significantly more i.e. 15.80 min in clonidine group compared to 13.14 min in dexmedetomidine group.

Time for complete motor blockade or Bromage 3 in the present study was significantly more for patients in clonidine group compared to dexmedetomidine group. Similar findings were reported by Bajwa SJ et al,[11] Shaikh SI et al,[12] and Kaur S et al.[14]

Bajwa SJ et al[11] found that there was decreasing trend in heart rate as well as mean arterial blood pressure in both groups and decrease was statistically significant in clonidine group ($p< 0.005$) when compared with dexmedetomidine group. Kaur S et al[14] found that only 2(4%) patients with plain ropivacaine and 5(10%) patients with dexmedetomidine plus ropivacaine had Bradycardia during first 40 min and was treated by giving injection atropine 0.6 mg intravenously. Later on, heart rate remained stable in both the groups. With plane ropivacaine 2(4%) patients and 4(8%) patients in ropivacaine combined with dexmedetomidine group had fall in blood pressure (SBP <90 mm of Hg) du during first 40 min interval which was corrected by giving vasopressors like ephedrine and intravenous fluids. Only 1(2%) patient in plain ropivacaine group and 3(6%) patients in ropivacaine combined with dexmedetomidine group required injection ephedrine hydrochloride intravenously and the dose difference was not statistically significant ($P > 0.05$). Ephedrine was given as 5 mg bolus and repeated according to blood pressure and total Ephedrine given in Group A was 10 mg and in Group B was 15 mg. Later on, blood pressure remained stable at all measured intervals. Swami SS et al[15] found that dexmedetomidine was more effective in reduction of heart rate compared to clonidine. These findings are comparable to the findings of the present study.

Table 1: Comparison of baseline parameters in two groups

Parameters	**Group A (N=50)**	**Group B (N=50)**	**T value**	**P value**
Age (years)	49.6±4.3	50±5.12	0.423	0.673
Weight (kg)	64.8±4.33	66.4±6.87	1.393	0.166
Duration of surgery (min)	113±10.54	113.2±9.57	0.099	0.92
Parameters	**Group A (N=50)**	**Group B (N=50)**	**Chi square**	**P value**
ASA grade I	24 (48%)	19 (38%)	0.6528	0.419
ASA grade II	26 (52%)	31 (62%)		
Abdominal hysterectomy	25 (50%)	25 (50%)	0.04	0.841
Vaginal hysterectomy	25 (50%)	25 (50%)		

Table 2: Comparison of various parameters in two groups

Variables		**Group A**	**Group B**	**T value**	**P value**
Time for onset of sensory and motor block	Time from injection to sensory level T10 (in minutes)	12.76±4.50	8.8±2.34	5.520	< 0.001
	Time for maximum sensory block (min)	19.1±5.94	11.7±2.63	8.054	< 0.001
	Onset time for Bromage 3 (min)	24.1±7.12	16.26±3.72	6.900	< 0.001
Mean SPO_2(%)	Preoperative mean SPO_2(%)	96.16±1.37	95.92±1.04	0.9866	0.32
	Intra-operative mean SPO_2(%)	95.98±0.82	96.02±0.68	0.2655	0.79
Postoperative block parameters	Time for 2 segment regression(min)	304.8±36.04	420±29.06	17.595	< 0.001
	Time for Bromage 1 (in min)	343.2±30.99	450.6±29.37	17.786	< 0.001
	Time for sensory regression to S1(min)	371.4±27.70	479.4±28.74	19.132	< 0.001
	Time for epidural top-up (in min)	390±26.41	499±23.33	18.124	< 0.001

Table 3: Comparison of highest sensory level achieved in two groups

Highest sensory level	**Group A**		**Group B**		**Chi square**	**P value**
	N	%	N	%		
T4	19	38	25	50		
T6	31	62	25	50	1.015	0.3159
Total	50	100	50	100		

Table 4: Comparison of side effects in two groups

Highest sensory level	**Group A**		**Group B**		**Chi square**	**P value**
	N	%	N	%		
Nausea	5	10	5	10	0.111	0.738
Shivering	4	8	3	6	0.153	0.695
Dry mouth	5	10	10	20	1.255	0.263
Hypotension	43	86	47	94	1.778	0.182
Bradycardia	21	42	31	62	3.245	0.0716

Table 5: Comparison of hemodynamic and sedation score parameters in two groups

Variables		**Group A**	**Group B**	**T value**	**P value**
SBP (mmHg)	Pre-op	124.88±6.10	126.28±3.52	1.399	0.164
	120 min	111.88±8.04	110.06±5.13	1.349	0.18
DBP (mmHg)	Pre-op	78.62±5.02	80.64±5.83	1.856	0.066
	120 min	67.79±4.68	66.96±2.24	1.131	0.26
MAP (mmHg)	Pre-op	93.64±4.33	95.32±4.35	1.935	0.055
	120 min	82.05±5.47	81.09±2.21	1.15	0.25
HR (bpm)	Pre-op	73.96±6.06	72.36±3.65	1.599	0.113
	120 min	72.70±6.67	70.38±4.77	2.00057	0.0482
RSS (min)	Pre-op	1.00±0	1.00±0	Not applicable	
	120 min	3.0±0	2.94±0.23	1.844	0.068

SBP=systolic blood pressure, DBP=diastolic blood pressure; MAP=mean arterial pressure; HR=heart rate; RSS=Ramsay sedation score

Saravana Babu MS et al[13] found that increase in the total duration of analgesia when dexmedetomidine is added as adjuvant when compared to clonidine. Duration is 407.00±47.06min in dexmedetomidine group and 345.01±35.02min in clonidine group. This is compared to be statistically significant. [p<0.0001]. Kaur S[14] found that duration of sensory blockade is 535.18+/-19.85min with dexmedetomidine ropivacaine where as it is 375.20+/-15.97min with plain ropivacaine. These values are compared to be statistically significant with p value < 0.0001. Shaikh SI[12] found that mean time for sensory regression to s1 with dexmedetomidine is 314.17± 18.87min and with clonidine group is 298.73± 20.68min [p=0.0038]. In our study total duration of analgesia until regression to S1 is 479.4±28.74min in dexmedetomidine group when compared to clonidine group with mean time of 371.4 ± 27.70min. Statistically significant difference with p value <0.001

Bajwa SJ et al[11] observed that dexmedetomidine [342.88 ± 29.16min] provided smooth and prolonged post-operative analgesia compared to clonidine (310.76 ± 23.75min] statistically significant [p<0.05]. Similar findings were observed by Saravana Babu MS et al[13] with duration of analgesia also prolonged in dexmedetomidine group (407.00±47.06 min) compared to clonidine group (345.01±35.02). In the study done by Kaur S et al[14]they observed prolonged post op analgesia 496.56+/-16.08min with ropivacaine mixed with dexmedetomidine compared with 312.64+/-16.21min with plain ropivacaine. Motor blockade is 385.92+/-17.71min with dexmedetomidine were as with plain ropivacaine it is 259.80+/-15.48min. Shaikh SI et al[12] also found that rescue analgesia was given earlier in clonidine group 307.97 ±22.54min when compared to dexmedetomidine group 342.97 ±18.03min. There is a statistically significant difference [p<0.00001]. In our study there was prolonged time to two segmental dermatomal regression (420 ± 29.06) in dexmedetomidine group as compared to clonidine group (304.8 ± 36.04) as well as return of motor power to bromage1 (450.6 ± 29.37) in dexmedetomidine group as compared to clonidine group (343.2 ± 30.99, therefore the time to rescue analgesia was comparatively shorter in clonidine group (390 ± 26.41) as compared to dexmedetomidine group (499 ± 22.33).

In the present study not even, a single case complained of pain during surgery and all the surgeries were completed within 3hours. Both these agents can be tried in epidural anesthesia for any type of hysterectomies. Dexmedetomidine is a preferred choice of adjuvant compared with clonidine but still a little higher dose of dexmedetomidine (1.5ug/kg) needed in hysterectomies than using 1ug/kg which is sufficient for lower limb surgeries as said by Kaur S et al[14] and Bajwa SJ et al.[11]

In the present study incidence of Side effects like nausea, shivering, dry mouth, hypotension and bradycardia was comparable in two groups i.e. there was not statistically significant difference in two groups (p > 0.05). Similar findings were reported by Bajwa SJ et al,[11] Shaikh SI et al.[12]

5. Conclusion

We conclude that Dexmedetomidine is preferred over Clonidine as adjuvant to bupivacaine administered epidurally in regard to onset of sensory blockade, motor blockade, duration of postoperative analgesia, sedation scores and hemodynamic stability in patients undergoing vaginal and total abdominal hysterectomies.

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7. Conflict of Interest

The authors declare they have no conflict of interest.

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Author biography

Veeramachaneni Rajesh, Assistant Professor

Revathi Lokala, Assistant Professor

Harshavardhan Venkatayogi, Assistant Professor

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