



A RANDOMISED CONTROL STUDY OF DEXMEDETOMIDINE VERSUS FENTANYL AS AN ANAESTHETIC ADJUVANT TO GENERAL ANAESTHESIA IN LAPAROSCOPIC SURGERIES

Anesthesiology

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ABSTRACT

Aim: To compare the effect of Dexmedetomidine and Fentanyl in relation to blunting of sympathetic response to intubation and induction while secondary variables are to study their effect on perioperative hemodynamic changes, operative conditions, recovery profile and side effects.

Methods: This study was conducted on 100 patients, divided into two groups (Group D and Group F) {50 Patients in each group} of either sex between 18 to 60 years of age, belonging to ASA physical status I – II, undergoing elective laparoscopic surgeries. Patients were randomised by using sealed envelope method. Group D : Patients received 1 µg/kg of Dexmedetomidine intravenous infusion as loading dose over 10 min before induction and 0.04-0.05 µg/kg/min of Dexmedetomidine as maintenance during surgery. Group F : Patients received 2 µg/kg of Fentanyl before induction and maintained with 0.02-0.03 µg/kg/min of Fentanyl intravenous infusion during surgery. In operating room parameters like Heart Rate (HR), Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP), SpO₂, EtCO₂ were recorded before and 10 minutes after infusion of drug i.e., dexmedetomidine or fentanyl. The said parameters were recorded at different time interval.

Results: Dexmedetomidine significantly attenuates stress response at intubation with lesser increase in HR (4.2% Vs 27%) and MAP (4.2% Vs 17.4%) as compared to fentanyl (p<0.05). Throughout intraoperative period of pneumoperitoneum

Conclusion: The study showed that haemodynamic changes during the intubation and laparoscopic surgeries were better controlled by Dexmedetomidine in comparison to Fentanyl.

KEYWORDS

Anaesthetic Adjuvant, Dexmedetomidine, Fentanyl, Laparoscopic Surgeries

INTRODUCTION

Laparoscopic or “minimally invasive” surgery is a specialized technique for performing surgery. In the past, this technique was commonly used for gynecologic surgery and for gall bladder surgery. Over the last 10 years the use of this technique has expanded into various other surgical procedures. In traditional “open” surgery the surgeon uses a single incision to enter into the abdomen. Laparoscopic surgery uses several 0.5-1cm incisions. Each incision is called a “port.” At each port a tubular instrument known as a trocar is inserted. Specialized instruments and a special camera known as a laparoscope are passed through the trocars during the procedure. At the beginning of the procedure, the abdomen is inflated with carbon dioxide gas to provide a working and viewing space for the surgeon. The laparoscope transmits images from the abdominal cavity to high-resolution video monitors in the operating room. During the operation the surgeon watches detailed images of the abdomen on the monitor. This system allows the surgeon to perform the same operations as traditional surgery but with smaller incisions.

In certain situations a surgeon may choose to use a special type of port that is large enough to insert a hand. When a hand port is used the surgical technique is called “hand assisted” laparoscopy. The incision required for the hand port is larger than the other laparoscopic incisions, but is usually smaller than the incision required for traditional surgery and Compared to traditional open surgery, patients often experience less pain, a shorter recovery period, and less scarring with laparoscopic surgery. Most intestinal surgeries can be performed using the laparoscopic technique. These include surgery for Crohn's disease, ulcerative colitis, diverticulitis, cancer, rectal prolapse and severe constipation.

Laparoscopic surgery is as safe as traditional open surgery. At the beginning of a laparoscopic operation the laparoscope is inserted through a small incision near the belly button (umbilicus). The surgeon initially inspects the abdomen to determine whether laparoscopic surgery may be safely performed. If there is a large amount of inflammation or if the surgeon encounters other factors that prevent a clear view of the structures, the surgeon may need to make a larger

incision in order to complete the operation safely.^[1]

Dexmedetomidine provides stable perioperative hemodynamic profile with decreased requirement of opioids. It may be suitable anaesthetic adjuvant when compared to Fentanyl.^[2] Dexmedetomidine is a highly selective α_2 agonist with properties of sedation, analgesia and anxiolysis, making it an ideal anaesthetic adjuvant.

Dexmedetomidine has recently been added to the anaesthesia armamentarium. It belongs to the class of α_2 agonists and possesses the properties of sedation, analgesia and opioid sparing effect. It differs from clonidine in being 1620 times more specific for α_2 receptors.^[3] Laparoscopic surgeries under general anaesthesia are associated with hemodynamic changes in the form of increased systemic vascular resistance which leads to hypertension, forcing the anaesthesiologist to increase the depth of anaesthesia (DOA), and at times even requires the use of vasodilators to control the rising blood pressure.^[4] Dexmedetomidine due to its distinct properties can be used as an anaesthetic adjuvant in the form of intravenous infusion.^[5] We studied the use of Dexmedetomidine in laparoscopic surgeries and evaluated its effects on hemodynamics, analgesic requirement and post op recovery.

Fentanyl is an opioid used as a pain medication and together with other medications for anaesthesia.^[6] Fentanyl is also made illegally and used as a recreational drug, often mixed with heroin or cocaine.^[7] It has a rapid onset and effects generally last less than an hour or two hours. Medically, Fentanyl is used by injection, as a patch on the skin, as a nasal spray, or in the mouth (as a oral lozenge). Common side effects include vomiting, constipation, sedation, confusion, hallucinations and injuries related to poor coordination. Serious side effects may include decreased breathing (respiratory depression), serotonin syndrome, low blood pressure, addiction, or coma. In 2016, more than 20,000 deaths occurred in the United States due to overdoses of Fentanyl and Fentanyl analogues, half of all reported opioid related deaths.^[8,9] Fentanyl works primarily by activating μ -opioid receptors. It is around 100 times stronger than morphine, and some analogues such as carfentanil are around 10,000 times stronger.^[10]

Fentanyl was first made by Paul Janssen in 1960 and approved for medical use in the United States in 1968.^[11] As of 2017, Fentanyl was the most widely used synthetic opioid in medicine.^[12] Fentanyl patches are on the WHO List of Essential Medicines, the most effective and safe medicines needed in a health system.^[13]

MATERIAL AND METHODS

After approval from The Ethical Committee of the institution, This Randomized control study was conducted at Swaroop Rani Nehru Hospital (associated to Moti Lal Nehru medical college, Prayagraj (Allahabad)) over a period of one year. This prospective study was conducted on 100 adult patients of either sex between 18 to 60 years of age, belonging to ASA physical status I – II, undergoing laparoscopic cholecystectomy.

Anaesthesia Protocol

In the preoperative room, I/V access was secured with a 20G cannula and infusion of Ringer's lactate was started. Inj Midazolam 30mcg/kg, inj Ranitidine 1mg/kg, inj Ondansetron 0.1mg/kg and inj Glycopyrrolate 0.2 mg was given intravenously (IV) half-an-hour prior to induction of anesthesia.

The study drugs were then prepared as follows.

About 2 ml (200 µg) of study drug Dexmedetomidine was diluted in 48ml of normal saline to make 50 ml (concentration 4 µg/ml.). About 4 ml (200 µg) of study drug Fentanyl was diluted in 46 ml normal saline to make 50 ml (conc. 4 µg/ml.)

After shifting to operation theatre, standard monitoring [i.e., electrocardiogram with two derivations, pulse oximetry (SpO₂), non-invasive arterial blood pressure measurement, End tidal CO₂ (EtCO₂), body temperature] was employed and baseline parameters recorded. This monitoring was continued till reversal and extubation. The prepared drug Dexmedetomidine or Fentanyl was given as follows:

Group D: Patients who were receive 1 µg/kg of Dexmedetomidine as loading dose within 10 min before induction and 0.04-0.05 µg/kg/min of Dexmedetomidine as maintenance during surgery.

Group F: Patients who were receive 2 µg/kg of Fentanyl before induction and maintained with 0.02-0.03 µg/kg/min of Fentanyl during surgery.

The patient was pre-oxygenated with 100% oxygen for three minutes. Anaesthesia was induced with Inj Propofol 2 mg/kg I.V. and Neuromuscular blockade was achieved with inj Atracurium 0.5 mg/kg I.V.

The patient was ventilated for three minutes with 100% O₂ and Isoflurane 0.8%. This was followed by laryngoscopy and tracheal intubation. Once tube position was confirmed, positive pressure ventilation was started with tidal volume 6-8 ml/kg and respiratory rate 12-14/minute with Drager Mix Fabius Plus Anaesthesia Workstation. The same parameters along with EtCO₂ were again recorded immediately after tracheal intubation and five minutes after tracheal intubation.

Depending upon the vital parameters, pulse and BP, maintenance infusion rate of Dexmedetomidine or Fentanyl was increased/decreased in a stepwise manner from 0.2-0.7 µg/kg/hour till the end of surgery.

Closed circuit breathing system with soda lime was used. Anaesthesia was maintained with Isoflurane 0.8%-1.0% and O₂, Nitrous oxide (40:60) along with Atracurium 0.1-0.2 mg/kg @ 10-20 min. for maintenance of blockade and along with infusion of Dexmedetomidine @ 0.04-0.05 µg/kg/min and Fentanyl @ 0.02-0.03 µg/kg/min in separate group, as needed to maintain mean arterial pressure between 65 and 85 mmHg. Ventilation was adjusted to maintain EtCO₂ between 30 and 35 mm Hg. Intraoperative sedation was augmented as and when required with Inj. propofol IV.

Parameters like ECG, HR, SBP, DBP, MAP, SpO₂, and EtCO₂ were continuously recorded at predetermined time intervals as follows: T⁰ (prior to infusion of study drug), T¹ (10 minutes after the study drug), T² (after Inj. of induction drug), T³ (After intubation), T⁴ (five minutes after intubation), T⁵ (after pneumoperitoneum), T⁶ (five minutes after

pneumoperitoneum), T⁷ (10 minutes after pneumoperitoneum), T⁸ (15 minutes after pneumoperitoneum), T⁹ (30 minutes after pneumoperitoneum), T¹⁰ (45 minutes after pneumoperitoneum), T¹¹ (60 minutes after pneumoperitoneum), T¹² (five minutes after release of pneumoperitoneum).

Adverse effects like bradycardia, tachycardia, hypotension, hypertension, if any, noted during operative procedure, were treated as follows:

Bradycardia - (HR < 55/min): Inj. Atropine 0.6 mg I.V

Tachycardia - (HR > 30% above baseline value): Inj. Propofol 20 mg I.V in titrated dose

Hypotension - (SBP < 60 mmHg): Inj. Ephedrine 6 mg I.V in titrated dose

Hypertension - (SBP > 140 mmHg): Deep plane of Anaesthesia with Inj. Propofol 20 mg I.V in titrated dose and increasing concentration of Isoflurane up to 1.2%.

Following this, inj. Ondansetron 4 mg I.V were given 15 min. before extubation for post operative nausea, vomiting.

At completion of surgery port site was infiltrated with 0.5% Bupivacaine 2-3 ml per port for postoperative analgesia. Fluid deficit, maintenance and loss were replaced with an infusion of lactated Ringer solution.

Infusion of drug (Dexmedetomidine or Fentanyl) was stopped and Isoflurane was discontinued 10 minutes before reversal. Residual paralysis was reversed with Inj. Neostigmine 0.05 mg/kg IV, and Inj. Glycopyrrolate 8 µg/kg IV. Patient was then extubated after thorough oral suction.

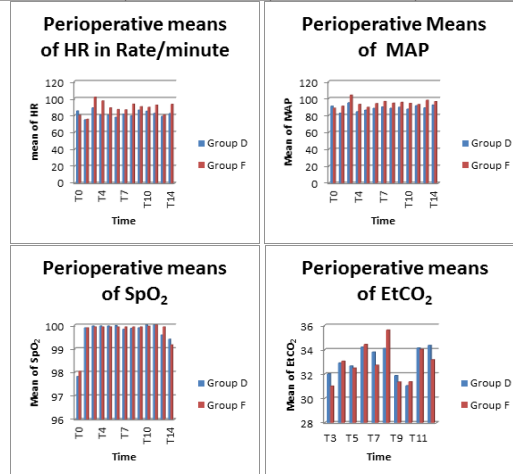
Parameters were again recorded at five minute (T¹³) and 10 minute (T¹⁴) after extubation.

Statistical analysis: Data was analysed using SPSS 20 (Statistical Package for the Social Sciences) software. Data was presented in the form of frequency, mean, standard deviation and graphs. Comparison of qualitative variables was done using Chi square or Fisher exact test whenever necessary. Comparison of quantitative variables was done using T-test. Significance will be considered if p-value is less than 0.05.

OBSERVATION AND RESULT

Table 1: Demographic profile

Parameter	Group - D	Group - F	P value
Age	42.22±12.84	38.58±13.60	0.172
Sex (F/M)	40/10	35/15	0.248



RESULTS

- Observed age in group D was 42.22±12.84 years and in group F was 38.58±13.60 years. Difference between mean of age in two groups was not significant (p value > 0.05). Out of total 50 patients in group D, 40 were female and 10 were male whereas in group F 35 were female and 15 were males. There is no statistical

- significance observed in gender and two groups (p value > 0.05). [Table 1]
- The increase in HR during laparoscopic cholecystectomy was less in Dexmedetomidine group in comparison to Fentanyl group. ($P < 0.05$) [Fig 1]
 - The increase in Mean Arterial Pressure during laparoscopic cholecystectomy was less in Dexmedetomidine group in comparison to Fentanyl group. ($P < 0.05$) [Fig 2]
 - There was no significant change in peripheral oxygen saturation (SpO_2) among Fentanyl and Dexmedetomidine group. ($P > 0.05$) [Fig 3]
 - There was no significant change in end tidal CO_2 ($EtCO_2$) among Fentanyl and Dexmedetomidine group. ($P > 0.05$) [Fig 4]

DISCUSSION

In our study Group D showed significant fall in HR, SBP, DBP, MAP from baseline value at all points of time intervals whereas it remained constantly high above baseline value in Group F (p -value < 0.05). The increase in HR and Mean Arterial Pressure during laparoscopic surgeries was less in Dexmedetomidine group in comparison to Fentanyl group. ($P < 0.05$) But there was no significant change in peripheral oxygen saturation (SpO_2) and end tidal CO_2 ($et CO_2$) among Fentanyl and Dexmedetomidine group. ($P > 0.05$) [Table 2-6]

In the study of **Vaswani et al. 2017**^[14], there was fall in HR, SBP, DBP and MAP more below baseline in Group D as compared to fall in HR, SBP, DBP and MAP in Group F at all points of time intervals

In the study of **Neil and Patel 2017**^[15], after intubation there was less rise in HR & DBP from baseline in Group D as compared to more rise in Group F (p -value < 0.05) which is statistically significant, after creation of pneumoperitoneum in intraoperative period, throughout the period of pneumoperitoneum, after release of pneumoperitoneum & post extubation at 5 min and 10 minutes, Group D showed significantly fall in HR & DBP from baseline at all time points, whereas in Group F showed constantly remained above the baseline throughout the intra operative period and the difference between two group is statistically significant as (p -value < 0.05) at all time points.

Similar results are observed in the study of **Vaswani et al. 2017 & Neil and Patel 2017**, no any significance difference observed in pre and post-operative SpO_2 values.

Similar results are observed in the study of **Vaswani et al. 2017 & Neil and Patel 2017**, no any significance difference observed in pre and post-operative $EtCO_2$ values.

CONCLUSION

we concluded that dexmedetomidine in compared to fentanyl causes greater attenuation of stress response to tracheal intubation, following pneumoperitoneum and in perioperative period resulting in greater reduction of HR, SBP, DBP, MAP than that of fentanyl, thus causing better haemodynamic stability in patients undergoing elective laparoscopic surgery. Dexmedetomidine also provides better sedation while maintaining patients arousability and has more analgesic sparing effect and causes lesser requirement of anaesthetic agent in perioperative period without much adverse effect.

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