



## A COMPARATIVE CLINICAL STUDY ON THE EFFECTS OF DEXMEDETOMIDINE AND NALBUPHINE ON HEMODYNAMICS OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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### ABSTRACT

**INTRODUCTION :** Owing to the hemodynamic response to tracheal intubation and pneumoperitoneum, laparoscopic surgery is not devoid of risks, many drugs have been used to blunt the pressor response to achieve a stable hemodynamics.

**AIMS AND OBJECTIVES :** This prospective, randomized study was designed to compare the effects of dexmedetomidine and nalbuphine on orotracheal intubation, hemodynamic responses and postoperative respiratory depression during laparoscopic cholecystectomy. Any other adverse effect of both the drugs was also studied.

**MATERIAL AND METHODS :** A total of 100 patients of 18-60 years, ASA grade I/II of either sex for elective laparoscopic cholecystectomy under general anaesthesia were included. The patients were randomly divided into two groups of 50 patients each. Group I received IV dexmedetomidine 1.0 ug/kg and Group II received IV nalbuphine 0.2 mg/kg over 10 mins diluted in 20ml normal saline. Hemodynamic parameters were recorded.

**RESULTS :** Control of HR, MAP in Group I was better than in Group II during laryngoscopy, intubation and PNP. Respiratory depression was not seen in either group. No patients had marked hypotension (MAP < 60 mmHg) or bradycardia (HR < 45 / min) in both groups but there were significant decrease in HR and MAP between the two groups during induction and after giving test drug.

**CONCLUSION :** The present study demonstrates the benefits of dexmedetomidine over nalbuphine in hemodynamic stability and analgesic quality in laparoscopic cholecystectomy. Thus establishing its utility for attenuation of pressor response.

**KEYWORDS :** dexmedetomidine, nalbuphine, hemodynamics, pneumoperitoneum, intubation

### INTRODUCTION

Laparoscopic surgeries form an essence of today's surgical practice because of its magnification, dexterity, less and cosmetic scar, less postoperative pain, and decreased hospital stay along with less morbidity and mortality.<sup>1,2</sup>

Laparoscopic surgeries are performed under General Anaesthesia with orotracheal intubation. Both tracheal intubation and insufflation of gas for creation of pneumoperitoneum in laparoscopic cholecystectomy cause profound hemodynamic instability.

Anesthetic maneuvers such as induction, laryngoscopy, tracheal intubation, and extubation involve sympathetic stimulation and autonomic reflex activity during general anesthesia.<sup>3,4</sup> In laparoscopic cholecystectomy, initial Trendelenburg position, creation of pneumoperitoneum (PNP), systemic absorption of CO<sub>2</sub>, and reverse Trendelenburg position cause pathophysiological changes in various systems of the body leading to increase in plasma level of nor-epinephrine, epinephrine, and plasma renin activity.<sup>5</sup>

Dexmedetomidine, an imidazole compound, displays specific and selective α<sub>2</sub> adrenergic receptor agonism.<sup>6</sup> In the past, xylazine and detomidine have been employed to induce analgesia and sedation in animals.<sup>7</sup> The analgesic, sedative, and sympatholytic properties of Dexmedetomidine renders it suitable for perioperative period.

Nalbuphine is an opioid with analgesic potency equal to morphine and its antagonistic potency is approximately 1/4th that of

naloxone. Its cardiovascular stability, longer duration of analgesia, no respiratory depression, less nausea and vomiting and potential safety in overdose makes it an ideal analgesic for use in balanced anaesthesia.<sup>8-11</sup>

Accordingly, this prospective, randomized study was designed to compare the efficacy of two drugs Dexmedetomidine and Nalbuphine representing two different groups in reducing the sympatho-adrenal stimulation during orotracheal intubation and pneumoperitoneum formation and throughout laparoscopic cholecystectomy. We are also studying the side effects that these drugs may have when used as premedication in laparoscopic cholecystectomy.

### MATERIAL AND METHODS

After approval from institutional ethical committee and getting informed written consent from the patients, this prospective randomized study was conducted on 100 healthy adult patients of ASA status I and II, of either sex, aged 18-60 and weight 40-80 kg, scheduled for elective laparoscopic cholecystectomy under general anaesthesia.

Patients with hypertension, morbid obesity, severe hepatic, renal, cardiac and endocrine dysfunction were excluded from the study.

The study was carried out in Surgery Operation Theatre (SOT) of Rajendra Institute of Medical Sciences, Ranchi. All the patients participating in the study were explained about the aims, objectives of the study in their language. Randomization in group allotment

was done by chit method.

**GROUP-A** - Dexmedetomidine (1 ug/kg body weight) IV given 10 minutes before induction after dilution in 20 ml normal saline.

**GROUP -B** - Nalbuphine(0.2mg/kg) IV given 10 minutes before induction after dilution in 20 ml normal saline.

All patients underwent systemic examination in pre anaesthetic check up one day prior to the day of operation.

The patients were kept nil orally overnight . On the day of surgery the patients were shifted after proper identification on a tilting table with an intravenous line with 18 gauge IV canula. Multipara monitor attached.In the operating room baseline parameters like pulse rate, SpO2 and blood pressure were recorded.

Preoxygenation for 3 min with 100% oxygen flow rate of 10 mL/min. Anaesthesia was induced with IV propofol 2 mg/kg and after performing check for ventilation ,after loss of eyelash reflex IV succinylcholine (1mg/kg) was given to facilitate direct laryngoscopy and intubation .

Anaesthesia was maintained with 40% oxygen ,60% nitrous oxide , 1% isoflurane and IPPV. Muscle relaxant used was vecuronium(0.08mg/kg) IV bolus with controlled ventilation in anaesthesia workstation.

After the completion of surgery adequate recovery from neuromuscular block was indicated by TOF more than 90% and patient was reversed with IV neostigmine (.05mg/kg) and glycopyrrolate (.04mg/mg of neostigmine). Proper suctioning was done and patients were extubated after adequate spontaneous respiration was observed.

Oxygenation was continued with 100% oxygen after extubation by face mask for 5-10 minutes. Patients were shifted to recovery room only after adequate reversal was seen.

**STATISTICAL ANALYSIS**

The results obtained in the study presented in tabulated manner and analysed using Microsoft Excel and SPSS software for Windows.

**RESULTS**

DEMOGRAPHIC VARIABLES (TABLE 1) in terms of mean age ,mean body weight,gender along with ASA status were comparable in between groups although was statistically significant higher females to male ratio and ASA I patients in study population among each group.

**TABLE 1 Showing demographic data of the two groups**

|            | GROUP A      | GROUP B      |
|------------|--------------|--------------|
| AGE(Yrs)   | 40.94        | 39.58        |
| WEIGHT(Kg) | 54.78 ± 6.10 | 55.36 ± 8.40 |
| GENDER     |              |              |
| Male       | 10           | 9            |
| Female     | 40           | 41           |
| ASA grade  |              |              |
| I          | 45           | 46           |
| II         | 5            | 4            |

**CHANGES IN PULSE RATE IN GROUP A AND GROUP B**

Baseline HR was comparable in both groups (TABLE 2),which was 85.26±6.36 and 86.12 ±6.47 respectively in both the groups. After infusion of dexmedetomidine ,HR decreased to 72.22± 7.16, and increased slightly to 73.12±7.55 after induction. But it increased to 88.44± 8.40 after intubation. There was significant increase during PNP which returned to baseline from about 35 mins in PNP ,thereafter decreased below the baseline.

In Group II after start of infusion of nalbuphine, HR decreased to 77.92±7.51. there was further decrease after induction to 77.90 ±10.92 and increase after intubation to 93.04±11.98. after PNP , HR remained above baseline till 40 mins, then it was near the baseline.

**TABLE-2.** Showing changes in pulse rate in GROUP A and GROUP B and comparison between both groups has been shown in this table.

|                        | Group A<br>(n=50)<br>Mean ± SD |        | (n=50)<br>Mean ± SD |         | P<br>Value |
|------------------------|--------------------------------|--------|---------------------|---------|------------|
| Baseline               | 85.26                          | ± 6.36 | 86.12               | ± 6.47  | 0.50       |
| After drug             | 72.22                          | ± 7.16 | 77.92               | ± 7.51  | 0.002      |
| After indu.            | 73.12                          | ± 7.55 | 77.90               | ± 10.92 | 0.12       |
| After Intub.           | 88.44                          | ± 8.40 | 93.04               | ± 11.98 | 0.028      |
| After PNP<br>Formation |                                |        |                     |         |            |
| 5 Min                  | 89.8                           | ± 7.45 | 94.02               | ± 7.59  | 0.006      |
| 10 Min                 | 90.95                          | ± 5.10 | 95.38               | ± 7.57  | 0.006      |
| 15 Min                 | 91.9                           | ± 5.59 | 95.9                | ± 7.52  | 0.003      |
| 20 Min                 | 92.37                          | ± 5.55 | 94.16               | ± 8.5   | 0.20       |
| 25 Min                 | 90.82                          | ± 5.07 | 95.06               | ± 8.42  | 0.003      |
| 30 Min                 | 92.76                          | ± 7.65 | 97.25               | ± 4.58  | 0.0006     |
| 35 Min                 | 84.98                          | ± 5.19 | 87.97               | ± 3.67  | 0.001      |
| 40 Min                 | 82.78                          | ± 4.83 | 86.76               | ± 4.29  | 0.0001     |
| 45 Min                 | 77.63                          | ± 3.99 | 84.04               | ± 5.15  | 0.0001     |
| 50 Min                 | 73.85                          | ± 5.38 | 85.90               | ± 5.96  | 0.0001     |

**CHANGES IN MEAN BLOOD PRESSURE (mm Hg) IN GROUP A AND B**

**Table 3** SHOWS THE VARIATION OF MAP(IN mmHg) IN BOTH THE GROUPS.

Baseline MAP was 95.88 ±4.14 and 95.31±4.38 respectively in both the groups. After giving dexmedetomidine , MAP decreased to 87.63±4.60 which further decreased to 81.73±3.32 after induction. After intubation MAP increased to 100.28 ±3.07. values increased in PNP and started to come towards baseline after 25 mins of PNP. In Group II ,MAP decreased from baseline to 90.22±4.32 after nalbuphine infusion and further decreased to 84.32 ± 4.32 after induction but then increased to 102.69±5.21 after intubation. After PNP , the MAP remained higher than baseline throughout surgery but was close to it from 40 mins of PNP.

**TABLE 3,** showing changes in Mean Blood Pressure in GROUP A and GROUP B and the comparison between the two groups.

|                 | Group A<br>Mean ± SD<br>n = 50 |        | Group B<br>Mean ± SD<br>n = 50 |        | P<br>Value |
|-----------------|--------------------------------|--------|--------------------------------|--------|------------|
| Baseline        | 95.88                          | ± 4.14 | 95.31                          | ± 4.38 | 0.51       |
| After drug      | 87.63                          | ± 4.60 | 90.22                          | ± 4.32 | 0.0005     |
| After Induction | 81.73                          | ± 3.32 | 84.32                          | ± 4.32 | 0.001      |
| After Intub     | 100.28                         | ± 3.07 | 102.69                         | ± 5.21 | 0.003      |

|                     |        |        |        |        |        |
|---------------------|--------|--------|--------|--------|--------|
| After PNP Formation |        |        |        |        |        |
| 5 Min               | 111.32 | ± 2.76 | 114.02 | ± 5.11 | 0.001  |
| 10 Min              | 111.40 | ± 1.71 | 114.02 | ± 5.11 | 0.0002 |
| 15 Min              | 107.96 | ± 1.73 | 110.28 | ± 4.98 | 0.03   |
| 20 Min              | 103.52 | 1.94   | 108.18 | 5.33   | 0.0001 |
| 25 Min              | 98.02  | ± 2.08 | 98.88  | ± 2.62 | 0.07   |
| 30 Min              | 96.51  | ± 2.20 | 97.82  | ± 2.32 | 0.005  |
| 35 Min              | 95.56  | ± 1.94 | 97.70  | ± 1.96 | 0.04   |
| 40 Min              | 96.41  | ± 2.44 | 96.70  | ± 1.96 | 0.61   |
| 45 Min              | 94.22  | ± 2.46 | 95.65  | ± 2.65 | 0.038  |
| 50 Min              | 93.70  | ± 2.47 | 96.02  | ± 3.07 | 0.0003 |

**R/R POST OP IN GROUP A AND GROUP B**

**TABLE 4,** showing postoperative respiratory rate for comparison of respiratory depression between patients of GROUP A and GROUP B

| Timing | Group A<br>Mean ± SD<br>n =50 |        | Group B<br>Mean ± SD<br>n =50 |        | P Value |
|--------|-------------------------------|--------|-------------------------------|--------|---------|
| 15 Min | 15.23                         | ± 0.63 | 15.21                         | ± 0.66 | 0.95    |
| 30 Min | 14.44                         | ± 0.82 | 14.66                         | ± 0.59 | 0.96    |
| 1 Hour | 13.4                          | ± 0.65 | 13.54                         | ± 0.71 | 0.94    |
| 2 Hour | 12.2                          | ± 0.38 | 12.14                         | ± 0.45 | 0.92    |

**SPO2 POST OP IN GROUP A AND GROUP B**

**TABLE 5,** showing changes in oxygen saturation post operatively in patients of GROUP A and GROUP B for comparison of respiratory depression.

| Timing | Group A<br>Mean ± SD<br>n = 50 |        | Group B<br>Mean ± SD<br>n = 50 |        | P Value |
|--------|--------------------------------|--------|--------------------------------|--------|---------|
| 15 Min | 99.80                          | ± 0.40 | 99.72                          | ± 0.61 | 0.90    |
| 30 Min | 99.88                          | ± 0.43 | 99.86                          | ± 0.49 | 0.91    |
| 1 Hour | 99.84                          | ± 0.54 | 99.82                          | ± 0.59 | 0.93    |
| 2 Hour | 99.86                          | ± 0.49 | 99.82                          | ± 0.59 | 0.97    |

**DISCUSSION**

The recent study by Manne GR et al (2014)<sup>12</sup> compared the clinical effects of two different doses of dexmedetomidine : 1.0 ug/kg given slow intravenous in 10 mins and 0.4 ug/kg given in 5 mins on hemodynamic responses. He found that the dose of 1.0 ug/kg was more effective. The rise in HR and MAP after intubation and PNP formation was 6.75% and 10.34% respectively.

In our study similar result was found as 1.0 ug/kg dexmedetomidine slow intravenous was given and results showed that this dose was effective in blunting hemodynamic responses.

In present study dexmedetomidine 1ug/kg diluted in 20 ml of normal saline ,infused in 10 minutes intravenously before induction. The selection of dose was in accordance with studies done by Kataria et al(2014)<sup>13</sup> who compared efficacy of dexmedetomidine with fentanyl and had noticed similar decrease in HR(8.76%) after infusion of dexmedetomidine, rise of MAP and HR(11.46%) after intubation and formation of pneumoperitoneum was much less in Dexmedetomidine group as compared to group receiving opioid. Our study was similar to the study done by Kwange et al<sup>14</sup> and results were also comparable ,as in our study also the heart rates of dexmedetomidine group was significantly lower than the other

group. In their study of comparison between Dexmedetomidine and lidocaine in laparoscopic cholecystectomy observed that dexmedetomidine group had significantly lower heart rates as compared to lidocaine group.

Chawda et al<sup>15</sup> concluded that nalbuphine 0.2mg/kg prevented a marked rise in HR( increased by 5.67%) and mean arterial pressure(increased by 7.89%) in orotracheal intubation.

Our study had similar results which showed that use of nalbuphine when used as premedication prevented a marked rise in above parameters. The incidence of above side effects was also similar to the above study.

Wasong C et al<sup>16</sup> studied the effect of nalbuphine in laparoscopic cholecystectomy and found lesser sedation, lesser respiratory depression and PACU stay in patients. Similarly Tuffanogullari et al<sup>17</sup> studied the effects of dexmedetomidine and found that it causes analgesia, slight sedation and almost no respiratory depression. Our study can be compared to study done by Wasong C et al<sup>16</sup> and study done by Tuffanogullari et al<sup>17</sup> since in our study also there was no incidence of respiratory depression.

Minai FN et al<sup>18</sup> who compared nalbuphine with placebo and noticed 20 % rise in MAP and HR in placebo. Our study results were similar to Minai FN et al<sup>18</sup> as in our study too the nalbuphine group was effective in controlling rise in MAP and HR(11.67% rise ) from the baseline similar to the above study .

**CONCLUSION**

From the above study it was concluded that dexmedetomidine is better than nalbuphine in maintaining a stable hemodynamics i.e mean blood pressure and heart rate were controlled better with dexmedetomidine while tracheal intubation and during surgery with pneumoperitoneum.

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