Comparative Study of Clonidine Vs Dexmedetomidine for Hemodynamic Stability and Postoperative Analgesia during Laproscopic Surgery

Pooja Gautam[1,2]

ABSTRACT

Introduction: Alpha-2 (α2) adrenergic receptor agonists, clonidine and dexmedetomidine, are widely used as adjuvants during anesthesia for analgesic, sedative, sympatholytic, and cardiovascular stabilizing effects. The aim of this study was to differentiate the effectiveness of intravenously administered clonidine and dexmedetomidine for hemodynamic stability and postoperative analgesia during laparoscopic surgery.

Materials and methods: This was a randomised, double blind and prospective study in which Group 1 included patients who received 2 µg/kg of clonidine dilute in 10 ml normal saline, given slow intravenous infusion over 10 minutes before induction of general anaesthesia. Group 2 patients received 1 µg/kg of dexmedetomidine diluted in 10 ml of normal saline, given slowly intravenous infusion over 10 minutes before induction of general anaesthesia.

Results: The data was presented as Mean ± SD. Groups were compared by independent student's t test. Groups were also compared by repeated measure analysis of variance (ANOVA) using general linear models (GLM). The mean scores of SBP were higher in group 1 among both the groups over the periods. The mean scores of DBP in both groups was similar over the periods with slightly being higher in Group 1 especially after 30 min to till end (Extubation) as compared to Group 2.

Conclusion: It can be concluded that α 2 agonists were found to be effective in attenuating the hemodynamic response to pneumoperitoneum during laparoscopic surgeries and provides reliable postoperative analgesia and sedation when used as a premedication agent.

Keywords: α2 Agonist, General Anesthesia, Pneumoperitoneum, Dexmedetomidine, Hemodynamics, Clonidine

INTRODUCTION

In terms of decreased tissue damage, early ambulation, decreased hospital stay and reduced analgesic needs, laparoscopic surgical procedures found to have several benefits towards the patients. The hallmark of laparoscopy is the creation of pneumoperitoneum with carbon dioxide (CO_2) which leads to stimulation of the sympathetic nervous system resulting in pathophysiological changes. These changes are characterized by increase in arterial pressure, systemic and pulmonary vascular resistance seen early after the beginning of intra-abdominal insufflation with little change in heart rate. This can become a risk factor for adverse cardiologic events in patients with pre-existing essential hypertension, ischemic cardiac disease, or increased intra-cranial or intra-ocular pressure.[1,2]

The α2 adrenoceptors belong to G-protein coupled family of transmembrane receptors and are present at both pre- and post-synaptic autonomic ganglia in the central and peripheral nervous systems. Binding of agonists, endogenous (norepinephrine) or exogenous (clonidine and dexmedetomidine), results in G-protein coupling with the inhibition of both adenylyl cyclase and phospholipase C activity and subsequent effects. Various α 2 agonists are used in modern anaesthesia practice because of several benefits like sedation, analgesia, attenuation of stress response and reduction in anaesthetic drug requirement.[3,4,5]

The two currently used drugs with dexmedetomidine are clonidine and dexmedetomidine with higher selectivity for α-2 receptor. Premedication with clonidine blunts the stress response to surgical stimuli and requirement of the narcotic and anaesthetic drug is also decreased. In addition, clonidine raises the cardiac baroreceptor reflex sensitivity to increase systolic blood pressure, and thus stabilizes blood pressure.

It was seen froom the previous literature that dexmedetomidine modulates the hemodynamic changes induced by pneumoperitoneum by inhibiting the release of catecholamines and vasopressin. Esmolol, an ultra-short-acting cardioselective β1- receptor antagonist, has been found to be effective in reducing the hemodynamic responses to perioperative noxious stimuli.[6,7,8]

From the previous literature, it has been observed that reduction in the heart rate, blood pressure, systemic vascular resistance (SVR) and cardiac output was found with clonidine, an imidazoline derivative which is a selective alpha-2 adrenergic agonist and a potent antihypertensive drug. This drug also inhibits the release of catecholamines and vasopressin modulating the hemodynamic changes induced by pneumoperitoneum in laparoscopic surgery.[9,10,11]

In the past, intravenous clonidine has been used as pre-medicant among neurosurgical patients, cataract surgeries

[1]Ex. Senior Resident Department of Anaesthesiology and Critical Care, Govt. Medical College, Haldwani, [2]Ex.junior Resident, Department of Anaesthesiology and Critical Care, S.N. Medical College, Agra, India

Corresponding author: Dr Pooja Gautam, Consultant Anesthesiologist, Combined Hospital, Tanakpur, Uttrakhand, India

How to cite this article: Pooja Gautam. Comparative study of clonidine vs dexmedetomidine for hemodynamic stability and postoperative analgesia during laproscopic surgery. International Journal of Contemporary Medical Research 2019;6(1):A1-A7.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.1.20

and orthopedic procedures which requires application of tourniquet but very few studies have used intravenous clonidine as pre-medicant for preventing adverse hemodynamic changes during laparoscopic cholecystectomy. Numbers of studies have been conducted on dexmedetomidine and sedation, ventilation and metabolic rate in volunteers, oxygen consumption in dexmedetomidine-premedicated patients and postoperative sympatholytic effects.[12,13] However, the role of dexmedetomidine in contemporary intraoperative anaesthesia practice is not established. The sedative and anxiolytic properties of dexmedetomidine as well as sympatholytic characteristics make this drug of particular interest for premedication.

Clonidine, a partial alpha-2 adrenoreceptor agonist has long been used to treat hypertension. In general anaesthesia clonidine given systemically has been found to decrease perioperative anaesthetic and analgesic requirement while, addition of clonidine to local anaesthetics during spinal anaesthesia, prolongs the duration of both motor and sensory blockadge.[14,15]

A newer highly selective alpha-2 adrenergic agonist Dexmedetomidine is under study as an intrathecal and epidural adjuvant as it provides stable haemodynamic condition, better quality of intra-operative and prolonged duration of post-operative analgesia with fewer side effects. Other uses like pre-medicant and as an adjunct to general anaesthesia as well as sedative agent in the intensive care unit have made it wonder drugs in anaesthesia. It has eight times higher alpha-2/alpha-1 selectivity ratio than that of clonidine.[16,17] Therefore, the aim of the present study was to compare the effectiveness of intravenously administered clonidine versus dexmedetomidine for hemodynamic stability and postoperative analgesia during laparoscopic surgery.

MATERIAL AND METHODS

The present study was performed on 70 cases in the Department of Anaesthesia and Critical Care, S.N. Medical College, Agra which were operated under laparoscopic surgery. This was a prospective, randomised, double blinded study which was conducted after getting approval from Institutional Ethics Committee and also an informed written consent was taken from the patients and from their attendants explaining about the purpose, method and risk of the study along with the rights to get enrolled in the study.

The age of the patients was between ≥ 20- 40 years for both the genders. ASA grades I and II and undergoing laparoscopic surgery were taken in the study. Patients who were unable to understand or cooperate with the study procedure as determined by investigator were not included in the study. Patients with neurologic, cardiovascular, renal hepatic diseases or diabetic mellitus and pregnant or breast feeding females were also not considered in the study. Duration of procedures lasting for more than 120 minutes and with anticipated difficult airway and also patients on anti-hypertensive, antipsychotics, analgesics or sedative medications were excluded from the study.

The patients were randomly allocated into two groups (35 each) using the computer generate random number table. Group 1 received 2 µg/kg of clonidine diluted in 10 ml of normal saline, given slowly intravenous infusion over 10 min. before induction of general anaesthesia. Group 2 received 1 µg/kg of dexmedetomidine dilute in 10 ml normal saline, given slow intravenous infusion over 10 minutes before induction of general anaesthesia. Electrocardiography, temperature and end tidal CO_2 was started and baseline cardio-respiratory parameters were also noted.

All patients were pre-medicated with intravenous ondensetron 4 mg, glycopyrrolate 0.2 mg and fentanyl 2µg/kg. In group 1, clonidine in 2µg/kg is diluted in 10 ml normal saline and was infused over 10 min. before induction and in group 2; dexmedetomidine 1µg/kg is diluted in 10 ml normal saline and infused over 10 min before induction.

After preoxygenation, general anaesthesia was induced with propofol 2 mg/kg by weight and endotracheal intubation was facilitated by vecuronium bromide 0.1 mg/kg intravenously and anaesthesia was maintained with oxygen and nitrous oxide in ratio of 33:66 and with halothane at 0.5-1% v/v. Muscle relaxation was maintained by vecuronium bromide 0.02 mg/kg intermittently thereafter.

Controlled mechanical ventilation was also done to maintain end tidal CO_2 between 30-40 mmHg. Intra-abdominal pressure during pneumoperitoneum was maintained between 12-14 mmHg. Patient was placed in supine position with 15° left lateral tilt and 30° head elevation. Intraoperative monitoring was also performed which included non-invasive arterial blood pressure, electrocardiography, capnography, pulse oximetry and temperature.

At the end of surgery, residual neuromuscular block was reversed by neostigmine in dose of 0.05mg/kg and glycopyrrolate in dose of 0.2mg per mg of neostigmine intravenously. Patients were extubated after complete reversal of neuromuscular blockade and restoration of spontaneous respiration and patients were then transferred to recovery room. Patient's sedation scores were noted according to Ramsay sedation scores at pre-induction and during postoperative period.

Ramsay Sedation Scale is as given below-

1. Anxious and agitated or restless or both.
2. Cooperative oriented and tranquil.
3. Drowsy but respond to commands.
4. Asleep, brisk response to light glabellar tap or loud auditory stimulus.
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Asleep or unarousable.

Pain were assessed on 10 point visual analogue score (VAS) at the end of surgery,15 min.,30 min.,45min.,60 min. and 90 min. Patients were observed in the post-operative room till VAS score of 5. Rescue analgesia in the form of injection Diclofenac sodium 75 mg IV first and inj. Tramadol 2mg/kg IV was given as second line of analgesic.

RESULTS

Table no. 1 shows the distribution of demographic details among the study subjects of both the groups. It was found that the age in group 1 was 36.28±12.56 and age in group 2 was 39.42±14.45. The male to female ratio was found to be 18:17 to 19:16 among both the groups. The weight was 54.00±08.33 and 56.37±08.89 followed by APAC II- score of 12.60±02.06 and 12.48±02.09. In the present study, it was found that Ramsay sedation mean scores were 3.34 and 3.11 among group 1 and group 2 which was not found to be statistically significant at p=0.42. (Table no. 2)

In the present study, Table no. 3 shows Ramsay score of 3 which was found to be more among group 2 followed by Ramsay score of 4. The least Ramsay score was 5 and 2 in Group 1 and Group 2. The mean score of SBP in both groups was equal over the periods with slightly being higher in Group 1 when compared to Group 2. Further, during the periods, the mean SBP in Group 1 ranged from 123.10 mmHg (20 min) to 130.63 mmHg (120 min) (variation of 7.53 mmHg.); while in Group 2, it ranged from 112.23 mmHg (11 min) to

Parameters	Group 1	Group 2
No.	35	35
Age (years)	36.28 ± 12.56	39.42 ± 14.45
Sex (M : F)	18:17	19:16
Weight (kgs)	54.00 ±08.33	56.37 ±08.89
Apace II-score	12.60 ± 02.06	12.48 ±02.09

Table no.1 shows the distribution of demographic details among 2 groups

Ramsay Sedation Score	Group 1	Group 2	p value
Mean	3.34	3.11	0.42
SD	1.41	0.93	

Table-2: Shows the distribution of Ramsay Sedation Score among 2 groups

Ramsay score	Group 1 (n)	Group 2 (n)
1	5	3
2	1	1
3	16	22
4	7	8
5	2	0
6	4	1
Total	35	35

Table-3: Shows the distribution of Ramsay Sedation Score among 2 groups

Observation Period		Group-I		Group-II		t-value	p-value
		Mean	SD	Mean	SD		
Baseline	0	124.37	20.47	120.83	10.12	-1.1555	0.2534
Pre-medication	5	126.6	5.26	120.89	3.77	5.1299	0.01
	10	127.17	2.82	122.10	9.94	2.903	0.006
Induction	11	125.69	7.45	112.23	8.76	6.9246	0.0001
Intubation	15	127.90	11.12	118.93	6.84	3.7431	0.0004
	20	123.10	11.45	118.54	3.22	2.2681	0.0289
Skin incision	30	124.37	6.53	119.54	5.26	3.4078	0.001
Co_2 insufflations	45	128.89	3.77	126.6	5.26	2.0935	0.04
	60	125.77	6.06	121.2	5.25	3.372	.0012
	75	127.2	5.28	122.83	7.72	2.7642	0.007
extubation	90	129.31	4.35	123.51	12.79	2.5399	0.0149
	105	128.6	4.64	124.63	9.03	2.3134	0.02
	120	130.63	7.05	127.69	4.68	2.0555	0.0443

Table-4: Shows Mean (SD) systolic blood pressure (mm/hg) of 2 groups over the periods

Observation time (min)		Group-I		Group-II		t-value	p-value
		Mean	SD	Mean	SD		
Baseline	0	85.69	2.92	84.63	1.83	1.8198	0.074
Pre-medication	5	82.97	3.43	82.77	2.31	0.2861	0.7758
	10	84.03	2.78	83.63	5.66	0.3753	0.7091
Induction	11	81.03	3.53	80.94	2.99	0.1151	0.9087
Intubation	15	81.43	2.32	81.6	4.19	-0.210	0.8345
	20	85.6	4.07	84.2	2.76	1.6843	0.0973
Skin incision	30	88.23	2.91	87.97	3.61	0.3317	0.7412
Co_2 insufflations	45	82.91	3.58	81.46	2.8	1.8874	0.0636
	60	85.6	3.27	84.94	1.57	1.0764	0.287
	75	85.57	4.22	84.8	2.65	0.9142	0.3645
extubation	90	86.54	3.17	85.34	2.26	1.8235	0.0731
	105	85.71	3.71	84.69	3.08	1.2515	0.2152
	120	83.51	2.9	82.37	2.43	1.7826	0.0793

Table-5: Shows distribution of Mean and SD diastolic blood pressure (mm/hg) among two groups

Observation)		Group-I		Group-II		t-value	p-value
Period	Time (min)	Mean	SD	Mean	SD		
Baseline	0	99.43	3.48	98.14	2.41	3.2005	0.0022
Pre-medication	5	96.06	3.89	96.8	2.25	-0.9742	0.3343
	10	96	4.44	94.69	2.41	2.7051	0.0092
Induction	11	94.6	3.9	93.74	2.81	1.0584	0.294
Intubation	15	95.63	3.3	94.89	2.71	3.7961	0.0003
	20	94	5.68	92.26	2.76	1.6301	0.1095
Skin incision	30	94.29	2.46	94.06	2.24	2.1872	0.0322
Co_2 insufflations	45	95.49	8.55	93.69	2.13	1.2086	0.2345
	60	91.57	2.59	90.97	1.92	1.101	0.2751
	75	92.23	2.24	91.74	1.79	3.0743	0.0031
extubation	90	101.66	6.92	99.2	2.46	2.7872	0.0079
	105	99.51	1.79	96.54	2.01	6.5282	0.060
	120	98.69	1.78	97.71	1.95	2.1959	0.0315

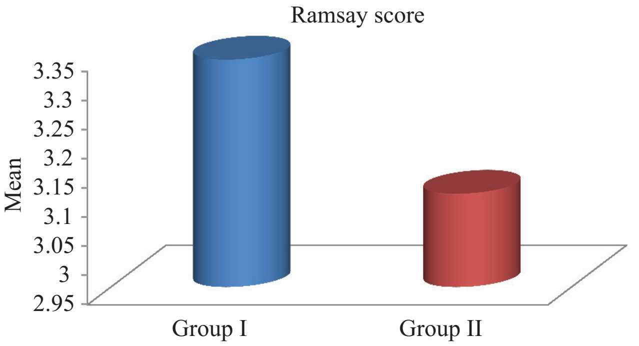
Table-6: Shows distribution of mean arterial pressure (mm/hg) over the period

Observation		Group-I		Group-II		t-value	p-value
Period	Time (min)	Mean	SD	Mean	SD		
Baseline	0	95.83	5.65	91.69	6.01	2.9692	0.0041
Pre-medication	5	79.11	5.08	85.51	4.65	-5.4978	<0.0001
	10	70.60	4.37	75.31	5.63	-3.9098	0.0002
Induction	11	72.63	5.14	76.89	8.05	-2.6387	0.0107
Intubation	15	76.17	4.36	82.23	2.22	-7.3276	<0.0001
	20	82.49	1.77	80.60	2.61	3.5456	0.0008
Skin incision	30	71.09	1.85	79.83	1.93	-19.3407	0.0001
Co_2 insufflations	45	76.17	2.67	80.91	1.80	-8.7086	<0.0001
	60	71.74	3.97	82.86	2.06	-14.7087	<0.0001
	75	73.60	3.35	82.29	2.49	-12.3168	<0.0001
extubation	90	76.23	3.24	83.97	2.20	-11.6922	<0.0001
	105	78.71	3.03	84.03	2.72	-7.7297	<0.0001
	120	81.09	3.06	85.57	2.00	-7.2502	<0.0001

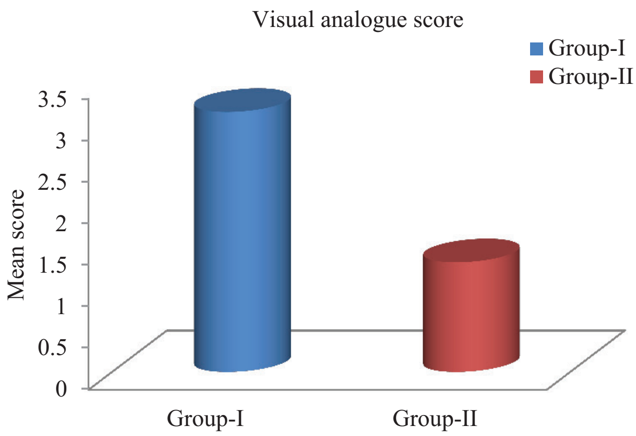
Table-7: Shows perioperative mean of heart rate (beats/min) among 2 groups

Adverse effects	Group 1	Group 2	p value
Bradycardia	3 (08.50%)	2(05.71%)	0.64
Hypotension	12 (34.28%)	4(11.40%)	0.02
Rebound hypertension	-	-	-

Table-8: Shows adverse effects observed during the study period among 2 groups



Graph-1: Shows Ramsay score among two groups



Graph-2: Shows Visual Analog Scale among two groups

127.69 mmHg (120 min) (variation of 16.60 mmHg). The mean SBP at baseline (pre- treatment) to other post periods (within groups), t test revealed similar (p< 0.05) SBP in both groups most of the time period not significant (Table no. 4). The mean score of DBP in both groups was found to be same over the periods with slightly being higher in Group 1 especially after 30 min till end (extubation) when compared to Group 2. Also, the mean DBP in Group 1 ranged from 81.03 mmHg (11 min) to 86.54 mmHg (90 min) (variation of 5.51 mmHg); while in Group 2 it ranged from 80.94 mmHg (11 min) to 87.97 mmHg (30 min) (variation of 6.03 mmHg). ANOVA showed insignificant effect among both the groups. Further, comparing the mean DBP at baseline (pre-treatment) to other post periods (within groups), t test also revealed similar (p>0.05) DBP in both groups at all post periods as compared to respective baseline was not different statistically (Table no. 5).

The Perioperative Mean Arterial Pressure (MAP) of two groups over the periods is depicted in Table no. 6. The mean MAP trend in both groups was similar over the periods with slightly being higher in Group 1 especially after 90 min to till end (extubation) as compared to Group 2. Further, during the periods, the mean MAP in Group 1 ranged from 91.57 mmHg (60 min) to 101.66 mmHg (90 min) (variation of 10.09 mmHg); while in Group 2 it ranged from 90.97 mmHg (60 min) to 98.14 mmHg (0 min) (variation of 7.17 mmHg).

The mean trend of HR in both groups was different over the periods with significantly lower in Group 1 especially from 45 min to till the end (extubation) of surgery as compared two groups. Further, the mean HR in Group 1 ranged from 71.09 beats/minutes to 95.83 beats/minutes (0 minutes) (variation of 24.74 beats/minutes); while in Group 2 it ranged from 75. 31 beats/minutes (10 min) to 91.69 beats/minutes (Table no. 7).

At the end of the surgery, the mean VAS of Group 2 differed and lowered significantly as compared to Group 1 (3.13 ± 1.40 vs. 1.32 ± 1.20, t=5.80; p<0.0001). In this study, bradycardia was observed in 3 patients (8.50%) in Group 1and 2 patients in Group 2 (5.71%) there was no significant difference between two groups (p=0.64) (Table no. 8).

Graph no. 1 shows that Ramsay score was found to be more among Group 1 as compared to Group 2. Graph no. 2 shows that visual analog scale was more in group 1 as compared to group 2.

DISCUSSION

During premedication and induction, to reduce these hemodynamic responses during laparoscopic surgeries, a wide variety of agents are being used. Various authors have conducted studies using beta blockers, α2 agonists, magnesium sulphate, opioid, vasodilators, and gasless approach to negate the hemodynamic variations. In the current study, the two most commonly used α-2 agonist in the anaesthetic practice were taken into consideration and comparison was done regarding their efficacy in reducing stress response and hemodynamic changes associated with laparoscopy and in postoperative pain relief.[18,19]

In our study, both the groups showed significant reduction in SBP as compared to baseline. It was also observed that the SBP was lower with dexmedetomidine at intubation, during pneumoperitoneum, at extubation and during postoperative period than clonidine, and this difference was found to be statistically significant. The fluctuations in SBP were also recorded in both the groups, which suggested that dexmedetomidine and clonidine stabilize the SBP and minimize the increase in SBP during various phases of anaesthesia and laparoscopy. These results are in concordance with the studies done by S. Kumar et al.[20]

In this study, there was increment in SBP at the time of extubation in clonidine which was not seen with dexmedetomidine. Thus, it was revealed that SBP stabilizing effect of dexmedetomidine lasted till extubation while clonidine was less effective in preventing the hemodynamic response to extubation. Similarly, clonidine and dexmedetomidine reduces the DBP and prevents its rise during early periods of procedure but does not suppress increase of DBP during extubation completely. These findings are consistent with the studies done by Dhurjoti Prasad et al.[21]

During the first phase of the procedure, regarding MAP, it was found that there was no significant difference in the two groups. At the end of procedure, both the drugs were equally effective in preventing the increase in MAP. The efficacy of clonidine was reduced as it was unable to suppress the increase in MAP in response to surgical stress completely.

The mean heart rate throughout the procedure was lower in clonidine as compared to dexmedetomidine and was found to be statistically significant. However, the heart rate was lower in both the groups as compared to baseline and was statistically significant. Instead of the more noticeable effect on heart rate, few of the patients suffered from significant bradycardia that received clonidine and also required treatment or dose reduction for bradycardia.

In patients suffering from coronary artery disease, the heart rate lowering effect of both the drugs reduced the myocardial oxygen demand of the patient which was very useful. Dexmedetomidine was found to be more effective in this situation and these findings were consistent with study done by Naz Anjum et al.[22] Thus, both the study drugs provided hemodynamic stability during laparoscopic surgeries and dexmedetomidine was equally effective as clonidine for this purpose. A study done by Pravin Ubale et al showed that using oral clonidine as premedication has similar results as found in the present study.[23]

Dexmedetomidine as a preanaesthetic medication and intraoperative infusion significantly attenuates sympathoadrenal response to tracheal intubation compared to clonidine and it was also seen in previous study. Previous study using clonidine 1 μg/kg intravenous showed attenuated hemodynamic stress response to pneumoperitoneum but not due to intubation and extubation.

To prevent the hemodynamic stress response to pneumoperitoneum, clonidine 2 μg/kg was given along with intubation and extubation. In this study, 2 μg/kg of clonidine and the response to laryngoscopy and intubation were prevented but the response to extubation was not suppressed completely although this difference was not statistically significant as compared to 1μg/kg dose of dexmedetomidine. So, 1μg/kg dose of dexmedetomidine was more effective than 1μg/kg of clonidine and its effect was comparable to 2 μg/kg of clonidine.

The mean VAS of the patients in clonidine was 3 at the end of procedure and all of the patients required analgesic after 60 minutes of surgery and 9/30 patients require rescue analgesia at extubation, while with dexmedetomidine, the mean VAS at the end of procedure was 1 and most patients had adequate analgesia up to 90 min. Thus, dexmedetomidine is far better analgesic as compared to clonidine regarding duration of analgesia.

The mean sedation scores at the end of the procedure were 3.34 and 3.11 respectively in clonidine and dexmedetomidine which was statistically insignificant. Thus, patients were equally sedated in dexmedetomidine as compared to clonidine. The patients in both groups were less sedated, required less postoperative monitoring and were more cooperative. This reflects the sedative property of dexmedetomidine than clonidine is proportional to their analgesic action so none of the patient requires any type of airway or ventilator support.

There was no complication noted in the study except bradycardia in 3 patients in clonidine and 2 patients in dexmedetomidine which was not statistically significant and did not require any intervention. It was found that hypotension was seen among 12 patients in clonidine and 4 patients in dexmedetomidine which was statistically significant and required some intervention. None of the patient had rebound hypertension. Therefore, both the drugs were found to be safe.

CONCLUSION

Both α 2 agonists were found to be effective in attenuating the hemodynamic response to pneumoperitoneum during laparoscopic surgeries and also provides reliable postoperative analgesia and sedation when used as a premedication agent.

REFERENCES

1. Unlugenc H., Gunduz M, Guler T, Yagmur O, Isik G. The effect of pre-anaesthetic administration of intravenous dexmedetomidine on postoperative pain in patients receiving patient-controlled morphine. European Journal of Anaesthesiology 2005; 5: 386-391.
2. Surendra Kumar Raikwar, Sandhya Evney, Aditya Agarwal. Comparision of Inj. Clonidine and Dexmedetomidine as an Adjuvant to Bupivacaine 0.5% (Plain) in Supraclavicular Brachial Plexus Block for Upper Limb Surgeries-A Clinical Study. International Journal of Contemporary Medical Research 2016; 3:3327-3330.
3. A. Naresh Babu, G. Harinath. A comparative study between clonidine and dexmedetomidine used as adjuncts to Ropivacaine for caudal analgesia in Pediatric patients. International Journal of Contemporary Medical Research 2015; 2:478-483.
4. Blobner M, Felber AR, Gogler S. Carbon-dioxide uptake from the pneumoperitoneum during laparoscopic cholecystectomy. Anesthesiology 1992; 77: 37–40.
5. Ramesh Pendela. A Comparative Study of Intrathecal Dexmedetomidine and Clonidine as an Adjuvant to Hyperbaric Bupivacaine in Surgeries for Fracture Femur and Tibia. International Journal of Contemporary Medical Research 2018; 5:12-14.
6. Lenz RJ, Thomas TA, Wilkins DG. Cardiovascular changes during laparoscopy: Studies of stroke volume and cardiac output using impedance cardiography. Anaesthesia. 1976; 31:4–7.
7. Anne Kiran Kumar, Mohammad Rahmathullah, Dilip Kumar Kulkarni, Gopinath Ramachandran. Efficacy of Adding Dexmedetomidine to Bupivacaine on Attenuating Hemodynamic Response to Skull Pin Placement for Performing Scalp Block. International Journal of Contemporary Medical Research 2017; 4:9-13.
8. Walder AD, Aitkenhed AR. Role of vasopressin in the haemodynamic response to laparoscopic cholecystectomy. Br J Anaesth. 1997; 78:264-266.
9. Frederic J. Gerges, Ghassan E. Kanazi, Samar I. Jabbourkhoury, Anesthesia for laparoscopy: a review. Journal of Clinical Anesthesia. 2006; 18: 67-78.
10. Singh Shivinder, Arora Kapil. Effect of oral clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. 2011; 55: 26-30.
11. Tripathi C Deepshikha, Shah S Komal, Dubey R Santosh, Doshi M Shilpa, Raval V Punit. Hemodynamic stress response during laparoscopic cholecystectomy: Effect of two different doses of intravenous clonidine premedication. J Anaesthesiol Clin Pharmacol. 2011; 27: 475-480.
12. Sarfraj Ahmad, Ananda Prakash Verma, Ram Pal Singh, Lakhvinder Singh Kang, Malti Agrawal, Shaheen Begum. Comparative Study of Efficacy of Clonidine added to Levobupivacaine and Levobupivacaine alone in Supraclavicular Brachial Plexus block for Upper Limb Surgery. International Journal of Contemporary Medical Research 2014; 1:7-13.
13. Panda Bijoy Kumar, Singh Priyanka, Marne Sourabh, Pawar Atmaram, Keniya Varshali, Ladi Sushma, Swami Sarita. Comparison study of Dexmedetomidine vs. Clonidine for sympathoadrenal response, perioperative drug requirements and cost analysis. Asian Pacific Journal of Tropical Disease 2012:1-6.
14. Amit Gupta, Kanhya Lal Gupta, Manish Yadav. To Evaluate the Effect of Addition of Dexmedetomidine to hyperbaric Bupivacaine Intrathecally in infraumblical Surgeries. International Journal of Contemporary Medical Research 2016; 3:2136-2138.
15. Aho M, ErkolaO, Kallio A, Schenin H et al. Comparision of dexmedetomidine and midazolam sedation and antagonism of dexmedetomidine with atipamezole. J Clin Anesth l993; 5:194-203.
16. Asad Mohammad, Sangeeta Goel, Anurag Singhal, Vibhor Rae. Clonidine as an Adjuvant to Ropivacaine in Supraclavicular Brachial Plexus Block: A Randomised Double Blinded Prospective Study. International Journal of Contemporary Medical Research 2016; 3:1293-1296.
17. Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous dexmedetomidine in humans: Sedation, ventilation and metabolic rate. Anaesthesiology1992; 77:1125-1133.
18. Davies DS, Wing LMH, Reid JL, Neill E, Tippett P, Dollery CT. Pharmacokinetics and concentration-effect relationships of intravenous and oral clonidine. ClinPharmacolTher 1977:21:593-601.
19. Hall JE, Uhrich TD, Ebert TJ. Sedative, analgesic and cognitive effects of clonidine infusions in humans. Br J Anaesth 2001; 86:5-11.
20. S Kumar et al. Comparative Study of Effects of Dexmedetomidine and Clonidine Premedication in

Perioperative Hemodynamic Stability and Postoperative Analgesia in Laparoscopic Cholecystectomy. The Internet Journal of Anesthesiology 2013; 33:1-8.
21. Dhurjoti Prosad Bhattacharjee, Sauvik Saha, Sanjib Paul, Shibsankar Roychowdhary, Shirsendu Mondal, Suhrita Paul. A comparative study of esmolol and dexmedetomidine on hemodynamic responses to carbon dioxide pneumoperitoneum during laparoscopic surgery. Anesth Essays Res 2016;10: 580–584.
22. Naz Anjum, Hussain Tabish, Saha Debdas, Hembrom P Bani Choudhuri, Rajat Ghosh Dastidar, Anjana Basu. Effects of dexmedetomidine and clonidine as propofol adjuvants on intra-operative hemodynamics and recovery profiles in patients undergoing laparoscopic cholecystectomy: A prospective randomized comparative study.
23. Pravin Ubale, Indrani Hemant Kumar. Effect of intravenous clonidine on hemodynamic changes in laparoscopic cholecystectomy: a randomized control study. Anaesth Pain & Intensive Care 2016; 20:182-186.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 04-12-2018; **Accepted:** 05-01-2019; **Published:** 16-01-2019