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Comparision of iv Dexmedetomidine V/S iv Clonidine In Hemodynamic Stability in Laparoscopic Surgery.

Disha Bhanderi*, Chandresh Shah, Bhavik Shah, Nidhi Mandowara.

B J Medical College, Civil Hospital, Ahmedabad, Gujarat, India

ABSTRACT

To compare and evaluate the efficacy of the two alpha agonists Clonidine and Dexmedetomidine in prevention of hemodynamic stress response to laryngoscopy, intubation and carbon dioxide pneumoperitoneum. Forty five patients of ASA I & II posted for laparoscopic surgery were studied. Patients were randomly allocated into 3 groups. Group I (Placebo group; n=15) were given Inj Normal Saline iv.Group II (Clonidine group; n=15) were given Inj Clonidine 1.5 mcg /kg iv 15 minutes before induction.Group III (Dexmed group; n=15) were given Inj Dexmedetomidine loading 1 mcg/kg over 10 minutes maintainance 0.4 mcg/kg/hr iv infusion before induction. Heart rate, blood pressure, oxygen saturation, $Etco_2$ were noted. Age, sex, weight and duration of surgery were comparable in all the three groups. The decrease in heart rate appeared more in Clonidine (group II) at all intervals when compared to Dexmedetomidine (group III) but the fall was found to be statistically significant only at end of pneumoperitoneum, and after reversal. The fall in mean blood pressure appeared more in Clonidine group at all intervals when compared to Dexmedetomidine group but the fall was not found to be statistically significant at any stage. Both Clonidine and Dexmedetomidine, maintained cardiovascular stability during laparoscopic surgery. But Clonidine was more effective in maintaining hemodynamic stability during the surgery.

Keywords: Clonidine, Dexmedetomidine, Hemodynamic stability, Laparoscopic surgery

Corresponding author

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INTRODUCTION

Laparoscopy is the technique of the new millennium.As a result of benefits of laparoscopic surgery over open surgery like reduction in post-operative pain and diminished postoperative disability, general surgery has under gone revolution [7]. Though laparoscopy offers much more benefits than conventional open surgery, it still causes stress hormone responses. Peritoneal insufflations induce alteration of hemodynamic parameters, characterized by decrease in cardiac output, elevation of arterial pressure and increase in systemic and pulmonary vascular resistance. Elevated stress hormones, cardiovascular instabilities and ventilatory impairment may prove detrimental in high risk patients with limited cardiopulmonary reserve [26]. To prevent hemodynamic responses of laryngoscopy, intubation and pneumoperitoneum, various pharmacological agents can be used. These involve[26] β-blockers-Atenolol, Esmolol; α-2 adrenoreceptor agonists-Clonodine, Dexmeditomidine; Opioids-Fentanyl, Remifentanyl; Vasodialator- Nitroglycerine, Nicardipine. In this study, we compare IV Clonidine and IV Dexmedetomidine in laparoscopic procedures to evaluate its effects on hemodynamic stability intraoperatively [1-15].

MATERIALS AND METHODS

After approval from the Institutional Ethics Committee, B. J. Medical College, & Civil Hospital,Ahmedabad and written informed consent of the patients, this study was conducted in a tertiary care B.J. medical college, Civil Hospital, Ahmedabad. A total of 45 patients of American Society of Anesthesiologists (ASA) physical status I & II, undergoing elective laparoscopic cholecystectomy with CO_2 pneumoperitoneum, were enrolled in this study. Patients in whom surgery could not be completed laparoscopically and open cholecystectomy done were excluded from the study.
These patients were randomly allocated to 3 groups

- **Group I** (Placebo group; n=15)
- **Group II** (Clonidine 1group; n=15)
- **Group III** (Dexmed group; n=15)

Patients were premedicated with Inj. Ondansetron 0.15 mg/kg i.v, Inj.Glycopyrrolate 4 mcg/kg i.v, Inj. Fentanyl 1.5 mcg/kg i.v in preoperative room. On arrival in the operation theatre, monitors were attached (heart rate, NIBP, oxygen saturation, ECG) and baseline vital parameters like heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded.

- Patients of group I were given Inj Normal Saline iv
- Patients of group II were given Inj Clonidine 1.5 mcg /kg iv 15 minutes before induction.
- Patients of group III were given Inj Dexmedetomidine loading 1 mcg/kg over 10 minutes maintainance 0.4 mcg/kg/hr iv before induction.

Anesthesia was induced with intravenous Thiopentone sodium (2.5%) 5-7 mg/kg followed by Inj. Succinylcholine 2 mg/kg to facilitate endotracheal intubation.Following induction of anaesthesia, a urinary catheter and a nasogastric tube were placed. For

maintainance O_2 and N_2O mixture with Isoflurane and Inj.Vecuronium bromide were used. CO_2 pneumoperitoneum was created and intra-abdominal pressure maintained at 14 mm Hg. Controlled ventilation was carried out to maintain normocapnia. Intraoperatively patients were monitored with continuous ECG, SBP,DBP,MAP,SPO_2, $EtCO_2$ at;

- Preoperative (M1)
- 10 min after starting Study Drug Infusion(M2)
- At Induction (M3)
- After intubation (M4)
- Before Pneumoperitoneum (M5)
- 10 min after pneumoperitoneum (M6)
- 20 min after pneumoperitoneum (M7)
- 30 min after pneumoperitoneum (M8) Then every 30 min till end of surgery
- End of Pneumoperitoneum (N1)
- After Reversal (N2)
- Postoperative in Recovery room (N3)

In case of acute and severe hemodynamic fluctuations, other medical interventions were carried out.

- When bradycardia (heart rate lower than 50 beats/min) occurred, Inj. Atropine 0.6mg IV (intra-venous) was administered.
- Hypotension (Mean Arterial Blood Pressure lower than 60 mmHg) was managed by decreasing Isoflurane concentration.
- Hypertension (Mean Arterial Blood Pressure greater than 110 mmHg) was managed by increasing Isoflurane concentration, Inj. NTG (Nitro Glycerine) infusion at the rate of 1-4 mcg/kg/min

Reversal: Inj. Neostigmine 0.05 mg/ kg + Inj. Glycopyrrolate 0.008 mg/ kg.

Extubation: After thorough oropharyngeal suction, Extubation was done when patient has established protective reflexes with adequate tidal volume and hemodynamic stability.
Patient vitals like Temperature, pulse, blood pressure, urine output were monitored and systemic examinations like respiratory, cardiovascular and central nervous system were done in post operative period.Patient was monitored for any side effect of drugs.All intraoperative and post operative complications were recorded properly.

Statistical analysis

Data was expressed as mean and standard deviation (SD). The homogenecity in three groups of mean and SD was analysed using student's t-test.Tables of mean and standard deviation were prepared for meaningful comparison of the three groups. A p value of less than or equal to 0.05 was considered as significant.

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RESULTS AND DISCUSSION

Table 1. Patient characteristics

Characteristics	Group I	Group II	Group III	'p' value
Age (Years)	43.27 ± 13.14	44.93 ± 8.16	45.93 ± 11.20	0.800
Weight (KG)	59.47 ± 8.57	59.27 ± 4.96	53.80 ± 7.31	0.057
Duration of surgery (Min)	68.13 ± 12.38	83.47 ± 27.67	79.53 ± 19.89	0.127

- Average age in Group I (Placebo Group) was 47.23 year, in Group II (Clonidine Group) was 44.93 year and in Group III (Dexmedetomidine Group) was 45.93 years. Average weight in Group I (Placebo Group) was 59.47 kg , in Group II (Clonidine Group) was 63.60 yr and in Group III (Dexmedetomidine Group) was 53.80kg.
- Average duration of surgery in Group I (Placebo Group) was 68.13 min, in Group II (Clonidine Group) was 83.47 min and in Group III (Dexmedetomidine Group) was 79.53 min.

Table 2. Sex distribution

Sex	Group I	Group II	Group III
Female	7 (46.67%)	6 (40%)	9 (60%)
Male	8 (53.33%)	9 (60%)	6 (40%)

- The sex distribution in the three groups have been depicted in the table above.

Table 3. Heart rate

Time	Group I	Group II	Group III	p value I-II	p value I-III	p value II-III
M1	88.13 ± 13.88	77.87 ± 8.03	87.73 ± 16.35	0.936	0.564	0.457
M2	86.27 ± 12.49	81.00 ± 12.07	86.80 ± 14.99	0.423	0.275	0.254
M3	87.73 ± 16.05	77.47 ± 13.13	84.00 ± 15.73	0.179	0.584	0.285
M4	108.47 ± 17.35	81.60 ± 10.40	87.00 ± 19.65	0.0001	0.002	0.261
M5	93.67 ± 15.50	73.47 ± 12.56	81.07 ± 19.18	0.005	0.0002	0.163
M6	90.87 ± 12.55	69.73 ± 11.55	83.57 ± 22.38	0.004	0.134	0.184
M7	90.87 ± 12.55	69.73 ± 11.55	83.57 ± 22.38	0.003	0.734	0.124
M8	94.20 ± 14.25	69.80 ± 11.35	80.93 ± 20.62	0.001	0.231	0.236
N1	83.00 ± 11.10	67.53 ± 12.22	82.93 ± 18.73	0.006	0.245	0.004
N2	102.93 ± 10.52	80.60 ± 8.83	97.64 ± 19.02	0.0002	0.003	0.0002
N3	86.40 ± 10.45	67.93 ± 9.87	76.29 ± 16.43	0.001	0.375	0.346

Group I (Placebo Group) and Group II (Clonidine Group)

Heart rate in Group I (placebo group) increased significantly when compared to Group II (Clonidine group), after intubation (M4), before pneumoperitoneum (M5), 10 min after pneumoperitoneum (M6), 20 min after pneumoperitoneum (M7), 30 min after pneumoperitoneum (M8), end of pneumoperitoneum (N1), after reversal (N2) and post operatively in recovery (N3) ($p=<0.05$)

Group I (Placebo Group) and Group III (Dexmedetomidine Group)

No statistically difference in heart rate was found between the two groups except after intubation (M4), before pneumoperitoneum (M5), after reversal (N2) ($p<0.05$), when

heart rate increased significantly in Group I (Placebo Group) compared to Group III (Dexmedetomidine Group)

Group II (Clonidine Group) and Group III (Dexmedetomidine Group)

The decrease in heart rate appeared more in Group II (Clonidine Group) at all intervals when compared to Group III (Dexmedetomidine Group) but the decrease was found to be statistically significant only at end of pneumoperitoneum (N1) and after reversal (N2) ($p<0.05$) when heart rate was found to be more in Group III (Dexmedetomidine group)

Table 4. Mean blood pressure

Time	Group I	Group II	Group III	P value	P value	P value
				I-II	I-III	II-III
M1	95.18 ± 8.65	96.07 ± 9.47	94.91 ± 8.67	0.936	0.637	0.263
M2	98.53 ± 8.36	96.67 ± 7.52	96.58 ± 8.86	0.779	0.537	0.536
M3	85.09 ±11.64	84.20 ± 9.44	86.20 ± 8.39	0.86	0.647	0.255
M4	117.98 ±14.03	91.69 ±10.97	90.22 ± 8.94	0.0001	0.002	0.436
M5	100.27 ±18.52	90.51 ±12.70	90.06 ±12.86	0.209	0.076	0.536
M6	109.64 ±12.03	94.62 ±11.08	99.50 ±17.05	0.014	0.325	0.896
M7	103.67 ± 6.82*	92.33 ± 9.32*	97.64 ± 16.34	0.034	0.363	0.256
M8	102.71 ± 8.93*	90.60 ± 10.25*	93.52 ± 11.87	0.007	0.435	0.637
N1	101.87 ± 6.15*	91.60 ± 10.15*	95.55 ± 13.01	0.025	0.324	0.622
N2	111.62 ± 8.70*	97.69 ± 7.23*	105.66 ± 14.22	0.003	0.003	0.235
N3	101.64 ± 8.26#	90.00 ± 6.19	91.95 ± 11.08	0.001	0.002	0.758

Group I (Placebo Group) and Group II (Clonidine Group)

Mean blood pressure (MAP) in Group I (Placebo Group) were significantly higher after intubation (M4), 10 min after pneumoperitoneum (M6),

20 min after pneumoperitoneum (M7), 30 min after pneumoperitoneum (M8), end of pneumoperitoneum (N1), after reversal (N2) and post operatively in recovery (N3) ($p=<0.05$) compared to Group II (Clonidine group).

Group I (Placebo Group) and Group III (Dexmedetomidine Group)

Mean blood pressure (MBP) in Group I (Placebo Group) were significantly higher after intubation (M4), after reversal (N2) and post operatively in recovery (N3) ($p=<0.05$) compared to Group III (Dexmedetomidine group)

Group II (Clonidine Group) and Group III (Dexmedetomidine Group)

There was no statistically significant difference in MBP between two groups. MBP between the two groups were found to be comparable.

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DISCUSSION [15-32]

- In our study we compared the efficacy of Dexmedetomidine and Clonidine on haemodynamic stability in patients undergoing Laparoscopic Cholecystectomy.
- We found a statistically significant change between Placebo (Group I) and Clonidine (Group II) groups as regards to heart rate after laryngoscopy and intubation (M4),before pneumoperitoneum (M5),10 min after pneumoperitoneum (M6) and throughout the period of pneumoperitoneum i.e. 20 min after pneumoperitoneum (M7), 30 min after pneumoperitoneum (M8). At end of pneumoperitoneum (N1), after reversal (N2), and post operative in recovery (N3) the change in heart rate were found to be significant.
- As regards to mean blood pressure statistically significant changes were found between Placebo (Group I) and Clonidine (Group II) groups similar to heart rate changes viz after laryngoscopy and intubation (M4),10 min after pneumoperitoneum (M6), 20 min after pneumoperitoneum (M7), 30 minafter pneumoperitoneum (M8). Again at end of pneumoperitoneum (N1), and after reversal (N2) the changes were found to be significant.
- When Dexmedetomidine group (Group III) was compared to Placebo Group (Group I) the heart rate and mean blood pressure were found to be statistically significant only after laryngoscopy and intubation (M4) and post operative in recovery (N3) and not at other intervals.
- The decrease in heart rate appeared more in Clonidine (group II) at all intervals when compared to Dexmedetomidine (group III) but the fall was found to be statistically significant only at end of pneumoperitoneum (N1), and after reversal (N2). The fall in mean blood pressure appeared more in Clonidine group at all intervals when compared to Dexmedetomidine group but the fall was not found to be statistically significant at any stage.
- In a study [32] Clonidine 4 mcg/kg and Dexmedetomidine 2.5 mcg/kg were given 40-50 min before the anticipated induction of anaesthesia and it was found that heart rate and mean arterial pressure were found to be lower in Clonidine and Dexmedetomidine group when compared to placebo group. In our study we found that heart rate and mean arterial pressure were significantly lower in the Clonidine group when compared to saline group than the Dexmedetomidine group. We used a lower dose of Clonidine and Dexmedetomidine.
- A study [23] compared the dose response relationship for one hour infusions of Clonidine 1, 2, and 4 mcg/kg/hr and placebo. Mean arterial pressure had increased by 10% over the baseline in the placebo group and mean arterial pressure decreased by 13% of the baseline in Clonidine 4mcg/kg/hr. In our study also in the placebo group the mean arterial pressure raised by 15 % above the baseline 60 mins after starting the infusion and decrease in mean blood pressure was found to be 6.2% in clonidine goup.
- Another study [24] found that Pneumoperitoneum results in an increase in MAP, SVR and PVR and a decrease in cardiac output. The increase in SVR is associated with a marked release of vasopressin and catecholamines. Clonidine given before pneumoperitoneum reduces the release of catecholamines and provides intraoperative hemodynamic stability Clonidine before creation of pneumoperitoneum, reduces catecholamine release thus significantly attenuated the

increase in mean arterial pressure and heart rate in comparison to placebo in a study where patients received 8 mcg/kg Clonidine infused over one hour before pneumoperitoneum. It was intended to study the propensity of Clonidine to modulate the haemodynamic changes during laparoscopic cholecystectomy. We had used a dose of 1.5 mcg/kg of Clonidine and our findings are correlated by this study.

- A study [20] compared three infusion doses of Dexmedetomidine 0.2, 0.4 and 0.8 mcg/kg/hr with saline in morbidly obese patients undergoing Laparoscopic Bariatric surgery. Mean arterial blood pressure values were maintained within ±25% of the preinduction baseline values by varying the inspired Desflurane concentration. It was found that intraoperative hemodynamic values were similar in the four groups, arterial blood pressure values were significantly reduced in the Dex 0.2, 0.4, and 0.8 groups compared with the control group on admission to the postanesthesia care unit (PACU) ($p<0.05$). In our study also, the mean blood pressure in Dexmedetomidine group was significantly less in PACU ($p<0.05$).

CUNCLUSION

Both Clonidine and Dexmedetomidine, maintained cardiovascular stability during laparoscopic surgery. But Clonidine was more effective in maintaining hemodynamic stability during the surgery. Moreover, Clonidine being more cost effective than Dexmedetomidine can be recommended for maintaining cardiovascular system stability during laparoscopic surgery.

REFERENCES

[1] Aantaa , Kanto J, Scheinin M, Kallio A, Scheinin H. Anesth Analg 1990; 70: 407-13
[2] Amirul I, Mozaffer H, AKM Akhtaruzzaman, UH Shahera Khatun. Journal of BSA January 2008;21(1) : 12-20.
[3] Bousquet P et al. Eur J Pharmacol 1981; 69: 389-92.
[4] Carabine UA et al. Anaesthesia and Analgesia 1991; 73: 633-637.
[5] Alex Bekker, Mary Stuaraitis et al. Anaesthesia and Analgesia 2008; 107; 1340-13477
[6] Ciaeeheri M et al. Acta Cardiol 1986; 38: 233-236.
[7] Bakhamees HS, Halafawy , El-Kerdawy H, Nevien M. Anesth 2007; 19 (3): 537-551
[8] Doze VA, Chen BX et al. Anaesthesiology 1989; 71: 75-79.
[9] Dipak rawal , Malini Mehta. Indian Journal of Anaesthesia 2002 ; 46 (2) , 124-129.
[10] Bhattacharjee, Sushil Nayek et al. J Anaesth Clin Pharmacol 2010; 26(1); 45-48
[11] Sharma RK. History of minimal access surgery.
[12] Lawrence CJ, lange SD. Anaesthesia1997; 52: 736-744
[13] Joris JL et al. J AM Coll Cardiol 1998; 32(5):1389-1396
[14] Joris JL et al. Anaesthesia and Analgesia : 1993; 76 : 1067-1071.
[15] Mehta JL et al. Arch med 1987; 147:389-90.
[16] Langer SZ et al. Biochem Pharmacol 1974; 23: 1793- 1800.
[17] Larsen JF et al. Br J Surg 2004; 91(7): 848-54
[18] Malek J, Knor J, Kurzova A et al. Rozhl Chir. 1999; 78 (6): 286-291.
[19] Manjushree R, Bimal H, Rita P, Dhurjoti PB. Indian Journal Of Anaesthesia. 2010; 54(2): 137-141.
[20] Tufanogullari B, et al. Anaesth Analg 2008; 106(6):1741-8.

[21] Laisalmi M, et al. Surg Endosc 2001; 15: 1331-5.
[22] Mrinmoy D , et al.. Indian Journal Of Anaesthesia. 2007 ; 51(3) : 205-207.
[23] Hall JE, Uhrich TD, Ebert TJ. BJA 2001; 86(1): 5-11.
[24] Jorris JL, et al. JACC 1998; 32(5):1389-96.
[25] Robert KS , Simon CH : Stoelting – Pharmacology And Physiology in Anaesthesia Practice. 4th edition 2006; 323-335.
[26] O'leary E, Hubbard K, Tormey W, Cunningham A. British Journal 1996; 76(5):640-4
[27] Pande P, et al. Am J Association 2007; 298 (22): 2644–53
[28] Paris A, Tonner PH: Current Opinion in Anaesthesiology 2005; 18 (4): 412–418
[29] Shivinder S, Kapil A. Indian Journal Of Anaesthesia. 2011 ; 55(1) : 26-30.
[30] Riker RR, et al. JAMA 2009; 301 (5): 489–99
[31] Ghignone M. Anesthesiology 1986; 64: 36-42.
[32] Taittonen MT, Kirvela OA, Aantaa R, Kanto JH. British journal of anaesthesia 1997; 78: 400-406.