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# A COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS CLONIDINE HAEMODYNAMIC CHANGES DURING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA

Forensic Medicine

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## ABSTRACT

**Introduction:** The alpha 2 adrenergic receptor agonist, dexmedetomidine and clonidine were found to inhibit the release of catecholamines and vasopressin and thus modulate the hemodynamic changes induced by pneumoperitoneum in laparoscopic cholecystectomy. The present study was conducted to compare the efficacy of dexmedetomidine vs clonidine on hemodynamic changes during laparoscopic cholecystectomy.
**Materials and methods:** A randomized, double-blind study was conducted on a total of 50 patients of ASA I and ASA II between the age group of 18 to 60 years. Group D, dexmedetomidine received 1ug/kg diluted in 20ml normal saline infused over 15 mins intravenously and Group C, clonidine 1ug/kg diluted in 20 ml normal saline over 15 mins intravenously. **Results:** There is no significant difference in Heart rate was observed in both group C and group D but Systolic BP, Diastolic BP and MAP were more stable in dexmedetomidine when compared to clonidine group. **Conclusion:** Dexmedetomidine in dose of 1microgram per kg as premedication significantly attenuates the haemodynamic changes during laparoscopic cholecystectomy under general anesthesia with more efficacy than Clonidine.

## KEYWORDS

Dexmedetomidine, Clonidine, Anaesthesia, Laparoscopic Cholecystectomy.

## INTRODUCTION

Laparoscopic cholecystectomy is a commonly performed surgery for cholelithiasis. It offers many benefits over conventional open cholecystectomy. However, this procedure is not risk-free from the anaesthetic point of view. Significant hemodynamic changes are observed during this procedure, which can be detrimental, especially in elderly and hemodynamically compromised patients (1) (2). Pneumoperitoneum affects, several homeostatic systems leading to an alteration in acid-base balance, cardiovascular & pulmonary physiology, and stress response(3). The cardiovascular changes associated with pneumoperitoneum are increased in mean arterial pressure, a decrease in CO, and an increase in SVR, which in turn compromises tissue perfusion. Various pharmacological agents are used to prevent hemodynamic changes associated with pneumoperitoneum(4). Nitroglycerine is used in the correction of reduction of CO associated with increased pulmonary occlusion pressure and systemic vascular resistance(5).IV clonidine has been used in the past as premedication in neurosurgical patients and orthopaedic procedures requiring the application of a tourniquet, but few studies are available which have used intravenous clonidine as premedication for preventing adverse hemodynamic changes during laparoscopic cholecystectomy(6). Dexmedetomidine is 8 times more specific for α2 receptors than clonidine and the improved specificity for the α2 adrenoreceptors, especially for the 2A subtype(7) (8). The present study was conducted to compare the efficacy of dexmedetomidine vs clonidine on hemodynamic changes in laparoscopic cholecystectomy.

**Figure 1: crumb rubber in cracker mill**

## MATERIALS AND METHODS

The study was conducted in the Department of Anesthesiology, Government general hospital, Guntur from January 2018 to December 2019.

A randomized, double-blind study was conducted on a total of 50 patients of ASA I and ASA II between the age group of 18 to 60 years undergoing elective laparoscopic cholecystectomy under general anesthesia. The sample size is calculated based on the mean duration of the Mean Heart rate. To detect a mean difference of 8 with a SD of 9.5(9). Considering Type I error (α) of 5% i.e. to detect a difference at the 95% confidence interval and Type II error (β) of 20% i.e. with a power of 80% for the study .keeping the ratio of two groups as 1.

$$n = 2(z1-\alpha/2 + z1-\beta)2 / (\mu 0 - \mu 1/\sigma)2$$

The sample size calculated per group is 24. So the minimum sample size required for this study is 48 and was rounded to 50.

Patients were randomly divided into 2 groups 25 members each

Group D – Dexmedetomidine group (n=25)
Group C – Clonidine group (n=25)

### INCLUSION CRITERIA:

1. ASA grade I and II
2. Age 18 to 60 years
3. Weight 30 – 80 years
4. The patient who gives informed valid consent
5. The patient is scheduled to undergo elective laparoscopic cholecystectomy.

### EXCLUSION CRITERIA

1. ASA grade III and IV
2. Risk of gastric aspiration
3. Smokers
4. Grossly obese patients
5. Patients with respiratory disease.

A pre-anesthetic evaluation of the patients was done to all patients. The monitoring and anesthetic technique was the same for all patients. Patients undergoing elective laparoscopic cholecystectomy who were fit for surgery and met the inclusion criteria were randomly divided into two groups i.e., group D and group C using computer-generated random numbers. The patients were not aware of whether s/he receiving dexmedetomidine or clonidine. The study drug was prepared by a senior anesthesiologist not involved with the study, and the observer was blinded for the study.

On arrival of the patient to the operating room, patients were connected to multi-channel monitors, which measures HR, SBP, DBP, MAP, ETCO2, SPO2, and ECG. A peripheral line with 18 G IV cannula was secured, and an infusion of normal saline was started. All patients were premedicated with injection glycopyrrolate 0.01mg/kg IV, injection fentanyl 1ug/kg IV, injection ondansetron 0.1mg/kg, and pre oxygenated with 100% oxygen for 3mins before induction with a tight-fitting mask using a closed circuit. After 15mins of administration of the study drug, anesthesia was induced with injection propofol 1% solution, and the dose required to produce verbal response was recorded. Injection atracurium 0.5 mg/kg IV was administered to facilitate intubation and produce muscle relaxation after 3mins of administration of atracurium, followed by laryngoscopy. After confirmation of tracheal intubation using etco2 and auscultation for bilateral equal air entry and the tube was secured, and anesthesia was maintained with 60% nitrous oxide and 40% oxygen and 1% of sevoflurane with a tidal volume of 8 to 10ml/kg and respiratory rate of 10 to 12 breaths per min.

Group dexmedetomidine received 1ug/kg diluted in 20ml normal saline infused over 15 mins intravenously and Group C, clonidine

1ug/kg diluted in 20 ml normal saline over 15 mins intravenously. In both, the groups' infusion started 30 mins before the induction of anesthesia. At the end of the surgery, patients were reversed with injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.01mg/kg. The patients were extubated when awake and breathing adequately and shifted to the recovery room. The parameters HR, SBP, DBP, MAP, SPO2 were recorded at baseline, before induction, after intubation, before the creation of pneumoperitoneum (P0), 10 mins, 20 mins, 30 mins after creation pneumoperitoneum, after extubation.

**STATISTICALANALYSIS:**

Non-parametric data were expressed in proportions; parametric data was represented as Mean ± SD. Statistical tests like the Independent sample T-test, Chi-Square was used wherever applicable. A P-value less than 0.05 is considered statistically significant. Data were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago., IL, trail version 17.0).

## RESULTS

**Table1: Distribution of variables Age, weight and Gender**

| | | Dexmedetomidine (N=25) | Clonidine (N=25) | P-value |
|---|---|---|---|---|
| Sex | Male | 12 | 12 | N.S (P=1) |
| | Female | 13 | 13 | |
| Mean Age (Years) | | 44.56±6.318 | 43.8±6.94 | N.S (P=0.6874) |
| Mean Weight(Kgs) | | 54.52±7.125 | 54.32±7.40 | N.S (p=0.9213) |

The selection of two groups was chosen in such a way that there is a similar distribution of gender, age, and weight.

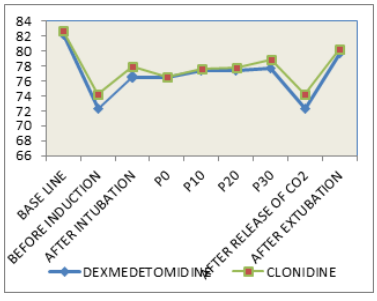



**Figure 1: Variations of heart rate at different time periods**

Heart rates were a little bit higher in the clonidine group when compared to the Dexmedetomidine group but this difference is statistically not significant all the time levels.

**Table 2: P values of heart rates at different time periods**

| | P-VALUE | Significance |
|---|---|---|
| BASELINE | 0.774 | NS |
| BEFORE INDUCTION | 0.377 | NS |
| AFTER INTUBATION | 0.538 | NS |
| P0 | 0.953 | NS |
| P10 | 0.873 | NS |
| P20 | 0.812 | NS |
| P30 | 0.573 | NS |
| AFTER RELEASE OF CO2 | 0.377 | NS |
| AFTER EXTUBATION | 0.767 | NS |

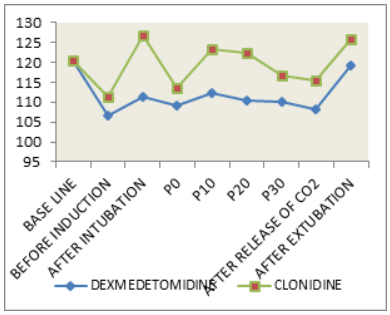



**Figure 2: Variations of Systolic Blood Pressure at different time periods**

There a significantly lower systolic blood pressure in the Dexmedetomidine group when compared to the clonidine group at all-time intervals except for the baseline.

**Table 3: P values of Systolic Blood Pressure at different time periods**

| | P-VALUE | Significance |
|---|---|---|
| BASELINE | 1.000 | NS |
| BEFORE INDUCTION | 0.024 | Sig |
| AFTER INTUBATION | 0.000 | Sig |
| P0 | 0.016 | Sig |
| P10 | 0.000 | Sig |
| P20 | 0.000 | Sig |
| P30 | 0.000 | Sig |
| AFTER RELEASE OF CO2 | 0.000 | Sig |
| AFTER EXTUBATION | 0.001 | Sig |

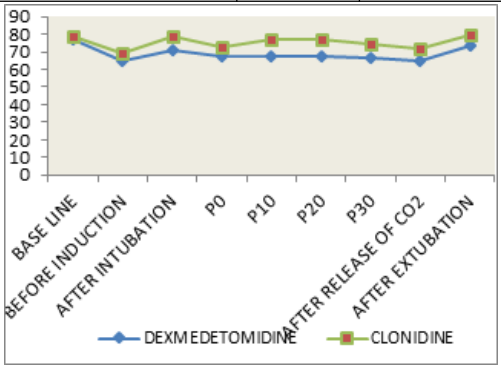


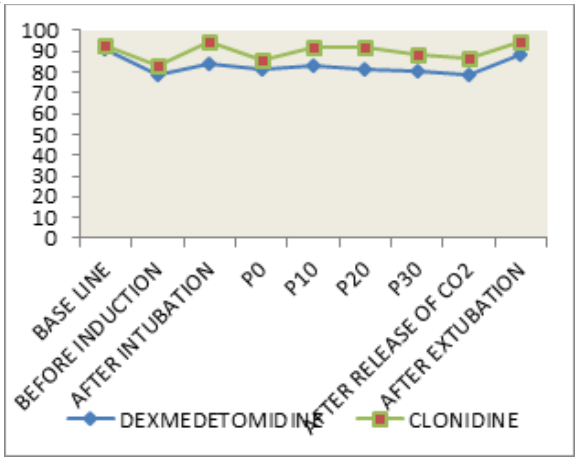

**Figure 3: Variations of Diastolic Blood Pressure at different time periods**

There is a significantly lower diastolic blood pressure in the Dexmedetomidine group when compared to the clonidine group at all-time intervals except for the baseline.

**Table 4: P values of Diastolic Blood Pressure at different time periods**

| | P-VALUE | Significance |
|---|---|---|
| BASELINE | 0.252 | NS |
| BEFORE INDUCTION | 0.002 | Sig |
| AFTER INTUBATION | 0.000 | Sig |
| P0 | 0.003 | Sig |
| P10 | 0.000 | Sig |
| P20 | 0.000 | Sig |
| P30 | 0.000 | Sig |
| AFTER RELEASE OF CO2 | 0.000 | Sig |
| AFTER EXTUBATION | 0.000 | Sig |

**Table 4: Variations of Mean Arterial Pressure at different time periods**




There is a significantly lower Mean Arterial Pressure in the Dexme detomidine group when compared to the clonidine group at all-time intervals except for the baseline.

There were no episodes of transient hypertension throughout perioperative and postoperative periods in both groups. Dexme detomidine group has less hypotension than the clonidine group.

**Table 5: Variations of Mean Arterial Pressure at different time periods**

| | P-VALUE | Significance |
|---|---|---|
| BASELINE | 0.372 | NS |
| BEFORE INDUCTION | 0.002 | Sig |
| AFTER INTUBATION | 0.000 | Sig |
| P0 | 0.001 | Sig |
| P10 | 0.000 | Sig |
| P20 | 0.000 | Sig |
| P30 | 0.000 | Sig |
| AFTER RELEASE OF CO2 | 0.000 | Sig |
| AFTER EXTUBATION | 0.000 | Sig |

Regarding variations of SpO2 at different time periods, there is no statistically significant difference has been observed in the two groups. There was no change in saturation in both the study and control groups during the drug infusion period. It was 94-97% in room air in both groups. In the post-op period both the groups received 5-6 liters/min oxygen and the saturation recorded include 99- 100% in both the groups. There was no incidence of desaturation in post-op, noted in either of the groups.

## DISCUSSION

The alpha2 agonists like clonidine, dexmedetomidine are assuming greater importance as anaesthetic adjuvant and analgesics (10). Mrinmoy Das et al, Chun-sung sung et al, Yu Hb et al, M Laisalmi et al used intravenous clonidine in laparoscopic cholecystectomy and they observed that clonidine significantly reduced MAP, HR & increase in SVR. They have opined that clonidine before pneumoperitoneum reduces catecholamines release and attenuates hemodynamic changes during laparoscopic cholecystectomy. Reena et al observed that dexamethasone is a good alternative than clonidine with more stable hemodynamics, better face mask acceptance; increased time for two-segment regression of sensory block, prolonged duration of analgesia when compared to clonidine(11). They also added that intravenous dexmedetomidine is an effective premedication drug than clonidine for children undergoing urogenital surgeries under spinal anesthesia. The results of our study are in agreement with above study and also studies of Jean L Joris et al, M Laisalmi et al, Malek et al, Mrinmoy Das et al.(10);(12);(13);(14) Velayudha Sidda Reddy et al in their study concluded that Premedication with intravenous dexmedetomidine is better than intravenous clonidine to provide intraoperative sedation and postoperative analgesia during bupivacaine spinal anesthesia(9). A single dose of intravenous dexmedetomidine resulted in an early onset action of bupivacaine, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the postoperative period, and stable cardiovascular parameters thereby making dexmedetomidine an effective adjuvant than clonidine for bupivacaine spinal anesthesia. Sukhminder Jit Singh Bajwa et al observed that dexmedetomidine is a better neuraxial adjuvant when compared to clonidine for providing early onset of sensory analgesia, adequate sedation, and prolonged postoperative analgesia(15). The present study is in similar lines with the above-mentioned studies.

### Limitations:

1. Patients belonged to ASA 1 and 2 criteria only.
2. Most patients were in the middle age group.
3. Patients with co-morbidities like hypertension and diabetes were all well controlled before surgery. Hence the advantage of using clonidine in hypertensive with inadequate control could not be appreciated.

## CONCLUSION:

The Dexmedetomidine group showed visible superiority over the Clonidine group in attenuating the hemodynamic changes during laparoscopic cholecystectomy under general anesthesia with minimal adverse effects.

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