# To Evaluate the Effectiveness of Intravenous Dexmedetomidine Infusion During Laproscopic Cholecystectomy. A Prospective Randomised Placebo Control Study

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## ABSTRACT

**Introduction:** Laparoscopic cholecystectomy is one of the commonest surgery performed under general anesthesia in our set up but maintaining the hemodynamic stability is challenging in these patients .Due to its well-known advantages like less post-operative pain, shorter hospitalization and faster functional recovery, laparoscopic cholecystectomy is also termed as patient friendly surgery. The Dexmedetomidine is a relatively new potent and highly selective α2-adrenoceptor agonist that has been used to provide sympatholysis, analgesia and sedation in the perioperative period. The present prospective, randomized study was designed to analyse the effect of IV dexmedetomedine on intraoperative hemodynamics, and the incidence of side effects in patients scheduled for laparoscopic cholecystectomy.

**Material and methods:** After obtaining approval from Hospital Ethics Committee, Study was conducted on 80 adult patients aged 18-60 years, of ASA grade I or II of either sex, scheduled for laparoscopic cholecystectomy under general anesthesia. Patients were randomized into two groups of 40 patients each. Patients of Group D received dexmedetomedine infusion (loading: 0.7µg/kg and maintenance: 0.4µg/kg/hr) and Group C (control group) received normal saline infusion with the same rate as group D. Patients were monitored for changes in heart rate, ECG, systemic blood pressure and $EtCO_2$, at baseline, at 5 min and 10 min after giving study drug bolus, after induction, intubation, skin incision and $CO_2$ insufflation. Thereafter, these changes were recorded at 15 min intervals till the end of surgery

**Results:** It was found that dexmedetomidine significantly reduces heart rate, systolic, diastolic and mean arterial blood pressure .It was observed that perioperative use of dexmedetomidine infusion maintained better hemodynamic stability as compared to the normal saline in control group and has sparing effect on other anaesthetic drug mainly on proppfol and fentanyl.

**Conclusion:** Dexmedetomidine infusion was a better option for maintaining hemodynamic stability during laparoscopic surgeries. Dexmedetomidine effectively attenuates haemodynamic stress response during laparoscopic cholecystectomy with reduction in requirement of concomitantly-administered anaesthesia maintaining drugs.


**Keywords:** Dexmedetomidine, Haemodynamic Stress Response, Laparoscopic Cholecystectomy

## INTRODUCTION

In the current era, laparoscopic cholecystectomy is considered the gold standard of treatment for symptomatic cholelithiasis, given the benefits of better postoperative pain profiles, lesser surgical wound complications and reduced hospital stay.[1] Laparoscopic surgeries have a number of advantages including reduced blood loss, smaller incision, reduced pain, shortened recovery time and reduced exposure of internal organs to possible external contaminants thereby reduced risk of acquiring infections but these are not completely devoid of disadvantages. Increase in intra-abdominal pressure and volume (pneumoperitoneum), extremes of patient positioning (reverse trendelenberg) and accumulation of carbon dioxide have profound effect on patient's hemodynamic, respiratory and metabolic functions.[2,3] To avoid these disadvantages, we added adjuvant viz dexmedetomedine in the perioperative period and observed its effects on intraoperative Hemodynamics. In December 1999, dexmedetomidine, a highly selective α2 agonist similar to clonidine but with a higher affinity for the α2 receptor, was approved for introduction into clinical practice as a short-term sedative (<24 hours).[4] α2 adrenergic agonists decrease sympathetic tone, attenuate neuroendocrine and hemodynamic responses to anaesthesia and surgery, reduce anaesthetic and opioid requirements and cause sedation and analgesia while allowing preservation of psychomotor function as the patient rests comfortably.[4]

The present prospective, randomized study was designed to evaluate the effect of intraoperative IV dexmedetomedine on intraoperative hemodynamics, and the incidence of side effects in patients scheduled for laparoscopic cholecystectomy.

## MATERIAL AND METHODS

After getting approval from Ethical Committee, the study was conducted on 80 patients belonging to ASA GRADE I and II patients aged 18-60 years of either sex, being admitted for laparoscopic cholecystectomy to be done under general

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anesthesia. An informed consent was taken from all the patients.

**Exclusion criteria**

1. A.S.A Grade III, IV and V
2. Patient refusal
3. Liver and renal dysfunction
4. Patient with cardiac dysarrhythmias
5. Patient with sinus bradycardia and on alpha blocker and calcium channel blockers.
7. Allergy to the drug under study

Patients were randomly selected into two groups of 40 each, according to computer generated random number table.

- Group D (dexmedetomedine group): Patients received dexmedetomedine infusion (loading: 0.7µg/kg and maintenance: 0.4µg/kg/hr)
- Group C (control group): Patients received normal saline infusion.

According to respective groups, infusions were started 10 minutes before induction of anaesthesia. After preoxygenation of 5 minutes patient induced with inj. fentanyl 2micrograms/kg and propofol 2mg/kg and the dose of propofol was recorded. Muscle relaxant vecuronium in dose of 0.1mg/kg was given and orotracheal intubation was performed after ventilating the patient and further set of recordings were done. Anaesthesia was maintained with 50% oxygen and 50% nitrous oxide, isoflurane at 1% volume.

During the intraoperative period both groups received IV fluids (R.L) @ 5ml/kg/hr Muscle relaxation was achieved with an infusion of vecuronium @ 1mics/kg/min

Patient were put on controlled mechanical ventilation to maintain $EtCO_2$ at 30 to 40mm Hg. In both groups, signs of inadequate anesthesia as increase in the arterial pressure greater than the targeted MAP or somatic responses as movement, tearing or sweating were treated with additional dose of fentanyl 1µg/kg .Propofol in bolus was given for heart rate above 100/min and MAP above 80mm Hg.

Patients were intra operatively monitored for heart rate, ECG, systolic blood pressure, diastolic blood pressure, peripheral oxygen saturation and $EtCO_2$. At 0, 5 mins, 10 mins, induction, intubation, skin incision, $CO_2$ insufflation, 5 mins after insufflation, 10 mins after insufflation and thereafter at every 15 mins till the end of surgery. Total dose of propofol and fentanyl used in surgery was noted.

At the start of surgical wound closure, the study drug infusion was stopped and the neuromuscular block was antagonized with neostigmine (0.05mg/kg) and glycopyrrolate (5 microgram/Kg). Patients were extubated and sent to PACU for further monitoring of vital parameter.

## STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences, IBM, 20.0 version.). Data was analysed for normality of distribution using Shapiro-Wilk test, p value < 0.05 indicated that data was not normally distributed, thus non parametric test of significance were applied. The comparison between the groups was done using Man whitney U test. p value < 0.05 was considered statistically significant .

## RESULT

In this prospective and randomized comparative study, 80

| | Group D (n=40) | | Control group (n=40) | | P value |
|---|---|---|---|---|---|
| | Mean | Standard deviation | Mean | Standard deviation | |
| Age (in years) | 38.5400 | 13.35269 | 39.9800 | 10.40141 | 0.067 |
| Weight (in kgs) | 63.4800 | 7.98274 | 65.1000 | 7.18914 | 0.084 |

**Table-1:** Description of mean age and weight of patients in the two groups.

| | | Group D (n=40) | Group C (n=40) |
|---|---|---|---|
| Gender | Male | 19 | 23 |
| | Female | 21 | 17 |
| P value – 0.274 | | | |

**Table-2:** Frequency distribution male and female patients in group D and group C

| | | Group D, (n=40) | | Group C, (n=40) | | P value |
|---|---|---|---|---|---|---|
| | | Mean | Standard deviation | Mean | Standard deviation | |
| Blood pressure in mm Hg | Baseline | 89.18 | 5.612 | 90.42 | 5.280 | 0.260 |
| | At induction | 78.64 | 4.452 | 85.30 | 4.747 | 0.000* |
| | After intubation | 80.02 | 3.126 | 87.44 | 3.939 | 0.000* |
| | At skin incision | 75.34 | 2.528 | 80.40 | 2.945 | 0.000* |
| | 5 minutes after pneumoperitoneum | 70 .96 | 2.166 | 76.10 | 2.533 | 0.000* |
| | 15 minutes after pneumoperitoneum | 68.1600 | 1.972 | 74.04 | 2.203 | 0.000* |
| | 30 minutes after pneumoperitoneum | 65.38 | 1.724 | 72.98 | 2.394 | 0.000* |
| | 45 minutes after pneumoperitoneum | 74.22 | 2.131 | 78.14 | 1.873 | 0.000* |
| | 60 minutes after pneumoperitoneum | 73.31 | 2.241 | 78.22 | 1.986 | 0.000 |
| | After deflation | 73.12 | 1.876 | 77.67 | 2.302 | 0.000 |

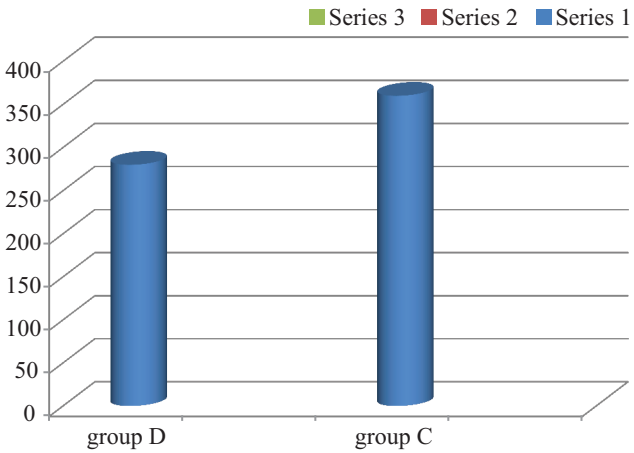
**Table-3:** Intra operative comparison of mean blood pressure (MBP)of patients in group D and group C at different points of time.

| | | Group D (n=40) | | Group C (n=40) | | P value |
|---|---|---|---|---|---|---|
| | | Mean | Standard deviation | Mean | Standard deviation | |
| Heart rate | Baseline | 88.18 | 5.612 | 89.42 | 5.280 | 0.260 |
| | At induction | 80.64 | 4.452 | 84.30 | 4.747 | 0.000* |
| | After intubation | 82.02 | 3.126 | 86.44 | 3.939 | 0.000* |
| | At skin incision | 74.34 | 2.528 | 78.40 | 2.835 | 0.000* |
| | 5 minutes after pneumoperitoneum | 70.96 | 2.166 | 76.10 | 2.533 | 0.000* |
| | 15 minutes after pneumoperitoneum | 68.1600 | 1.972 | 74.04 | 2.203 | 0.000* |
| | 30 minutes after pneumoperitoneum | 65.38 | 1.724 | 72.98 | 2.394 | 0.000* |
| | 45 minutes after pneumoperitoneum | 74.22 | 2.131 | 78.14 | 1.873 | 0.000* |
| | 60 minutes after pneumoperitoneum | 73.33 | 2.040 | 78.10 | 2.735 | 0.000 |
| | After deflation | 73.45 | 1.982 | 77.34 | 1.897 | 0.000 |

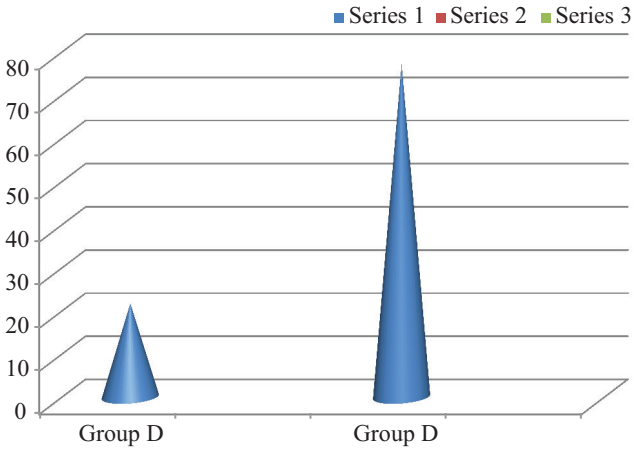
**Table-4:** Intra operative comparison of Mean Heart Rate of patients in group D and group cat different points of time

| Analgesic Requirement | Group D | Group C | P value |
|---|---|---|---|
| Propofol requirement (in total surgery) | 280 ± 25.43 | 360 ± 36.72 | 0.000* |
| Additional analgesic requirement (fentanyl in mics) | 21.67 ± 22.75 | 77.17 ± 27.87 | 0.000* |

**Table-5:** Comparison of total propofol requirement, additional analgesic requirement in both the groups




**Graph-1:** Comparison of total propofol requirement(in mg) in both the groups.




**Graph-2:** Comparison of additional analgesic requirement (inj fentanyl in mics) in both the groups.

patients of age group18 – 60 yrs of both sex of ASA grade I and II were included (table-1).

All patients were comparable in regards to their demographic profile. All patients were comparable in two groups according to age wise distribution, sex wise distribution and ASA grading.

The baseline mean blood pressure (p value =0.260) and heart rate was not significantly different between the groups but at induction, at intubation, during pneumoperitoneum they were significantly lower in group D than in control group (p value - <0.05) (table-2,3).

So there was statistically significant difference in Mean blood pressure between the two groups (p value < 0.05). The total mean dose of propofol required in Group D was 280 ± 25.43 mg versus in Group C 360.67 ±36.72 mg (Figure 1). This was statistically significant (p<0.05).

## DISCUSSION

Various physiological methods and pharmacological agents have been used for controlling haemodynamics in laparoscopic surgery with varying success. Dexmedetomidine, a relatively new α2 agonist, provides dose dependent sedation, analgesia, sympatholysis, anxiolysis and controlled hypotension without relevant respiratory depression

In this prospective and randomized comparative study, 80 patients of age group18 – 60yrs of both sex of ASA grade I and II were included.

All patients were comparable in regards to their demographic profile. All patients were comparable in two groups according to age wise distribution, sex wise distribution and ASA grading. (Table 1,2)

In our study, the primary objective was to assess the effect of perioperatively administered IV Dexmedetomidine in attenuating stress respose in laproscopic cholecystectomy. Results in the study showed that patients in group D had reduced mean arterial blood pressure and heart rate in comparision to control group with no episodes of severe hypotension

It was observed that perioperative use of dexmedetomidine maintained better hemodynamic stability as compared to the control group during laparoscopic cholecystectomy

Srivastava VK, et al in their study emphasized the use of dexmedetomidine and esmolol for attenuation of hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy and concluded that Dexmedetomidine is more effective than esmolol in preventing such hemodynamic responses in laparoscopic surgery.[5] Their results are similar to results of our study. Inaddition dexmedetomidine also reduce the induction dose of propofol and intraoperative fentanyl requirement for analgesia.

Bhattachargee et al, conducted a study to evaluate the efficacy of dexmedetomidine to provide perioperative haemodynamic stability in patients undergoing laparoscopic cholecystectomy. Their results showed that dexmedetomedine do maintain hemodynamic stability during the intraoperative period of laparoscopic cholecystectomy.[6] Ghodki et al, conducted an observational study using dexmedetomedine as an anaesthetic adjuvant in laparoscopic surgeries. They monitored the depth of anesthesia (DOA) using entropy to avoid unwanted awareness under anesthesia. They concluded that dexmedetomidine is an effective anesthetic adjuvant that can be safely used in laparoscopy without the fear of awareness under anesthesia.[7]

The total mean dose of propofol in Group D was 280 ± 25.43 mg versus in Group C was 360.67 ±32.72 mg (Figure 1,2). This was statistically significant ($p<0.05$). The mean average dosage of propofol required was 4.10 ± 0.19 mg kg-1 hr-1 in Group D, while it was 5.40 ± 0.24 mg kg-1hr-1 in Group C. This was statistically significant ($p<0.05$) (table 4,5). Thus dexmedetomidine reduced the requirement of propofol. This observation is supported by Poonam Ghodki, Shalini Thombre, Shalini Sardesai, Kalpana Harnagle who studied effects of dexmedetomidine as an adjuvant in laparoscopic surgery using entropy monitoring. They also found a reduction in propofol dose in dexmedetomidine group.[8]

## CONCLUSION

So from the above observation and results it may be concluded that:

Dexmedetomidine infusion resulted in a steady and smooth reduction in mean blood pressure and reduced heart rate, with no episodes of severe hypotension. Dexmedetomidine successfully maintained hemodynamic stability, with reduced requirements of propofol and fentanyl but without dexmedetomidine infusion higher doses of propofol and fentanyl were required to maintain hemodynamic stability.

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