

**Estimation of Blood Glucose As An Indirect Assessment For Attenuation Of Stress Response By Dexmedetomidine Versus Fentanyl Premedication During Laparoscopic Appendectomy: A Clinical Study**

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**Abstract**

**Background:** Anaesthesia and surgery-induced neuroendocrine stress response can be modulated by appropriate premedication. The present study was done to assess the clinical efficacy of dexmedetomidine versus fentanyl premedication for attenuation of neuroendocrine stress response by analysing the perioperative variation of blood glucose level during Laparoscopic appendectomy under general anaesthesia.

**Methodology:** 40 patients of ASA physical status I or II of either sex, aged between 20-60 yrs scheduled to undergo elective Laparoscopic appendectomy under general anaesthesia were randomly divided by envelope method into one of the 2 groups of 20 patients each (group D and group F). Patients allocated in group D (n = 20) were given IV infusion of dexmedetomidine 1µg/kg in 100 ml normal saline and Group F (n = 20) were given IV infusion of fentanyl 2 µg/kg in 100 ml normal saline over a 15 min period before the induction of general anaesthesia. Serial random blood sugar estimation was done perioperatively. Heart rate and mean arterial pressure were recorded at various time intervals.

**Results:** Our study demonstrated that, there was increment in mean RBS value from the basal value, 30 mins after beginning of surgery, 28% and 31% in Group D and group F respectively, both of which were statistically significant. 10 mins following extubation there was 39% increase from the basal value in group F which was clinically and statistically significant (p <0.001) and 33% increase from the basal value in Group D which was also significant statistically (p <0.001).

**Conclusion:** Both dexmedetomidine and fentanyl premedication attenuated the neuroendocrine stress response of laparoscopic appendectomy under general anaesthesia, as assessed by analysing the variation of blood glucose levels. The dexmedetomidine premedication was better when compared to fentanyl premedication.

**Keywords:** Hyperglycemia, neuroendocrine response, dexmedetomidine, fentanyl

**Introduction**

The body reaction to surgery and trauma is in the form of widespread endocrinal, metabolic and biochemical reactions which are known as *stress response*<sup>1</sup>. The stress response to surgery is characterised by increased secretion

of pituitary hormones and activation of sympathetic nervous system. The overall metabolic effect of endocrine response is increased catabolic hormones resulting in hypermetabolism, with the acceleration of most of the biochemical reactions<sup>2</sup>. Hyperglycemia is a feature of the metabolic response to surgery and depends on patient's age, anaesthetic technique, severity of tissue trauma, type and magnitude of surgery, total operative time, amount of intraoperative blood loss, and postoperative pain<sup>3,4</sup>.

Laparoscopic appendectomy is one of the most commonly practiced surgeries in the present era due to its well-known advantages like less post-operative pain, shorter hospitalization and faster functional recovery. Trendelenburg position, creation of pneumoperitoneum with CO<sub>2</sub>, potential for systemic absorption of CO<sub>2</sub> during Laparoscopic appendectomy is associated with sympathetic stimulation and stress response<sup>5</sup>.

The anaesthetist as a specialist of perioperative medicine deals with injured and surgical patients who are under huge stress. The choices of premedication and anaesthetic techniques are able to influence the neurohormonal stress response by modulating the pathophysiological pathways<sup>6</sup>. Various agents in the form of opioid analgesics, benzodiazepines, beta blockers, calcium channel blockers and vasodilators have been used to achieve this objective with variable success<sup>7,8</sup>.

Dexmedetomidine is a highly selective  $\alpha_2$  agonist with sedative, sympatholytic and analgesic properties. Hence, it can be a very useful adjuvant in anaesthesia as stress response buster, sedative and analgesic<sup>9</sup>.

Fentanyl, a potent, synthetic opioid analgesic is a strong agonist at the  $\mu$ -opioid receptors. IV fentanyl is extensively used for anesthesia and analgesia, most often in operating rooms and ICUs.

The primary aim of this study was therefore, to investigate the influence of dexmedetomidine and fentanyl

premedication on modulation of neuroendocrine stress response during laparoscopic appendectomy under general anaesthesia by analysing the variation of perioperative serial blood glucose levels.

### **Methodology**

After ethical committee approval and informed consent, a prospective randomized observational study was conducted in 40 patients belonging to ASA physical status I or II of either sex, aged between 20 to 60 yrs scheduled for elective laparoscopic appendectomy under general anaesthesia. Thorough pre- anaesthetic evaluation and routine investigation were carried out before taking up the patient for surgery. Patients belonging to ASA physical status III and IV, those with diabetes mellitus and complicated surgeries of more than 2.5 hours were excluded from the study.

Patients were premedicated with Tab Ranitidine 150 mg at night before surgery and at the morning of the surgery, Tab Lorazepam 1 mg at night before surgery and Inj Glycopyrrolate 0.2mg IM 1 h before the surgery.

On arrival to operation room, random blood sugar (RBS) estimation of the patient was done using glucometer. Routine, hemodynamic monitoring was performed by automatic blood pressure measurements, five-lead ECG monitor, and finger pulse oximetry and baseline readings were recorded. An intravenous (IV) infusion of ringer lactate was started, followed by IV midazolam 1 mg. Group D patients (n = 20) were given IV infusion of dexmedetomidine 1 $\mu$ g/kg in 100 ml normal saline and Group F patients (n = 20) were given IV infusion of fentanyl 2  $\mu$ g/kg in 100 ml normal saline over a period of 15 minutes (mins) before the induction of general anesthesia.

After preoxygenation, the anaesthesia was induced with propofol 2 mg/kg IV and tracheal intubation was facilitated by vecuronium 0.1 mg/kg IV. Anaesthesia was

maintained with isoflurane 1-1.5% and 60% nitrous oxide in oxygen. The patient's lungs were initially mechanically ventilated with a tidal volume of 8 ml/kg, a respiratory rate of 12 breaths/min, and I: E ratio of 1:2 in volume controlled mode. Five mins after securing the airway and abdominal insufflations by CO<sub>2</sub>, the lung mechanics were adjusted to maintain normocapnia (an EtCO<sub>2</sub> value of 35-40 mmHg) and IAP maintained between 12 and 15 mmHg. Muscle relaxation was supplemented with IV vecuronium bromide. All patients were covered to maintain normothermia.

Blood samples were estimated using glucometer for RBS levels preoperatively, 30 mins after beginning of surgery and 10 mins post extubation.

All patients were assessed for changes in hemodynamic parameters by measuring heart rate (HR), Oxygen saturation (SPO<sub>2</sub>), SBP, DBP and MAP prior to premedication (Baseline), after Premedication/ Pre-Induction, after induction, after intubation, at 5, 20, 40, 60, 80, 100 and 120 mins after pneumoperitoneum and post extubation .

Intraoperatively, patients were monitored for any bradycardia or tachycardia, hypotension or hypertension and it was managed as required. The residual neuromuscular block was reversed with neostigmine 0.05 mg/kg IV and glycopyrrolate 0.01 mg/kg IV and the trachea extubated when respiration was adequate and patient was able to obey simple commands. All patients received Paracetamol 1g intravenously at the end of procedure after RBS estimation. The patients were transferred to PACU and observed for any hemodynamic abnormalities, respiratory depression (respiratory rate <8 breaths/min), or hypoxemia (SPO<sub>2</sub> < 94%), shivering, nausea, and vomiting, and managed accordingly.

**Statistical Analysis**

20 patients in each group were taken to obtain the power 0.80. Qualitative data analysed by Chi-square test. Quantitative data analysed by Unpaired 't' test. The Statistical software SPSS 20.0 was used for the statistical analysis of the data.

**Results and Observations**

A total of 40 patients were randomly assigned to two groups of 20 patients each. Both groups were comparable in age, weight, height, and gender. There was no difference between groups for anaesthetic technique and mean operative time as shown in **table 1**

**TABLE 1: Demographic Data**

	Group D Dexmedetomidine	Group F Fentanyl	P Value
Age(years)	33.15±8.02	32.95±7.84	0.574
Weight(kg)	60.75±8.43	62.35±8.06	0.533
Gender Ratio(M:F)			
Duration of Surgery	90.45±8.43	91.9±12.48	0.713

All values in Mean ± Standard Deviation

Preoperative mean RBS level was 93.9 and 94.05 mg/dl in group D and group F respectively which was not statistically significant. After 30 min of beginning of surgery, mean RBS in 119.5 and 129.65 mg/dl in group D and group F respectively which was stastically significant (p <0.001). After extubation, mean RBS in 115 and 122.65 mg/dl in group D and group F respectively which was also stastically significant (p <0.001). Mean RBS levels are shown in table 2.

**TABLE 2: Mean RBS levels at various time intervals**

Time interval/Groups	Group D Dexmedetomidine	Group F Fentanyl	P Value
Preoperatively	93.90±6.793	94.05±7.181	0.128

30min after beginning of surgery	119.5±11.958	129.65±10.833	0.058
10min after extubation	115±8.326	122.65±8.152	<0.001

All values in Mean ± Standard Deviation

The mean HR was lower in group D after intubation, after pneumoperitoneum at 5, 20, 40, 60, 80 and 100 mins and post extubation than compared to group F which was clinically and statistically significant. Hemodynamic variables recorded at various time intervals during the study are shown in table 3.

**TABLE 3: Heart Rate and MAP at various time Intervals**

Parameters	Heart Rate (Beats/min)	Mean arterial Blood pressure (mm of Hg)		
		Group D Dexmedetomidine	Group F Fentanyl	Group D Dexmedetomidine
Baseline	75.4±9.43	73.8±6.61	96.85±5.414379	94.81667±6.591218
After Premedication	65.3±7.582	68.05±6.126	83.16±5.038	88.61±9.014
After Induction	62.4±7.556	65.65±5.669	78.45±5.336	83.95±8.556
After Intubation	68.3±6.514	73.15±5.153	88.15±4.344	90.5±8.345
5min after pneumoperitoneum	66.9±6.632	72.45±5.643	87.05±5.062	96.76±7.395
20min after pneumoperitoneum	65.65±6.73	71.45±5.246	86.65±5.052	96.88±8.146

40min after pneumoperitoneum	61.95±6.46	72.4±5.942	81.4±9.241	97.03±9.498
80min after pneumoperitoneum	63.5±5.68	74.55±5.216	80.4±4.38	98.4±10.117
120min after pneumoperitoneum	68±4.062	76.00±7.583	84±6.284	97.93±13.088
After Extubation	73.75±7.419	81.95±7.817	92.1±7.379	103.41±9.083

All values in Mean ± Standard Deviation

**Discussion**

The present study compares the clinical efficacy of dexmedetomidine versus fentanyl premedication for attenuation of neuroendocrine stress response by analysing the variation of perioperative blood glucose level during laparoscopic appendectomy under general anaesthesia.

Blood glucose concentration increased during and after surgery in both groups, which is a common metabolic response to surgical trauma. This increment, however, was more pronounced in fentanyl group than in dexmedetomidine group. In our study, intravenous dexmedetomidine 1 µg/kg or fentanyl 2 µg/kg has effectively modulated the neuroendocrine response of laryngoscopy and laparoscopy.

Observation of our study is in accordance with Gupta *et al.* that blood concentration of glucose had increased significantly in the fentanyl group, than in the dexmedetomidine group<sup>10</sup>.

Bessey *et al.* have suggested that increased circulating concentrations of catecholamines, glucagons, and cortisol can evoke the changes in carbohydrate metabolism, occurring immediately after trauma<sup>11</sup>. The characteristic metabolic effect of cortisol is to decrease the rate at which insulin activates the glucose uptake system; hence,

surgical stress led to greater activation of neuroendocrine response and hepatic gluconeogenesis under perioperative conditions, which corresponds to hemodynamic behavior and postoperative pain<sup>2</sup>. Iwaska et al. have observed impaired glucose tolerance and diminished insulin secretion in response to intravenous glucose during prolonged radical neck surgery<sup>12</sup>.

Thorell et al. have recently investigated that how intensive insulin therapy leads to normoglycemia in critically ill trauma patients. Multiple theories have been proposed for better outcome of trauma patients, including a decreased infection rate, reduced endothelial dysfunction, and reduced hyperglycemic axonal damage<sup>13</sup>.

Post-operative blood glucose level increased in both the groups, but was more pronounced in fentanyl group than dexmedetomidine group.

### **Conclusion**

We conclude that, both dexmedetomidine and fentanyl premedication have effectively attenuated the neuroendocrine stress response of laparoscopic appendectomy under general anesthesia, as assessed by analysing the variation of blood glucose levels. The dexmedetomidine premedication was better when compared to fentanyl premedication.

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