"STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL"

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LIST OF ABBREVIATIONS

ADH	Antidiuretic hormone
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CBF	Cerebral blood flow
CO	Cardiac Output
CO_2	Carbon dioxide
DBP	Diastolic Blood Pressure
FRC	Functional Residual Capacity
HR	Heart Rate
HS	Highly significant
IAP	Intra-abdominal pressure
ICP	Intracranial pressure
MAP	Mean Arterial Pressure
NBM	Nil by mouth
NS	Not significant
S	Significant
S.D.	Standard deviation
SBP	Systolic blood pressure
SVR	Systemic vascular resistance
SV	Stroke volume
SpO_2	Saturation of peripheral oxygen (%)
RSS	Ramsay Sedation Score
mcg	Microgram
mg	Milligram

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ABSTRACT

Title:

Study of effect of intranasal dexmedetomidine on stress response to pneumoperitoneum in laparoscopic surgeries: A one year double blinded hospital based randomised clinical trial.

Background:

Insufflation in laparoscopic surgeries may cause sympathetic stimulation, which can cause tachycardia and hypertension. Dexmedetomidine, a potent alpha-2 adrenoceptor agonist is gaining popularity to abolish this pressor response. This study explores the effect of intranasally used dexmedetomidine on stress response to pneumoperitoneum.

Aims and Objectives:

To determine the effect of intranasal dexmedetomidine on stress response to pneumoperitoneum in laparoscopic surgeries and to determine the side effects of the study drug if any.

Methodology:

A randomized control trial at KLES Prabhakar Kore Hospital & Medical Research Centre included 64 ASA I and II patients, aged 18-60 years, undergoing laparoscopic surgeries under General Anaesthesia. Patients were divided into two groups of 32 each. Group 1 received 1.5 mcg/kg of intranasal dexmedetomidine and Group 2 received similar volume of intranasal normal saline ten minutes prior to shifting to OT. Hemodynamic parameters (SBP, DBP, MAP, HR & SpO2) were

recorded 5minutes before the insertion of ports, during insufflation of abdomen and then every 5 minutes after for 30 minutes. Sedation status in both groups were assessed by an observer using the Ramsay sedation scale (RSS) in the pre-operative area. Statistical analysis compared results.

Results:

Variables were analysed using mean and standard deviation, unpaired and paired t-tests, Chi-square or Fisher's exact test. Intragroup analysis in dexmedetomidine group showed no strong evidence of difference in hemodynamic parameters from baseline with $p > 0.05$ whereas saline group showed statistically significant difference from baseline with $p < 0.05$. Intergroup analysis showed Hemodynamic changes were significantly less in Dexmedetomidine group as compared to saline group with $p<0.05$.

Conclusion:

Intranasal Dexmedetomidine was found to be effective in attenuating the hemodynamic response occurring due to creation of pneumoperitoneum in laparoscopic surgeries under General Anaesthesia.

Keywords:

Dexmedetomidine, Laparoscopy, Intranasal, General Anaesthesia, Pneumoperitoneum.

INTRODUCTION

Laparoscopic surgeries have gained popularity due to their numerous postoperative advantages, including faster recovery, reduced tissue trauma, avoidance of large surgical incisions, shorter hospital stays, and lower healthcare costs.

However, anaesthetic management in these patients presents challenges due to the cardiopulmonary alterations that occur during laryngoscopy, intubation, pneumoperitoneum, and the specific patient positioning required for different laparoscopic procedures The insufflation of carbon dioxide triggers an increase in plasma levels of catecholamines, prostaglandins, vasopressin, and enzymes of the renin-angiotensin system, all of which contribute to the physiological stress response. The rise in intra-abdominal pressure can negatively impact the cardiovascular system, leading to reduced cardiac output, increased blood pressure, and a rise in systemic and pulmonary vascular resistance, resulting in hypertension and tachycardia. Additionally, peritoneal insufflation induces significant ventilatory and respiratory changes, further exacerbating the stress response.[1]

When patients are positioned in extreme Trendelenburg, venous return from the head decreases, potentially increasing intracranial and intraocular pressures. The placement of laparoscopic ports and abdominal insufflation can also trigger arrhythmias, while peritoneal stretching may cause a marked increase in vagal tone.[2] These hemodynamic disturbances can heighten the risk of myocardial ischemia.[3]

Different methods have been employed with varying degrees of efficacy to mitigate sympathetic reactions. These include increasing the depth of anaesthesia using higher concentrations of inhalational & intravenous anaesthetic agents, administering higher doses of opioids, and utilizing antihypertensive medications and beta-adrenergic blockers.

Dexmedetomidine, an alpha-2 adrenergic agonist, is increasingly used for sedation due to its sedative and analgesic properties without causing respiratory depression. When administered as an intravenous adjuvant, it helps attenuate the pressor response associated with laryngoscopy, intubation, and pneumoperitoneum during laparoscopic surgeries, thereby promoting hemodynamic stability. However, its widespread use has been restricted by adverse hemodynamic effects such as hypotension, bradycardia, and, in rare cases, cardiac arrest. Additionally, its sedative action has been linked to delayed recovery when given intravenously. To minimize these side effects, alternative administration routes have been explored as a potential solution.[4]

The intranasal route offers several advantages, including ease of administration, effective drug absorption, reduced first-pass metabolism, and high patient acceptance.[5]

Given these benefits, this study attempts to assess the impact of intranasal dexmedetomidine in mitigating hemodynamic fluctuations following pneumoperitoneum creation in laparoscopic procedures.

AIMS AND OBJECTIVES

Aim:

To assess the Effectiveness of Intranasal Dexmedetomidine in Reducing the Stress Response to Pneumoperitoneum in Laparoscopic Surgeries.

Objectives:

Primary objective:

To determine the effect of intranasal dexmedetomidine on stress response to pneumoperitoneum in laparoscopic surgeries with respect to systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate.

Secondary objectives:

To identify the side effects of study drug.

REVIEW OF LITERATURE

1. "Bhattacharjee *et al*. studied the effectiveness of dexmedetomidine in maintaining hemodynamic stability in patients undergoing laparoscopic cholecystectomy" and found that intravenous infusion of 0.2 µg/kg/hr of dexmedetomidine 5 minutes before induction, attenuated mean arterial pressure and heart rate and maintained hemodynamic stability.[6]
2. A study conducted by "Ye, *et al*. in 2021 where they researched the effects of intravenous dexmedetomidine on intraoperative hemodynamics, recovery profile and postoperative pain in patients undergoing laparoscopic cholecystectomy" found that the administration of dexmedetomidine before anaesthesia induction can attenuate the stress response during intubation, pneumoperitoneum and extubation and maintain the hemodynamics more stable. [7]
3. "Vora, *et al*. in 2015 investigated the effect of intravenous dexmedetomidine on attenuation of hemodynamic changes and it's effects as adjuvant in anaesthesia during laparoscopic surgeries" and found that Dexmedetomidine, provided a stable hemodynamic profile in the perioperative period and effectively blunted the pressor response to intubation and extubation. Intraoperatively it decreased the requirement of volatile agents and analgesics. Since it is useful in attenuating stress response to intubation and extubation we believe it is useful in attenuating stress response to pneumoperitoneum.[8]
4. "Panchgar *et al.* in 2017 studied the effect of intravenous dexmedetomidine on hemodynamic parameters during perioperative period in patients undergoing laparoscopic surgery". They found that dexmedetomidine infusion in the dose of 1 µg/kg body weight as bolus over 10 min and 0.5 µg/kg/h intraoperatively as

maintenance dose controlled the hemodynamic stress response in patients undergoing laparoscopic surgery. [9]

5. "Yuen, *et al.* in 2007 did a Double-Blind, Crossover Assessment of the Sedative and Analgesic Effects of Intranasal Dexmedetomidine" and found that it is a convenient and safe alternative to parenteral administration. They have demonstrated that 1 and 1.5 mcg/kg of intranasally administered dexmedetomidine produced clinically significant sedation and better hemodynamic stability which is a desired effect for our study.[5]
6. "Niyogi S, *et al*. in 2019 conducted a study to compare the attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine" by IV (0.5 mcg/kg) and intranasal (1 mcg/kg) route. They found that both are equally efficacious for reducing hemodynamic response during laryngoscopy & intubation.[4]
7. "Jayaraman L *et al*. in 2013 conducted a comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery" and found that intranasal dexmedetomidine can obtund hemodynamic response to laryngoscopy and intubation.[10]
8. Kumar *et al.* in 2023 compared the effect of 0.5 μ/kg of intravenous dexmedetomidine & 1 μ/kg of intranasal dexmedetomidine on reducing stress response to laryngoscopy & endotracheal intubation & found that they were both equally efficient.[11]
9. "A Comparative Study Between Intranasal and Intravenous Dexmedetomidine on Hemodynamic Responses During Endotracheal Intubation" by M.K. *et al*. was done in 2022 using IV dose of dexmedetomidine 0.5mcg/kg and IN dose of

1mcg/kg and found that dexmedetomidine can be utilized as a premedication to lessen hemodynamic surges during endotracheal intubation with more or less the same efficacy via intranasal and intravenous routes.[12]

10. Tayung *et al.* in 2024 compared intranasal vs intravenous administration of dexmedetomidine for attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation and found that when given through intranasal route at a dose of 1 µg/kg body weight, a forty minutes before induction of anaesthesia, it produced similar hemodynamic changes as when given through intravenous route as infusion at a dose of 0.5 µg/kg body weight in patients undergoing major surgeries under general anaesthesia.[13]
11. Vaswani, *et al.* in 2017 did a "Comparative Study of the Effect of intravenous Dexmedetomidine (0.5 mcg/kg) Vs. Fentanyl (0.5 mcg/kg) on hemodynamic response in Patients Undergoing Elective Laparoscopic Surgery" and found that, dexmedetomidine when compared to fentanyl caused greater attenuation of stress response to tracheal intubation, following pneumoperitoneum and in perioperative period. However, Intravenous dexmedetomidine is associated with side effects such as bradycardia and hypotension which needs to be addressed.[1]
12. A study done by Li *et al*. in 2018 compared the pharmacokinetic & pharmacodynamic profile of i.v. administration of 1 mg kg -1 dexmedetomidine with two different modes of intranasal administration (atomiser or by drops from syringe) and found that there is no difference in bioavailability with atomisation or nasal drops. A similar degree of sedation can be achieved by either method.[14]

Intravenous dexmedetomidine has been found to attenuate stress response to tracheal intubation, following pneumoperitoneum and in perioperative period.[1,7] Since intravenous dexmedetomidine is associated with side effects, intranasal

dexmedetomidine has been studied to show similar effects with fewer adverse effects.[11,12] Since not enough studies have been done on intranasal dexmedetomidine for attenuation of stress response to pneumoperitoneum, this study was undertaken.

BASIC SCIENCES

LAPAROSCOPIC SURGERY:

The laparoscopic approach has become a standard of care for many abdominal surgical procedures. Compared with laparotomy, laparoscopy allows smaller incisions, reduces the perioperative stress response, reduces postoperative pain, and results in shorter recovery time.

Anaesthetic concerns for patients undergoing laparoscopic and robotic surgery differ from those for patients undergoing open abdominal surgery.

Laparoscopy requires creation of a pneumoperitoneum by insufflation of gas, usually carbon dioxide (CO_2), to open space in the abdomen for visualization and surgical manipulation. CO_2 insufflation can be performed blindly using a Veress needle or by placement of a port under direct vision through a small subumbilical incision. The gas source is connected to the needle or port; intraabdominal pressure (IAP) is monitored as gas is insufflated, aiming for a pressure $\leq$15 mmHg to minimize physiologic effects.

Physiologic effects of the pneumoperitoneum, absorption of CO_2, and positioning required for surgery can influence intraoperative care and outcomes. In addition, some laparoscopic procedures take longer than the open alternative.

PHYSIOLOGICAL EFFECTS OF LAPAROSCOPY

Cardiovascular changes —

Table 1: Cardiovascular changes during laparoscopy [15,16,17]

Parameters	Change	Causes
Systemic vascular resistance and mean arterial pressure	Increased	• Hypercarbia • Neuroendocrine response (ie,increased catecholamines, vasopressin, and cortisol) • Mechanical factors (ie, direct compression of aorta)
Cardiac filling pressures	Increased	• Increased intrathoracic pressure secondary to pneumoperitoneum. • Increased sympathetic output due to neuroendocrine response and hypercarbia.
Cardiac filling volumes	Variable; increased or no change	Interaction among: • Increased intravascular volume resulting from compression of liver and spleen. • Reduced preload and venous return. • Positioning. • Patient's preexisting status.
Cardiac index	Variable; decreased or no change	Interaction among: • Increased afterload. • Decreased venous return. • Decreased cardiac filling. • Increased intravascular volume. • Positioning. • Patient's preexisting status.
Cardiac rhythm	Bradyarrhythmias Tachyarrhythmias	• Peritoneal stretch - vagal • Hypercarbia. • Hypoxia. • Capnothorax. • Pulmonary embolism.

These effects are generally well tolerated by healthy patients. However, significant intraoperative cardiac dysfunction can occur in older patients and in those with cardiopulmonary disease (eg, chronic obstructive pulmonary disease [COPD], congestive heart failure, pulmonary hypertension, valvular heart disease).

Studies of hemodynamic events during laparoscopy in patients with significant cardiopulmonary disease have reported an increase in mean arterial pressure (MAP), systemic vascular resistance (SVR), and central venous pressure (CVP), with decreases in cardiac output (CO) and stroke volume (SV) during peritoneal insufflation.[18,19,20,21,22]

Compared with healthy patients, those with cardiopulmonary disease may require more pharmacologic interventions and more intensive monitoring to respond to these changes.

Cardiovascular changes during laparoscopy relate to the increase in intraabdominal pressure (IAP) associated with carbon dioxide (CO_2) insufflation, effects of positioning, and of absorption of CO_2, as follows:

- **Effects of pneumoperitoneum:** Pneumoperitoneum and the associated increase in IAP result in neuroendocrine and mechanical effects on cardiovascular physiology.
  - Neuroendocrine effects – Increase in IAP results in catecholamine release and activation of the renin–angiotensin system with vasopressin release. This increases MAP in most patients and may contribute to increases in SVR and pulmonary vascular resistance (PVR) [23]. Vagal stimulation, from insertion of the Veress needle or peritoneal stretch with gas insufflation, can result in bradyarrhythmias.

Bradycardia is common in this setting, while atrioventricular dissociation, nodal rhythm, and asystole have been reported [24].

- Mechanical effects – Mechanical aspects of laparoscopy are dynamic; the resulting cardiovascular effects depend on the patient's preexisting volume status, insufflation pressure, and position. Compression of arterial vasculature with pneumoperitoneum increases SVR and PVR, with variable effects on CO and blood pressure (BP) [25,26,27]. Hypercarbia caused by CO_2 absorption may also increase SVR and PVR; in most cases, minute ventilation is increased to prevent hypercarbia, but the increase in intrathoracic pressure that accompanies ventilator adjustments may further increase SVR and PVR. Cardiovascular effects tend to resolve quickly as pneumoperitoneum is maintained.

- **Effects of positioning:** Laparoscopic surgery is often performed in head-up (eg, for cholecystectomy) or head-down (eg, pelvic surgery) positions to allow the intraabdominal organs to fall away from the surgical field. Extremes of position can affect cardiovascular function.

  - Head up – The head-up position (ie, reverse Trendelenburg) leads to venous pooling, tends to reduce venous return to the heart [26,28], and may result in hypotension, especially in patients who are hypovolemic.

  - Head down – The-head down position (ie, Trendelenburg) position increases venous return and cardiac filling pressures [29].

- **Effects of hypercarbia:** Absorption of CO_2 during laparoscopy can have direct and indirect cardiovascular effects. The direct effects of hypercarbia and associated acidosis include decreased cardiac contractility, sensitization to arrhythmias, and systemic vasodilation. Indirect effects are the result of

sympathetic stimulation, and include tachycardia and vasoconstriction, which may counteract vasodilation [26].

Pulmonary changes —

Pneumoperitoneum with CO_2 and surgical positioning are associated with changes in pulmonary function and gas exchange:

Table 2: Pulmonary changes during laparoscopic surgery [15]

Parameter	Change	Causes
Lung volume (ie, functional residual capacity)	Decrease	• Elevation of diaphragm • Increased intraabdominal pressure • Positioning
Lung compliance	Decreased Increased pleural pressure Increased airway pressure	• Elevation of diaphragm • Increased intraabdominal pressure
PCO_2	Increased, depending on ventilation	• CO_2 absorption
PO_2	Variable	• Interaction among: • Atelectasis • Hypoxic pulmonary vasoconstriction • Preoperative pulmonary status
Tracheal position	Cephalad displacement, possible mainstem intubation	• Increased intraabdominal pressure • Trendelenburg position

These changes can result from increased IAP with pneumoperitoneum and from absorption of CO_2.

During laparoscopy, minute ventilation must be increased to compensate for absorption of CO_2. Hyperventilation may be difficult for patients with COPD, asthma, and/or severe obesity, especially in Trendelenburg position. In patients with

COPD and in older patients, end-tidal CO_2 ($ETCO_2$) may not accurately reflect arterial partial pressure of CO_2; in such patients, arterial blood gases may be required to monitor ventilation.

The absorption and elimination of CO_2 in patients with severe obesity appears to be similar to patients without obesity [30]. Arterial oxygenation decreases and alveolar– arterial oxygen gradient increases in anesthetized patients with obesity when placed in Trendelenburg position, though CO_2 insufflation tends to slightly reverse these effects [31].

- **Changes in pulmonary mechanics** – Pneumoperitoneum causes cephalad displacement of the diaphragm and mediastinal structures, which reduces functional residual capacity (FRC) and pulmonary compliance, resulting in atelectasis and increased peak airway pressures. These effects are exacerbated with steep Trendelenburg positioning (eg, during pelvic surgery) and are reduced with reverse Trendelenburg positioning (eg, during cholecystectomy and gastric surgery). The changes in pulmonary compliance may be less with retroperitoneal insufflation (eg, during renal or adrenal procedures) compared with intraperitoneal insufflation.

- **Ventilation/perfusion matching** – The reduction in FRC and atelectasis associated with laparoscopy may theoretically lead to shunting and ventilation/perfusion mismatch; however, in healthy patients, these effects are minimal and well tolerated, even with steep Trendelenburg positioning [17,29,32].
- **Endotracheal tube position** – Pneumoperitoneum and Trendelenburg positioning may cause cephalad movement of the carina, which can result in mainstem endobronchial migration of the endotracheal tube, hypoxia, and high inspiratory

pressure [33,34]. In addition, endotracheal tube cuff pressure increases in some patients during laparoscopy [35].

Regional circulatory changes –

- **Splanchnic blood flow** – The mechanical and neuroendocrine effects of pneumoperitoneum can decrease splanchnic circulation, resulting in reduced total hepatic blood flow and bowel perfusion. However, hypercapnia can cause direct splanchnic vasodilatation. Thus, the overall effects on splanchnic circulation are not clinically significant [36,37]
- **Renal blood flow** – The creation of a pneumoperitoneum results in reduction in renal perfusion and urine output associated with renal parenchymal compression, reduced renal vein flow, and increased levels of vasopressin[38,39,40]. When IAP is kept under 15 mmHg, renal function and urine output generally normalize soon after pneumoperitoneum deflation, without histologic evidence of pathologic changes. The effects of laparoscopy on renal function for patients with preexisting renal disease have not been studied. In most cases, we believe that the benefits of a minimally invasive surgical approach outweigh theoretical concerns about the effect of increased intraabdominal pressure on renal function.
- **Cerebral blood flow** – Increased intraabdominal and intrathoracic pressures, hypercarbia, and Trendelenburg positioning can all increase cerebral blood flow (CBF) and intracranial pressures (ICP) [41]. In healthy patients undergoing prolonged pneumoperitoneum and steep Trendelenburg position, cerebral oxygenation and cerebral perfusion remain within safe limits [42]. In patients with intracranial mass lesions or significant cerebrovascular disorders (eg, carotid atherosclerosis and cerebral aneurysm), the increase in ICP may have clinical

consequences. Therefore, in this patient population, we maintain strict normocapnia during laparoscopy.

- **Intraocular pressure** – Intraocular pressure (IOP) increases with pneumoperitoneum and increases further when the patient is positioned in Trendelenburg [43,44,45].

DEXMEDETOMIDINE [46]

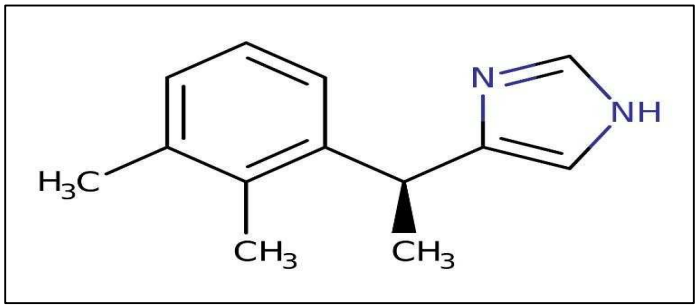


Figure 1: Chemical structure of Dexmedetomidine

Dexmedetomidine is the S-enantiomer of the veterinary sedative medetomidine. It is a highly selective α2-adrenoceptor agonist demonstrating an α2:α1 selectivity ratio of 1620:1. This makes it eight times more selective for the α2-adrenoceptor than clonidine.

Clinical Trials and FDA Approval:

The drug underwent clinical trials in the 1990s. It was first approved by the U.S. Food and Drug Administration (FDA) in 1999 under the brand name Precedex. Initially, its use was limited to short- term sedation (less than 24 hours) in mechanically ventilated patients. However, over time, its clinical indications have expanded. By 2008, the FDA approved dexmedetomidine for sedation of non-intubated patients prior to and/or during surgical and other procedures, and later its use was extended to longer sedation durations.

Drug actions

Sedation and anxiolysis:

These properties are mediated via agonism of α2-adrenoceptors primarily in the locus coeruleus of the pons where it results in dose-dependent inhibition of norepinephrine release. It is postulated that this results in disinhibition of the ventrolateral preoptic nucleus which then releases inhibitory neurotransmitters. This pathway is part of the complex circuitry governing natural sleep, resulting in a quality of sedation with dexmedetomidine which more closely resembles normal physiological sleep than the more familiar GABA-ergic sedatives (propofol and the benzodiazepines). This sedation is characterized by preserved muscle tone and ventilation, by spontaneous and evoked movements, and by awakening by external stimuli. Once roused, patients are cooperative and can typically obey simple instructions. Once the external stimulus is discontinued, patients resume the previous level of sedation. Electroencephalogram studies have further confirmed that the sedative effects of dexmedetomidine mimic stage 2 non-rapid eye movement sleep.[47]

Analgesia:

It is likely that dexmedetomidine exerts effects at various sites in the pain pathway, but its main site of action is at the level of the spinal cord where stimulation of α2-receptors in the substantia gelatinosa of the dorsal horn reduces the release of nociceptive neurotransmitters such as substance P.

Effects on organ systems:

The cardiovascular effects of the drug are biphasic. At higher rates of infusion, such as during administration of a loading dose, the predominant effect is hypertension due to activation of α2B receptors on vascular smooth muscle. This is

superseded by hypotension and bradycardia as a result of the centrally mediated inhibition of sympathetic outflow. Case reports of bradycardia leading to asystole after loading dose administration of the drug in conjunction with multiple other have been found in the literature.[48] Cardiovascular adverse effects associated with dexmedetomidine may be expected to be more pronounced in hypovolemic patients, in those with diabetes mellitus or chronic hypertension, in the elderly and in those with high vagal tone.

A defining feature of the sedative action of dexmedetomidine is its minimal effect on ventilation, even when given in doses 10 times the maximum recommended.[49] In addition, MRI studies have shown that the airway remains patent during dexmedetomidine sedation.

Owing to actions on peripheral α2-adrenoecptors, dexmedetomidine also has decongestant and antisialagogue effects. It may theoretically reduce bowel motility.

Dexmedetomidine suppresses shivering, possibly due to agonism of α2B receptors in the hypothalamus. It exerts a diuretic effect by inhibiting the action of ADH at the collecting duct.

Despite its imidazole structure, dexmedetomidine has not been found to cause any clinically significant adrenal suppression.

Pharmacokinetics:

Administration is possible via multiple routes, with a bioavailability of 16% when given orally, 65% nasally, and 82% buccally. It is 94% protein bound with the unbound drug freely crossing the blood–brain barrier to exert its central effects, with a distribution half-life of 6 min. It undergoes glucuronidation, hydroxylation, and N-methylation in the liver to inactive metabolites which are then renally excreted. Hepatic impairment therefore should prompt a dose reduction due to decreased

protein binding and metabolism, while renal impairment and renal replacement therapy requires no dose adjustment. It has a terminal elimination half-life of ∼2 h with clearance estimated at 39 litre/h. Its steady-state volume of distribution (118 litres) is increased in patients with low plasma albumin concentration, prolonging the terminal half-life and context- sensitive half-time in such patients. [50]

Drug administration:

The dexmedetomidine intravenous infusion is begun at a rate of 0.5-1.0 μg/kg/hr and is then adjusted according to response within the dose range 0.2–1.0 μg/kg/hr. In contrast to its use in anaesthesia, it is recommended that no loading dose is given when used for sedation in the ICU. After dose adjustment, a new steady- state sedation level may not be reached for up to 1 h.

The IV formulation is also efficacious when administered by the intranasal route in both children and adults. Intranasal dexmedetomidine is associated with a slower and more gradual onset than IV administration. The intranasal route is more convenient as it is painless, odourless and tasteless. Intranasal drug can penetrate the blood brain barrier and reach the central nervous system directly. Due to the higher vascularity of the nasal mucosa, dexmedetomidine may access the systemic circulation rapidly, bypassing the first-pass metabolism of liver.[10] Although IV administration results in much higher peak plasma concentrations and earlier onset, the depth of sedation is similar once it occurs. A more gradual onset may actually be desirable in avoiding the α1 agonist effects seen with rapid IV administration (hypertension and bradycardia).[51,52]

A study done by Li et al in 2018 compared the pharmacokinetic (PK) and pharmacodynamic (PD) profile of IV administration of 1 mg/kg/hr dexmedetomidine with two different modes of intranasal administration (atomiser or by drops from

syringe) and found that there is no difference in bioavailability with atomisation or nasal drops. A similar degree of sedation can be achieved by either method.[14]

Perioperative use:

Sedative Premedication:

Its anxiolytic, sedative, sympatholytic, and antisialagogue properties, along with a lack of respiratory depression make dexmedetomidine suitable for premedication. The drug also acts as an anaesthetic-sparing agent and obtunds the pressor response to intubation. Its versatility in route of administration is an advantage in paediatric premedication where intranasal administration of 1μg/kg/hr dexmedetomidine was shown to be as effective a sedative as midazolam 0.5 mg/kg/hr orally, with modest hemodynamic effects.[53] Dexmedetomidine also has a reversal drug for its sedative effect called as atipamezole, which acts by increasing the central turnover of noradrenaline.[54]

Anaesthetic and Opioid-sparing agent:

Dexmedetomidine decreases anaesthetic requirements and is opioid sparing. These properties are particularly useful in certain patient populations where the respiratory- depressant properties of opioids may be particularly detrimental, such as in bariatric surgery.

Sympatholysis:

A Cochrane review in 2009 [55] examined the theoretical benefits of α-agonists in obtunding the perioperative stress-induced increase in sympathetic activity, and thereby reducing cardiac complications of surgery. The authors found that perioperative α2- agonists reduced mortality and myocardial ischemia, with the greatest benefit seen in patients undergoing vascular surgery. There was, however, an increase in perioperative hypotension and bradycardia with drug administration.

A study by Vaswani, et al in 2017 Comparison of the Effect of intravenous Dexmedetomidine (0.5 mcg/kg) Vs. Fentanyl (0.5 mcg/kg) on hemodynamic response in Patients Undergoing Elective Laparoscopic Surgery found that, dexmedetomidine when compared to fentanyl caused greater attenuation of stress response to tracheal intubation, following pneumoperitoneum and in perioperative period.[1] Continuous infusion of dexmedetomidine throughout the extubation period has been used for emergence phenomena.

Postoperative Analgesia:

Postoperative dexmedetomidine infusions have been used to supplement other forms of analgesia in patients in whom opioid-induced respiratory depression would be potentially deleterious. A small randomized controlled trial of thoracic surgical patients found less supplemental epidural opioid was needed in the group who also received an IV dexmedetomidine infusion.

Neuroanaesthesia:

Dexmedetomidine is routinely used in our centre for neurosurgical procedures requiring intraoperative patient cooperation, that is, awake craniotomy for supratentorial tumour resection or deep brain stimulator implantation. It does not suppress epileptiform activity in patients undergoing electrocorticography and so is useful in epilepsy surgery.

Dexmedetomidine administration has no effect on intracranial pressure. Although there were initial concerns that it may reduce cerebral blood flow leading to ischemia, multiple studies have demonstrated a reduction in cerebral blood flow and cerebral metabolic rate. It does not affect somatosensory evoked potentials or motor- evoked potentials and so may be a useful anaesthetic-sparing agent and analgesic supplement in scoliosis surgery. Experimental studies show dexmedetomidine has neuroprotective

effects in hypoxic–ischaemic and traumatic brain injury models. This neuroprotection appears to be afforded by the action of the drug on α2A-receptors and at imidazoline receptors. [56]

Regional Anaesthesia Adjuncts:

A limited number of studies have shown a prolongation of regional nerve block when dexmedetomidine was added to the local anaesthetic.

Adverse Effects:

While dexmedetomidine is generally well-tolerated, it can cause several side effects, particularly related to its cardiovascular effects.

- Hypotension: As a sympatholytic, it can significantly reduce blood pressure, especially in volume- depleted patients or those concurrently receiving other vasodilators.
- Bradycardia: The drug can slow the heart rate, which may be severe in some cases, particularly if patients are predisposed to bradycardia or are taking other medications that reduce heart rate.
- Dry Mouth: Common with alpha-2 agonists due to reduced salivary secretion.
- Transient Hypertension: Initial administration can lead to transient hypertension before the onset of central sympatholysis.
- Nausea and Vomiting: Can occur, although less frequently than with other sedatives and anaesthetics.[57]

In medical practice, dexmedetomidine's benefits are maximised when used judiciously, with careful monitoring of vital signs to manage its blood pressure and heart rate effects. Its ability to provide sedation and pain relief while allowing patients to remain responsive and breathe independently makes it a valuable tool in various clinical settings.

MATERIALS AND METHODS

Study Design: Double Blind Randomised Clinical Trial

Source of Data: Study was performed on subjects between 18-60 years, of both sexes, ASA grade I & II, posted for laparoscopic procedures under GA in "Dr. Prabhakar Kore's Hospital and Medical Research Centre and KLE's Dr. Prabhakar Kore Charitable Hospital, Belagavi" over 1 year.

Period of study: January 2024 to December 2024

Sample Size: 64.

Sampling technique:

The sample size formula based on mean and SD at 95% confidence interval and 95% power is,

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 (SD_1^2 + SD_2^2)}{(\bar{x}_1 - \bar{x}_2)^2}$$

Where $Z_{1-\alpha/2}$ = the level of significance and $Z_{1-\beta}$ = the power of the test. For 5% level of significance $Z_{1-\alpha/2}$ =1.96 and $Z_{1-\beta}$ = 1.64 for 95% power of the test. Heart rate at 5 mins was used for calculation. $\bar{x}_1$ = mean of control group (87.06) and $\bar{x}_2$ = mean of treatment group at 5 minutes (77.46). SD_1 is the SD of the control group (11.3) and SD_2 is SD of the treatment group. (9.66). Therefore, sample size = 64. There were 2 groups with 32 cases in each.

The above computation was based on a 2019 study by "Niyogi S. et al. to compare attenuation of hemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine by IV (0.5 mcg/kg) and IN (1 mcg/kg) route. [4]"

Inclusion Criteria:

- ASA I & II.
- Patients of 18-60 years.
- Subjects scheduled for laparoscopic procedures under GA with endotracheal tube.
- Provides consent.

Exclusion Criteria:

- Patient refusal or unable to give consent.
- ASA physical status III & above.
- Patients with nasal deformities.
- Patients allergic to study drug.

STUDY PROTOCOL:

Ethical Committee approval was obtained, 64 patients scheduled for laparoscopic procedures under GA were studied. Informed consent was obtained, subjects were randomised into 2 groups using computer generated randomisation table. The allocation remained concealed to the patient as well as the assessor.

GROUP 1: received 1.5 mcg/kg of intranasal dexmedetomidine

GROUP 2: received similar volume of intranasal normal saline

A pre-anaesthetic evaluation was conducted prior to the procedure.

Investigations: Complete Blood Counts, Serum Creatinine, Fasting Blood Sugars for all patients. ECG for patients above 40 years of age. All subjects were given Ranitidine (150mg) & Alprazolam (0.5mg) orally, previous night.

The day of procedure, NPO status was confirmed and all subjects moved to pre operative room and IV RL maintenance fluid started using 18G wide bore line. Baseline readings of SBP, DBP, MAP and HR were recorded. Ten minutes prior to shifting to OT, patients in,

1)GROUP 1: was given 1.5 mcg/kg of IN dexmedetomidine in undiluted form, made from parenteral preparation (100 µg/ml) administered equally to both nostrils in equal volume in supine head down position using a tuberculin syringe,

2) GROUP 2: received similar volume of intranasal normal saline.

Hemodynamic parameters were recorded. Sedation status in both groups, was assessed by an observer using the Ramsay sedation scale (RSS) in the pre-operative area.

Once moved to OT, routine monitors were connected and baseline readings taken. Premedicated with IV Glycopyrrolate 0.005 mg/kg, IV Midazolam 0.05 mg/kg and IV Fentanyl 2mcg/kg. Induced with IV propofol 2mg/kg and IV succinylcholine 2mg/kg after 3 mins preoxygenation with 100% Oxygen to allow tracheal intubation. Anaesthesia was maintained with 50% O2-N2O mixture, isoflurane 1-1.2 MAC, inj. vecuronium 0.1mg/kg followed by top ups of $1/4^{th}$ the loading dose.

Hemodynamic parameters (MAP, SBP, DBP and HR) were recorded 5minutes before the insertion of ports, during insufflation of abdomen and then every 5 minutes for 30 minutes. Both groups received IV Paracetamol 15mg/kg for pain relief.

During extubation Inj. neostigmine (0.05mg/kg) & Inj. Glycopyrrolate (0.01mg/kg) were given to reverse the neuromuscular blockade. Patients were extubated once the clinical criteria was met and were moved to recovery room.

In group 2, cardiovascular changes were managed either by increasing the dose of isoflurane or giving IV fentanyl 0.5mcg/kg top up.

Ramsay Sedation Score [58]

A popular tool for determining a patient's level of sedation, especially in critical care and surgical situations, is the Ramsay Sedation Score (RSS). It offers a quick and efficient method for determining the level of sedation. Measurements were taken before induction.

Each of the six RSS levels denotes a distinct level of patient responsiveness & sedation:

1. Score 1: Anxious or restless
2. Score 2: In a state of tranquil
3. Score 3: Only Responds to commands
4. Score 4: Loud vocal stimulus or light glabellar tap elicits brisk response
5. Score 5: loud vocal stimulus or light glabellar tap elicits sluggish response
6. Score 6: Not responsive to both tapping and vocal stimulus

Statistical Analysis:

This study compared two groups by first calculating mean and standard deviation for continuous numerical elements. Intergroup comparisons were performed using unpaired Student's t-tests, whereas paired Student's t-tests were employed to assess numerical elements within same group. Categorical elements were expressed as frequencies, ratios, and percentages, with correlation among outcomes, clinical parameters, and demographic characteristics analyzed via the Chi-square test. Discrete elements were summarized using medians and compared using nonparametric methods. Graphical representations were provided to effectively illustrate these comparisons, and a p-value <0.05 was deemed statistically significant.

RESULTS

This research titled **"STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL**" was conducted in the "Department of Anaesthesiology, Jawaharlal Nehru Medical College, KAHER, Belagavi" from August 2023 to August 2024 in 64 subjects randomized into 2 groups of 32 each.

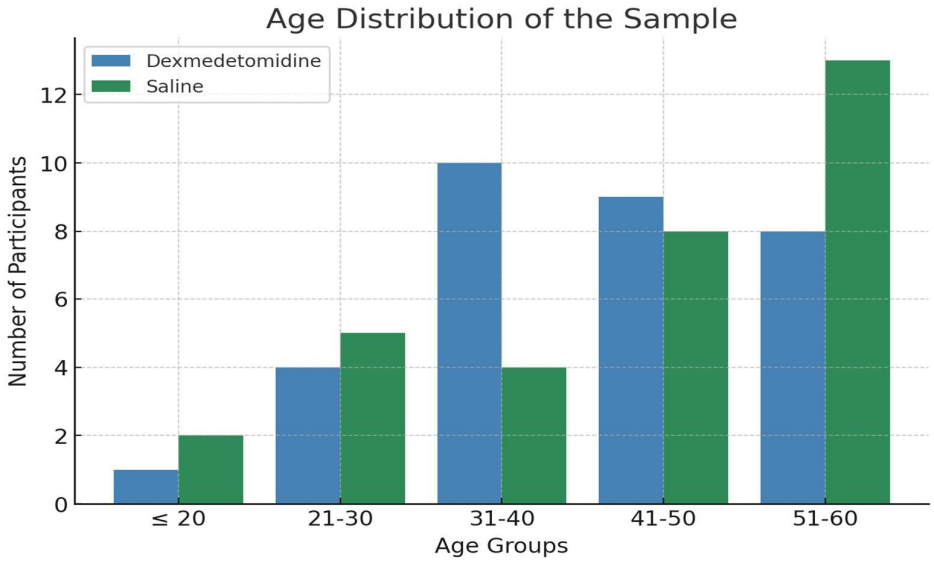
The data was organized using Microsoft Excel, and statistical evaluation was conducted using SPSS 26.0 and R environment (version 4.4.2). Graphs and tables were created using Microsoft Excel and Word.

1. **AGE DISTRIBITION:**

AGE(YRS)	**Group 1 DEXMEDETOMIDINE**		**Group 2 SALINE**		**TOTAL**
≤ 20	1	3.13%	2	6.25%	3
21 - 30	4	12.5%	5	15.63%	9
31 - 40	10	31.25%	4	12.5%	14
41 - 50	9	28.13%	8	25%	17
51 - 60	8	25%	13	40.63%	21
Total	32	100%	32	100%	64
Pearson chi-square = 4.27, p-value = 0.371					

Table 1: Mean Age Distribution of Group 1 and Group 2

The age distribution in each group is classified into 5 sub groups. From the above table we can see that in subjects ≤ 20 years, dexmedetomidine group has 1 and saline group has 2. There were 4 subjects in 21 – 30 years age group in dexmedetomidine group and 5 in saline group. In 31 – 40 years age group, 10 subjects in dexmedetomidine group and 4 subjects in saline group were noted. In 41 – 50 years age group 9 subjects in dexmedetomidine group and 8 subjects in saline group were seen. In age group of 51 – 60 years, there were 8 patients in dexmedetomidine group and 13 patients in saline group. Since the p-value (**0.371**) is higher than common significance level, there is **no significant association** between age groups.



Graph 1: Age distribution of the Sample

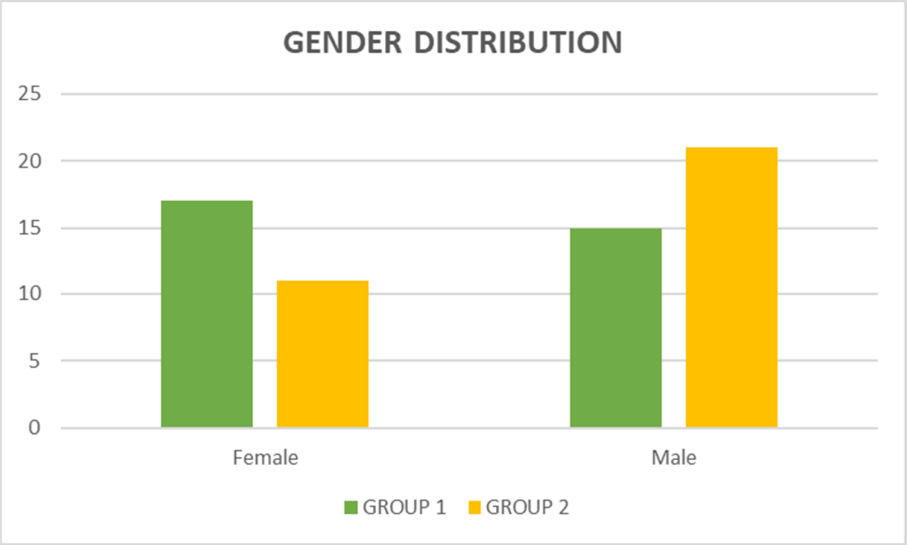
2. **GENDER DISTRIBUTION:**

There were 17 female patients and 15 male patients in dexmedetomidine group and 11 female patients and 21 male patients in saline group.

P-value (0.208) being >0.05, indicates **no significant association** between gender and group assignment.

GENDER	**Group 1 DEXMEDETOMIDINE**		**Group 2 SALINE**	
Female	17	53.13%	11	34.38%
Male	15	46.86%	21	65.63%
Total	32	100%	32	100%
Pearson chi-square = 1.59, p-value = 0.208				

Table 2: Mean Gender Distribution of Group 1 and Group 2



Graph 2: Gender distribution of the sample

3. **SYSTOLIC BLOOD PRESSURE:**

GROUP 1 (DEXMEDETOMIDINE)

Timepoint	SBP (Mean)	SBP (SD)	P value	INFERENCE
Baseline	125.00	11.19	-	-
T0	114.22	11.06	0.0005	S
TP	122.00	11.00	0.288	NS
T5	126.69	10.80	0.543	NS
T10	122.97	9.17	0.433	NS
T15	120.47	8.55	0.078	NS
T20	118.75	8.97	0.019	S
T25	118.84	8.52	0.019	S
T30	117.50	8.77	0.005	S

Table 3 : Mean Systolic Blood Pressure of Group 1

From the above chart we can see that in dexmedetomidine group the mean SBP at baseline was 125.00mmHg. At T0 there was a fall in SBP post induction , and then subsequent moderate rise in SBP during creation of pneumoperitoneum (TP, T5, T10, and T15) but <20% from baseline with $p > 0.05$, implying no strong evidence of a difference from Baseline. T20, T25, and T30 show statistically significant changes ($p < 0.05$), suggesting meaningful reductions.

GROUP 2 (SALINE):

Timepoint	SBP (Mean)	SBP (SD)	P value	INFERENCE
Baseline	127.53	10.43	-	-
T0	113.94	10.45	0.00001	HS
TP	131.00	10.70	0.199	NS
T5	143.84	11.52	0.000001	HS
T10	144.53	12.77	0.000002	HS
T15	135.00	10.9	0.009	S
T20	128.00	6.80	0.832	NS
T25	126.53	9.29	0.688	NS
T30	124.91	8.74	0.284	NS

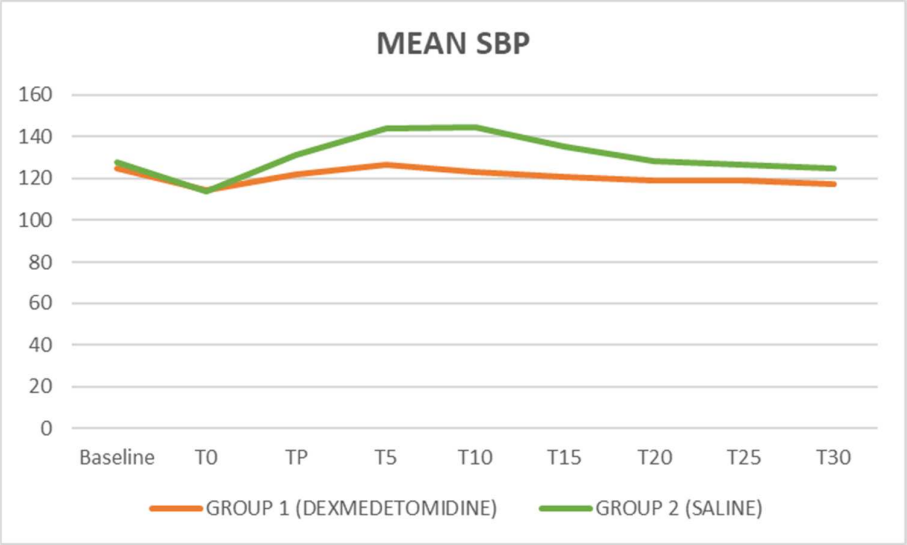
Table 4: Mean Systolic Blood Pressure of Group 2

In the saline group, mean SBP at baseline was 127.53mmHg which had a statistically significant fall at T0 post induction. T5, T10, and T15 show statistically significant increase in SBP post creation of pneumoperitoneum ($p < 0.05$). T20, T25, and T30 are not significant ($p > 0.05$), suggesting no strong evidence of a difference from Baseline as intervention was done.

	GROUP 1 (DEXMEDETOMIDINE)		GROUP 2 (SALINE)			
Time	**Mean**	**SD**	**Mean**	**SD**	**p-value**	**Inference**
Baseline	125.00	11.19	127.53	10.43	0.353	NS
T0	114.22	11.06	113.94	10.45	0.917	NS
TP	122.00	11.00	131.00	10.70	0.0015	S
T5	126.69	10.80	143.84	11.52	<0.001	HS
T10	122.97	9.17	144.53	12.77	<0.001	HS
T15	120.47	8.55	135.00	10.9	<0.001	HS
T20	118.75	8.97	128.00	6.80	<0.001	HS
T25	118.84	8.52	126.53	9.29	0.001	S
T30	117.50	8.77	124.91	8.74	0.001	S

Table 5: Mean Systolic Blood Pressure of Group 1 and Group 2

Baseline and T0 show no significant difference ($p > 0.05$), indicating both groups started at similar SBP levels. TP to T30 show statistically significant differences ($p < 0.05$), meaning that Dexmedetomidine (Group 1) had a significantly decreased SBP response compared to Saline (Group 2). Very strong significance is observed at T5, T10, T15 & T20 ($p < 0.000001$), suggesting a major difference in SBP between groups at these points.



Graph 4: Mean SBP

4. **DIASTOLIC BLOOD PRESSURE:**

GROUP 1 (DEXMEDETOMIDINE)

Timepoint	DBP (Mean)	DBP (SD)	P value	INFERENCE
Baseline	78.16	16.56	-	-
T0	74.31	8.99	0.257	NS
TP	82.2	12.1	0.274	NS
T5	84.78	10.66	0.067	NS
T10	81.44	8.71	0.329	NS
T15	79.69	7.20	0.635	NS
T20	77.72	6.99	0.891	NS
T25	77.81	7.19	0.913	NS
T30	76.50	6.03	0.598	NS

Table 6: Mean Diastolic Blood Pressure of Group 1

In the dexmedetomidine group, mean DBP at baseline was 78.16 mmHg. This chart suggests that DBP changes over time were not significantly different from the Baseline with an increase of less than 20% at TP, T0, T5 & T10.

GROUP 2 (SALINE)

Timepoint	DBP (Mean)	DBP (SD)	P value	INFERENCE
Baseline	79.81	7.14	-	-
T0	76.47	7.03	0.069	NS
TP	87.59	7.65	0.0002	S
T5	96.13	9.70	<0.00000001	S
T10	95.38	10.44	<0.0000001	S
T15	90.19	7.39	0.0000028	S
T20	85.75	5.88	0.0010	S
T25	83.03	5.29	0.049	S
T30	82.16	6.22	0.170	NS

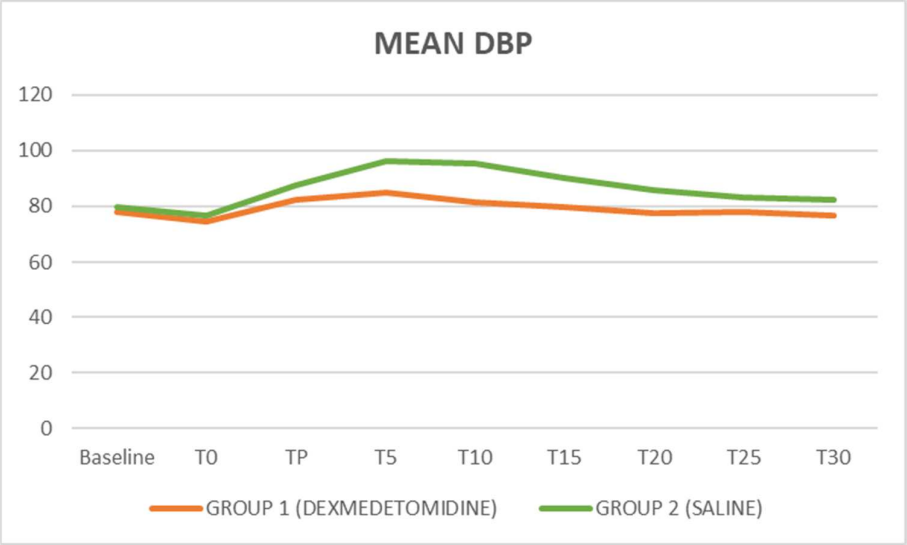
Table 7: Mean Diastolic Blood Pressure of Group 2

In saline group, mean DBP at baseline was 79.81 mmHg which had a statistically significant rise at TP, T5, T10, T15, T20, and T25 with $p < 0.05$.

	GROUP 1 (DEXMEDETOMIDINE)		GROUP 2 (SALINE)			
Time	**Mean**	**SD**	**Mean**	**SD**	**p-value**	**Inference**
Baseline	78.16	16.56	79.81	7.14	0.607	NS
T0	74.31	8.99	76.47	7.03	0.288	NS
TP	82.2	12.1	87.59	7.65	0.037	S
T5	84.78	10.66	96.13	9.70	0.000036	S
T10	81.44	8.71	95.38	10.44	<0.01	S
T15	79.69	7.20	90.19	7.39	<0.01	S
T20	77.72	6.99	85.75	5.88	<0.01	S
T25	77.81	7.19	83.03	5.29	0.0016	S
T30	76.50	6.03	82.16	6.22	0.00047	S

Table 8: Mean Diastolic Blood Pressure of Group 1 and Group 2

B**aseline and T0 are not significant** ($p > 0.05$), indicating both groups had similar DBP values at the start. **TP to T30 show statistically significant differences** ($p < 0.05$), meaning Dexmedetomidine (Group 1) and Saline (Group 2) had significantly different DBP responses over time suggesting a major impact of Dexmedetomidine on DBP.



Graph 5: Mean DBP

5. **MEAN ARTERIAL PRESSURE:**

GROUP 1 (DEXMEDETOMIDINE)

Timepoint	Mean	SD	P value	INFERENCE
Baseline	93.77	13.01	-	-
T0	87.61	9.07	0.016	S
TP	95.53	11.08	0.119	NS
T5	98.75	10.29	0.041	S
T10	95.28	8.43	0.767	NS
T15	93.28	6.97	0.441	NS
T20	91.39	7.04	0.386	NS
T25	91.48	6.88	0.179	NS
T30	90.16	6.31	0.495	NS

Table 9: Mean of Mean Arterial Pressure of Group 1

The mean MAP at baseline was 93.77 mmHg and at All other time points (TP, T10, T15, T20, T25, T30) MAP was not significant ($p > 0.05$), meaning MAP changes at these points were not statistically different from Baseline.

GROUP 2 (SALINE)

Timepoint	MAP (Mean)	MAP (SD)	P value	INFERENCE
Baseline	95.71	7.69	-	-
T0	88.95	7.41	<0.000001	HS
TP	102.19	8.37	0.00018	S
T5	112.03	10.14	<0.00000001	S
T10	111.76	10.81	<0.00000001	S
T15	105.00	8.19	0.000054	S
T20	99.6	5.95	0.0083	S
T25	97.53	6.11	0.245	NS
T30	96.40	6.52	0.798	NS

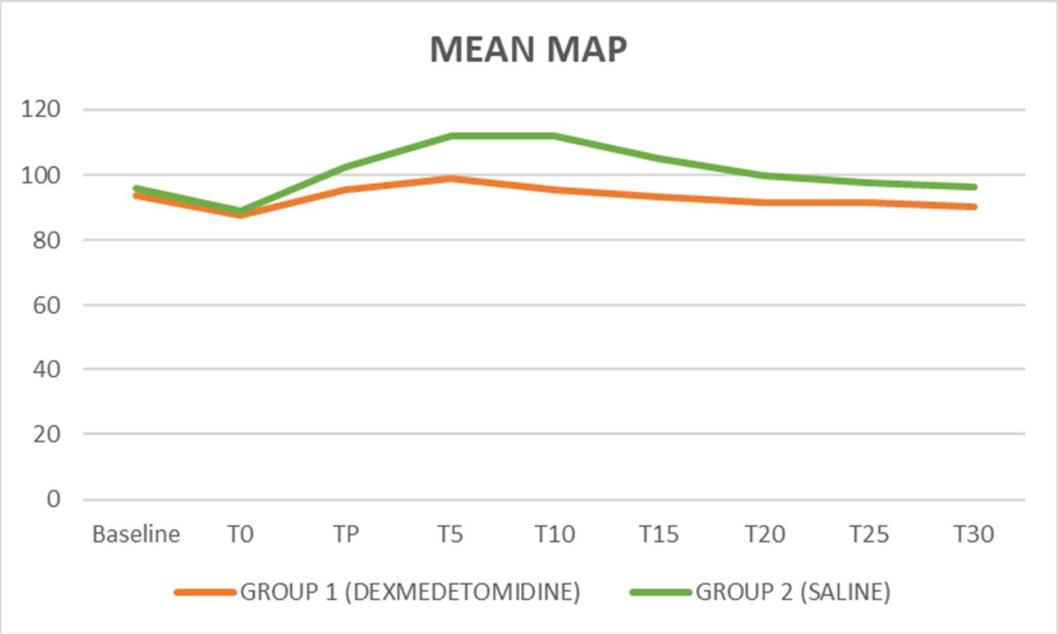
Table 10: Mean of Mean Arterial Pressure of Group 2

The mean MAP at baseline was 95.71 mmHg and showed a statistically significant increase ($p < 0.05$) at T0 to T20.

	GROUP 1 (DEXMEDETOMIDINE)		GROUP 2 (SALINE)			
Time	**MEAN**	**SD**	**MEAN**	**SD**	**p-value**	**Inference**
Baseline	93.77	13.01	95.71	7.69	0.363	NS
T0	87.61	9.07	88.95	7.41	0.042	S
TP	95.53	11.08	102.19	8.37	0.032	S
T5	98.75	10.29	112.03	10.14	<0.0001	S
T10	95.28	8.43	111.76	10.81	<0.0001	S
T15	93.28	6.97	105.00	8.19	<0.01	S
T20	91.39	7.04	99.6	5.95	<0.01	S
T25	91.48	6.88	97.53	6.11	0.00083	S
T30	90.16	6.31	96.40	6.52	0.00099	S

Table 11: Mean of Mean Arterial Pressure of Group 1 and Group 2

Baseline is not significant (p = 0.363), meaning MAP was similar between the groups before intervention. **TP to T30 show significant differences (p < 0.05),** indicating MAP changes differed between the Dexmedetomidine and Saline groups at most time points with dexmedetomidine group showing lower MAP than saline group.



Graph 6: Mean MAP

6. **HEART RATE:**

GROUP 1 (DEXMEDETOMIDINE)

Timepoint	HR (Mean)	HR (SD)	P value	INFERENCE
Baseline	81.09	9.53	-	-
T0	67.03	5.92	<0.01	S
TP	71.97	5.88	0.00015	S
T5	74.03	7.70	<0.01	S
T10	73.03	7.41	0.00134	S
T15	72.72	7.82	0.0033	S
T20	71.13	8.30	0.0003	S
T25	71.53	12.34	0.078	NS
T30	70.16	7.78	<0.01	S

Table 12: Mean Heart Rate of Group 1

In dexmedetomidine group, mean heart rate at baseline was 81.09 bpm. It was observed that there was notable reduction ($p<0.05$) in HR compared to baseline.

GROUP 2 (SALINE)

Timepoint	HR (Mean)	HR (SD)	P value	INFERENCE
Baseline	76.38	7.20	-	-
T0	74.03	6.54	0.188	NS
TP	83.19	5.89	0.0053	S
T5	94.13	8.41	<0.00001	S
T10	95.16	10.33	<0.00001	S
T15	87.88	9.51	<0.00001	S
T20	82.19	7.84	0.0085	S
T25	78.00	6.30	0.430	NS
T30	76.47	5.27	0.403	NS

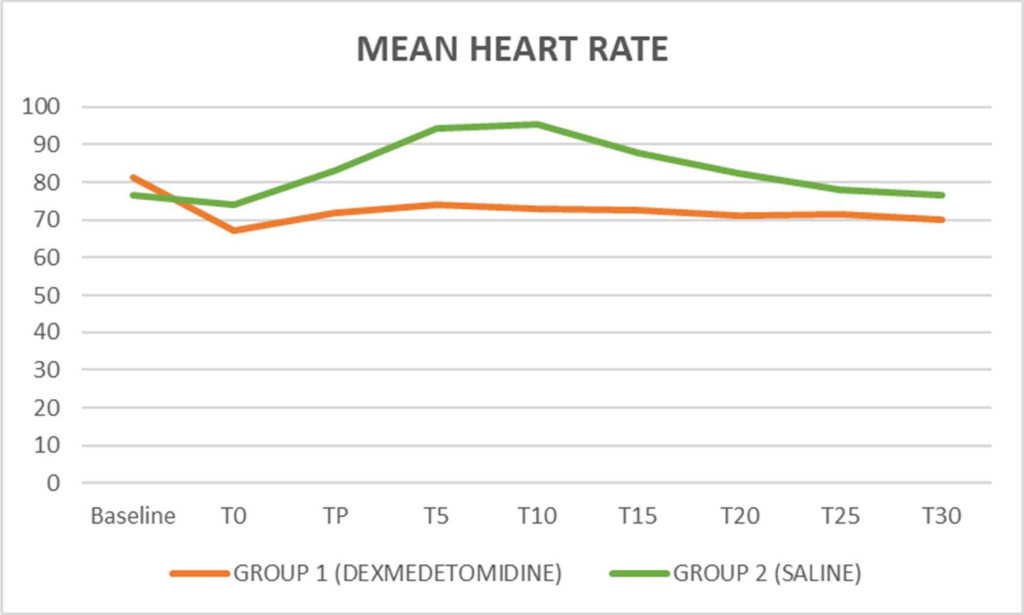
Table 13: Mean Heart Rate of Group 2

Mean heart rate in saline group at baseline is 76.38 bpm. **TP, T5, T10, T15, and T20 are significant ($p < 0.05$),** indicating a statistically significant HR increase from baseline.

	GROUP 1 (DEXMEDETOMIDINE)		GROUP 2 (SALINE)			
Time	**MEAN**	**SD**	**MEAN**	**SD**	**p-value**	**Inference**
Baseline	81.09	9.53	76.38	7.20	0.313	NS
T0	67.03	5.92	74.03	6.54	0.0001	S
TP	71.97	5.88	83.19	5.89	0.0001	S
T5	74.03	7.70	94.13	8.41	0.0001	S
T10	73.03	7.41	95.16	10.33	0.0001	S
T15	72.72	7.82	87.88	9.51	0.0001	S
T20	71.13	8.30	82.19	7.84	0.00033	S
T25	71.53	12.34	78.00	6.30	0.065	NS
T30	70.16	7.78	76.47	5.27	0.0011	S

Table 14: Mean Heart Rate of Group 1 and Group 2

Dexmedetomidine group saw a consistently substantial ($p<0.001$) decrease in heart rate when compared to the other group at almost all times.



Graph 7: Mean Heart Rate

7. **OXYGEN SATURATION:**

With respect to SpO2 levels, both the groups have been comparable. There was no fall in SpO2 levels and was maintained at 98-100% in the two groups.

8. **RAMSAY SEDATION SCORE:**

RSS	Group 1	Group 2
Pre-Induction	1(30), 2(2)	1(32)
Total	32	32
Pearson chi-square = 2.065, p-value = 0.473		

Table 15: Ramsay Sedation Score

The Ramsay Sedation Score was assessed in two groups preoperatively, and no significant difference was found between the two groups. All patients showed a score of 1 with only 2 subjects in Group 1 showing RSS of 2.

No side effects were seen in Group 1 such as nausea, vomiting or allergic reaction.

DISCUSSION

Our study titled "STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL" aimed to evaluate the efficacy of intranasal dexmedetomidine in reducing the stress response to pneumoperitoneum. A total of 64 patients classified as ASA I & II were randomly assigned to 2 groups of 32 each. Group 1 was given 1.5 mcg/kg intranasal undiluted dexmedetomidine prepared from injectable formulation (100mcg/ml). Ten minutes prior to induction, a 1 ml tuberculin syringe was used to drip an equal dosage of intranasal medication into each nostril while the patient was supine. Group 2 received an intranasal administration of the same volume of saline. Hemodynamic parameters were monitored. SBP, DBP, MAP, HR & SpO2 were recorded 5 minutes prior to insertion of ports, during insufflation of abdomen and then every 5 minutes for 30 minutes.

The aim of this study was to find an alternative route to administer dexmedetomidine without the adverse effects of intravenous route and evaluate its efficacy in reducing stress response to laparoscopic insufflation.

Dexmedetomidine is a highly selective α2 adrenergic agonist. It produces sedation, anxiolysis, analgesia and sympatholysis via brain and spinal cord's α2 A, α2 B and α2 C receptors. Stimulation of α2A receptors in brainstem vasomotor centre leads to sympathetic outflow suppression causing hypotension and bradycardia.

There are several ways to administer dexmedetomidine like intraoral, intranasal, intravenous, and intramuscular. Sedation, severe bradycardia and hypotension are the primary drawbacks of intravenous usage. The intranasal method is more practical because it requires no intravenous infusion and is painless, odourless

and tasteless. Intranasal medications can directly access the CNS and cross the blood-brain barrier. Dexmedetomidine can access the systemic circulation quickly by avoiding the liver's first pass metabolism because of rich vascularity of nasal mucosa.[11,12,13,14]

In a study by "Li et al., on the pharmacokinetics & pharmacodynamics of intranasal dexmedetomidine" demonstrated a delayed and steady onset compared to intravenous route.[14] While rapid IV administration leads to elevated peak plasma levels and quicker onset, our study favoured the gradual onset of the intranasal route to avoid the α2 agonist effects associated with rapid IV delivery, such as hypotension and bradycardia.

Additionally, study evaluating dexmedetomidine via nasal route as a sedative premedication reported effective perioperative anxiety control without prolonging anaesthetic recovery.[59] IN dexmedetomidine has shown to be a safe option for procedure related sedation in pediatric dental patients, offering high patient cooperation and swift recuperation, without recorded incidents of O2 desaturation or apnoea.

This trend was also evident in our research where there were no desaturation episodes after intranasal administration.

Based on these we can understand that IN dexmedetomidine is as efficacious as intravenous route and is linked with mild sedation with no respiratory depression, anxiolysis and minimal hypotension and bradycardia. Hence, we used intranasal route in our study.

Regarding the dosage of intranasal dexmedetomidine, 18 subjects part of a A Double-Blind, Crossover Assessment trial by Yuen et al to assess the sedative, analgesic and hemodynamic effect of different doses of dexmedetomidine were divided into three groups and given either a placebo or intranasal dexmedetomidine 1mc/kg and 1.5 mcg/kg. It has been shown that both the dexmedetomidine groups showed good reduction in hemodynamic parameters during the procedure. These results prompted us to select 1.5 mcg/kg as the dose for our trial.[5]

In a study on the onset time and duration of action of intranasal dexmedetomidine, Yuen et al. demonstrated that the effect of Dexmedetomidine began within 25 (25-30) minutes and lasted for approximately 85 (35-100) mins. According to these findings, it is suggested that administering IN dexmedetomidine 25 to 40 mins prior to stimulus can achieve the desired outcome.[60] Additionally, Yuen et al. reported that when administered 40-45 mins preoperatively, 91% of children experienced adequate sedation. In comparison with the above article, in our study intranasal dexmedetomidine was administered 30 minutes before creation of pneumoperitoneum or 10 minutes before shifting to OT.

Regarding the observations in our study, following intranasal administration, vitals were recorded every 10 mins before shifting to OT. The concept behind this being the pharmacokinetics and pharmacodynamics of intranasal route which is associated with slow and gradual onset resulting in achieving peak concentrations slowly. Also since the hemodynamic variations were not as much compared to intravenous route as evidenced in other studies. Parameters were noted every 5mins after shifting to OT till 30 minutes after pneumoperitoneum.[4]

In our study, randomisation was done using a computer generated list. Since it was double blinded, both the patient and the observer were blinded. They did not know which group they were assigned to. The drug was prepared by another fellow doctor and given intranasally. This helped in avoiding any bias during the study.

In our study it was noted that the age and gender were equally comparable between the two groups. With respect to SBP, DBP, MAP & HR, substantial difference was seen among both groups.

With respect to SBP, both the groups showed reduction in SBP post induction and then a statistically significant rise during and after creation of pneumoperitoneum but the rise in dexmedetomidine groups was less clinically substantial. By comparing the two groups it can be seen that dexmedetomidine had a significantly reduced SBP response than saline group. T5, T10, T15 & T20 showed $p < 0.000001$ suggesting a major difference in SBP between groups at these points.

On studying the DBP data, the dexmedetomidine group showed insignificant rise in DBP whereas the saline group had a statistically significant rise at TP, T5, T10, T15, T20, and T25 with $p < 0.05$ indicating the need for intervention. On comparing the two groups, it can be seen that dexmedetomidine group was superior in avoiding major DBP changes over time.

On comparing MAP in two groups, statistically notable increase in saline group was seen needing intervention whereas in dexmedetomidine group the rise in MAP was not statistically different from baseline at all times. Significant difference in the two groups was seen from T5 to T20 with $p<0.001$ indicating better hemodynamic control in dexmedetomidine group.

With respect to heart rate between the groups, dexmedetomidine group maintained heart rate lower than baseline which was statistically significant ($p<0.05$). Saline group had substantial HR increase from baseline at TP, T5, T10, T15, and T20 with $p < 0.05$. On comparison it was determined to have statistically significant fall in dexmedetomidine group at almost all time points.

Also, SpO2 readings were maintained between 98-100% in all patients throughout the study.

The Ramsay Sedation Score was assessed preoperatively and the score was noticed to be 1 or 2 in patients in dexmedetomidine group and 1 in all subjects in saline group.

Bhattacharjee et al. conducted a study that found an IV infusion of DEX 0.2 mcg/kg/hr, 5 minutes before induction, effectively reduced the rise in MAP and HR during and after pneumoperitoneum. This contributed to improved perioperative hemodynamic stability during laparoscopic procedure.[6]

The efficacy of intranasal dexmedetomidine has also been proven in adult patients during both LA and GA. “Jayaraman et al. in a comparative study evaluated the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery”. They noted that intranasal dexmedetomidine was effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation in adult obese patients.[10]

Similarly, in a study done by “Niyogi et al for comparison of intranasal and intravenous dexmedetomidine for attenuation of stress responses to laryngoscopy and endotracheal intubation” using IV (0.5 mcg/kg) and intranasal (1mcg/kg)

dexmedetomidine, found that both the routes were equally efficacious in attenuating stress response to laryngoscopy and intubation.[4]

Likewise in our study as well intranasal DEX was efficient in diminishing pressor response to pneumoperitoneum when compared to Saline group.

No side effects were seen in Group 1 such as nausea, vomiting or allergic reaction. Patients receiving Dexmedetomidine showed bradycardia however, it was not clinically significant to warrant any intervention.

Limitations:

A few limitations may be considered in this study.

- Power of the study maybe lesser due to smaller sample sizes.
- The results may be better validated if it was done in ASA III and above patients as well since the response could be varied compared to ASA I and II patients.
- Not being a multicentre study limits its generalizability as the study was only conducted at one centre.

Future scope:

We believe that intranasal dexmedetomidine can prove to be an ideal drug because of the many advantages over the intravenous route. These benefits could also be used before performing regional blocks in adult and paediatric patients due to good analgesia and anxiolysis without respiratory depression. Further multicentre studies maybe done on intranasal route of administration as compared with intravenous route on larger study populations.

Thus, we found that intranasal dexmedetomidine was efficient in mitigating pressor response to pneumoperitoneum in laparoscopic surgeries without any significant side effects.

CONCLUSION

Our study showed that hemodynamic parameters (SBP, DBP, MAP & HR) were more stable in dexmedetomidine group than saline group. The reduction in heart rate was not clinically significant enough to necessitate intervention in dexmedetomidine group. We conclude that intranasal dexmedetomidine is beneficial for attenuation of stress response to pneumoperitoneum in laparoscopic surgeries without notable side effects. Intranasal route is effective, easy to administer and comfortable to the patient**.**

SUMMARY

The present study focused on assessing the efficacy of intranasal route of administration of a dexmedetomidine.

The study aimed to study the effect of intranasal dexmedetomidine on stress response to pneumoperitoneum in laparoscopic surgeries under general anaesthesia. Additionally any side effects of the study drug were noted. This randomised controlled trial included 64 patients, “ASA grade I” and “II”, ages 18 to 60, who were treated at “KLES Prabhakar Kore Hospital & Medical Research Centre in Belagavi”. Participants were randomly assigned into 2 groups of 32 each.

GROUP 1: received 1.5 mcg/kg of intranasal dexmedetomidine

GROUP 2: received similar volume of intranasal normal saline

Hemodynamic parameters (SBP, DBP, MAP, HR and SpO2) were noted 5 mins before creating pneumoperitoneum, during abdominal insufflation and then every 5 minutes till 30mins.

We observed that intranasal dexmedetomidine significantly helped attenuate the stress response to pneumoperitoneum with respect to SBP, DBP, MAP and HR, especially from TP to T15.

According to the study's findings, patients undergoing laparoscopic procedures can achieve hemodynamic stability during abdominal insufflation using intranasal dexmedetomidine as a premedication without any side effects.

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ANNEXURE 1: CONSENT FORM

KAHERs

JNMC, BELAGAVI

"STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL"

Name of student/principal investigator: DR. _____

Name of guide investigators: DR. _____

Objective:

To study the effect of intranasal Dexmedetomidine on hemodynamic parameters during pneumoperitoneum in patients undergoing laparoscopic surgery.

Explanation of procedure:

If you agree to enroll in my study, I will ask you present, past and family history. Then you will be clinically examined in detail. You will be allotted into one of the two groups randomly using computer generated software.

GROUP 1: will receive 1.5 mcg/kg of intranasal dexmedetomidine

GROUP 2: will receive similar volume of intranasal normal saline if they were to receive Dexmedetomidine.

Withdrawal from participation in the study:

Participation in this study in voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study:

You will not have nor get any benefits by Participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person to identify you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Cost of investigations done during the course of study will be paid by the principal investigator.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purpose and/or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, in future or in case of study related injury or illness, you are free to contact:

If you have any questions or complaints with regard to your right as study participant you may contact DR HARSHA HEGDE, Chairperson, Ethical committee of JNMC, 0831-2473777 extension 4052.

Legal rights: By signing this consent form, we are not waiving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study **"STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL**". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the
participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE II – PROFORMA

"STUDY OF EFFECT OF INTRANASAL DEXMEDETOMIDINE ON STRESS RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES: A ONE YEAR DOUBLE BLINDED HOSPITAL BASED RANDOMISED CLINICAL TRIAL"

GROUP ALLOTTED: **1** **2**

Date of examination: IP No.:

Name:

Age: gender: occupation:

Address:

PRE-ANAESTHETIC EVALUATION:

Chief complaints:

Past history:

- H/o co-morbidities and drug intake:
- H/o previous surgeries where difficult airway was encountered:
- Previous Anaesthetic experience:

General physical examination:

Height(cm): Weight(kgs): BMI:

Pallor: Icterus: Cyanosis:

Clubbing: Temperature:

BP: PR: RR: SPO2:

SYSTEMIC EXAMINATION:

- CVS:
- RS:
- GIT:
- CNS:

AIRWAY ASSESSMENT:

Teeth: Jaw movements:

INVESTIGATIONS:

Hb(gm/dl): TLC: Platelet count:

Serum creatinine: FBS: Chest x-ray:

ECG:

PREOPERATIVE PHYSICAL STATUS:

ASA GRADE I II III IV V

DIAGNOSIS:

PROPOSED SURGERY:

RSS(Ramsay Sedation Score) – 1 2 3 4 5 6

VITALS	SBP	DBP	MAP	HR	SPO2
BASELINE					
5 MINS BEFORE PNEUMOPERITONEUM					
AT THE TIME OF PNEUMOPERITONEUM					
5 MINS					
10 MINS					
15MINS					
20 MINS					
25 MINS					
30 MINS					

SBP - Systolic blood pressure

DBP - Diastolic blood pressure

MAP - Mean arterial pressure

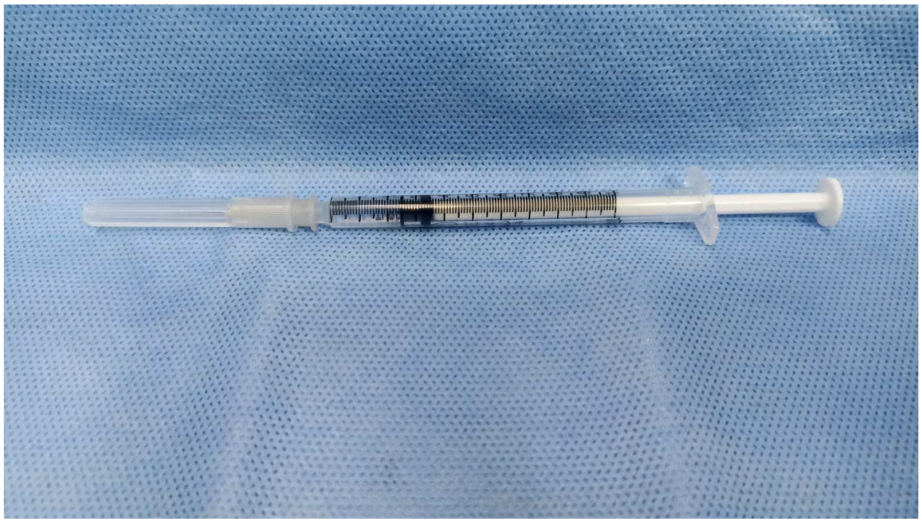
HR - Heart rate

SPO2- Peripheral oxygen Saturation

INVESTIGATOR	
WITNESS	
ANAESTHESIOLOGIST	

ANNEXURE III – PHOTOGRAPHS

Photograph 1: Dexmedetomidine Ampoule



Photograph 2: Tuberculin Syringe

ANNEXURE IV – KEY TO MASTERCHART

ASA	American Society of Anesthesiologists
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
MAP	Mean Arterial Pressure
HR	Heart Rate
SpO2	Peripheral Oxygen Saturation
M, F	Male, Female

ANNEXURE V – MASTERCHART

GROUP 1

SL NO	AGE (YRS)	SEX	ASA GRADE	DIAGNOSIS	SURGERY	BASELINE					T0					TP					T5				
						SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2
1	49	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	110	70	83	72	100	100	60	73	68	100	120	80	93	69	100	118	74	89	74	100
2	47	M	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	140	98	112	78	100	110	80	90	70	100	130	90	103	72	100	142	94	110	66	100
3	38	F	1	UTERINE PROLAPSE	TOTAL LAPAROSCOPIC HYSTERECTOMY	122	84	97	74	100	108	72	84	68	100	110	77	88	70	100	130	88	102	68	100
4	63	M	1	CHOLELITHIASIS + EPIGASTRIC HERNIA	LAP CHOLECYSTECTOMY+ HERNIOPLASTY	136	84	101	74	100	122	72	89	68	100	121	80	94	66	100	132	90	104	68	100
5	21	F	1	BROAD LIGAMENT FIBROID	DIAGNOSTIC LAPAROSCOPY AND PROCEED	120	70	87	88	100	112	76	88	72	100	116	82	93	78	100	127	88	101	79	100
6	36	F	1	UMBILICAL HERNIA	LAP HERNIA REPAIR	99	66	77	69	100	135	88	104	62	100	147	104	118	71	100	139	94	109	78	100
7	48	M	1	STUMP APPENDICITIS	DIAGNOSTIC LAPAROSCOPY AND PROCEED	129	75	93	81	100	116	78	91	64	100	111	73	86	70	100	123	87	99	72	100
8	27	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	120	0	40	82	100	110	70	83	77	100	130	90	103	80	100	128	88	101	81	100
9	61	F	2	CALCULOUS CHOLECYSTITIS	LAP CHOLECYSTECTOMY	140	90	107	80	100	122	72	89	70	100	138	90	106	79	100	132	88	103	80	100
10	37	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	140	100	113	82	100	93	62	72	72	100	110	73	85	67	100	128	96	107	64	100
11	33	M	1	HIATUS HERNIA	LAPAROSCOPY AND PROCEED	108	82	91	68	100	110	70	83	54	100	129	109	116	59	100	120	84	96	64	100
12	27	M	1	RIGHT INGUINAL HERNIA	LAPAROSCOPIC HERNIA REPAIR	115	81	92	80	100	98	59	72	71	100	101	56	71	68	100	101	57	72	69	100
13	21	M	1	LEFT INGUINAL HERNIA	LAPAROSCOPIC HERNIA REPAIR	130	82	98	75	100	96	55	69	61	100	95	58	70	67	100	102	64	77	63	100
14	49	M	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	128	80	96	80	100	114	70	85	72	100	126	88	101	77	100	124	82	96	78	100
15	46	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	128	88	101	82	100	120	82	95	71	100	132	90	104	78	100	128	86	100	68	100
16	34	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	118	74	89	90	100	106	71	83	80	100	121	87	98	84	100	116	82	93	81	100

17	**31**	**F**	**1**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**130**	**88**	**102**	**86**	**100**	**120**	**90**	**100**	**66**	**100**	**122**	**84**	**97**	**78**	**100**	**130**	**93**	**105**	**68**	**100**
18	**20**	**M**	**1**	**B/L VARICOCOELE**	**DIAGNOSTIC LAPAROSCOPY AND PROCEED**	**127**	**73**	**91**	**87**	**100**	**105**	**66**	**79**	**76**	**100**	**125**	**82**	**96**	**79**	**100**	**104**	**67**	**79**	**74**	**100**
19	**45**	**M**	**1**	**UMBILICAL HERNIA**	**LAP HERNIA REPAIR**	**122**	**82**	**95**	**82**	**100**	**112**	**80**	**91**	**68**	**100**	**128**	**88**	**101**	**72**	**100**	**122**	**86**	**98**	**69**	**100**
20	**53**	**F**	**2**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**132**	**82**	**99**	**78**	**100**	**128**	**78**	**95**	**61**	**100**	**124**	**72**	**89**	**78**	**100**	**132**	**84**	**100**	**76**	**100**
21	**54**	**M**	**1**	**ACUTE APPENDICITIS**	**LAP APPENDICECTOMY**	**110**	**70**	**83**	**80**	**100**	**118**	**89**	**99**	**65**	**100**	**122**	**104**	**110**	**71**	**100**	**142**	**117**	**125**	**81**	**100**
22	**60**	**M**	**1**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**116**	**86**	**96**	**67**	**100**	**122**	**88**	**99**	**54**	**100**	**134**	**98**	**110**	**62**	**100**	**128**	**88**	**101**	**68**	**100**
23	**57**	**M**	**2**	**INGUINAL HERNIA**	**LAP AND PROCEED**	**132**	**74**	**93**	**82**	**100**	**128**	**72**	**91**	**71**	**100**	**130**	**70**	**90**	**72**	**100**	**128**	**74**	**92**	**70**	**100**
24	**61**	**F**	**2**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**142**	**92**	**109**	**72**	**100**	**128**	**82**	**97**	**63**	**100**	**134**	**88**	**103**	**68**	**100**	**140**	**90**	**107**	**70**	**100**
25	**62**	**M**	**1**	**CA STOMACH**	**DIAGNOSTIC LAP AND PROCEED**	**110**	**70**	**83**	**72**	**100**	**96**	**66**	**76**	**64**	**100**	**108**	**70**	**83**	**68**	**100**	**114**	**74**	**87**	**70**	**100**
26	**44**	**M**	**2**	**UMBILICAL HERNIA**	**LAP HERNIA REPAIR**	**138**	**84**	**102**	**76**	**100**	**128**	**80**	**96**	**62**	**100**	**128**	**82**	**97**	**66**	**100**	**136**	**88**	**104**	**68**	**100**
27	**32**	**F**	**1**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**110**	**70**	**83**	**82**	**100**	**112**	**74**	**87**	**71**	**100**	**114**	**76**	**89**	**76**	**100**	**122**	**80**	**94**	**92**	**100**
28	**39**	**F**	**1**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**132**	**82**	**99**	**76**	**100**	**122**	**76**	**91**	**68**	**100**	**122**	**74**	**90**	**68**	**100**	**132**	**86**	**101**	**82**	**100**
29	**33**	**F**	**1**	**APPENDICITIS**	**LAP APPENDICECTOMY**	**124**	**80**	**95**	**72**	**100**	**100**	**70**	**80**	**64**	**100**	**112**	**76**	**88**	**70**	**100**	**130**	**88**	**102**	**82**	**100**
30	**33**	**F**	**1**	**CHOLELITHIASIS**	**LAP CHOLECYSTECTOMY**	**122**	**82**	**95**	**70**	**100**	**114**	**72**	**86**	**62**	**100**	**115**	**74**	**88**	**66**	**100**	**128**	**84**	**99**	**72**	**100**
31	**47**	**M**	**1**	**INGUINAL HERNIA**	**LAP HERNIA REPAIR**	**132**	**90**	**104**	**82**	**100**	**126**	**88**	**101**	**69**	**100**	**132**	**90**	**104**	**80**	**100**	**144**	**92**	**109**	**94**	**100**
32	**44**	**F**	**2**	**SUPRAUMBLICAL REPAIR**	**DIAGNOSTIC LAP AND PROCEED**	**138**	**72**	**94**	**88**	**100**	**124**	**70**	**88**	**61**	**100**	**126**	**74**	**91**	**74**	**100**	**132**	**80**	**97**	**80**	**100**

T10					T15					T20					T25					T30					RSS
SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	pre induction
114	70	85	70	100	108	68	81	68	100	110	70	83	66	100	107	68	81	67	100	106	66	79	68	100	1
132	88	103	64	100	130	84	99	66	100	122	76	91	64	100	124	72	89	63	100	125	70	88	66	100	2
120	88	99	68	100	122	81	95	66	100	118	70	86	66	100	116	70	85	64	100	112	78	89	65	100	1
126	88	101	66	100	124	84	97	64	100	125	86	99	67	100	122	80	94	65	100	120	82	95	64	100	1
135	94	108	72	100	134	92	106	88	100	135	92	106	84	100	129	86	100	82	100	129	85	100	79	100	1
131	90	104	79	100	118	80	93	68	100	117	80	92	67	100	116	80	92	69	100	115	79	91	67	100	1
119	81	94	79	100	121	86	98	77	100	124	78	93	85	100	119	83	95	72	100	113	72	86	72	100	1
126	84	98	77	100	128	82	97	92	100	122	82	95	88	100	128	88	101	87	100	126	80	95	88	100	1
128	80	96	78	100	124	82	96	74	100	126	84	98	72	100	122	82	95	74	100	120	84	96	72	100	1
105	75	85	64	100	105	81	89	72	100	97	75	82	64	100	96	74	81	65	100	97	69	78	68	100	1
122	82	95	66	100	124	84	97	72	100	122	82	95	74	100	124	82	96	72	100	126	82	97	72	100	1
101	58	72	67	100	102	61	75	73	100	103	63	76	62	100	105	63	77	60	100	103	64	77	62	100	1
103	66	78	59	100	102	66	78	61	100	101	66	78	61	100	101	65	77	59	100	101	65	77	60	100	1

120	**82**	**95**	**79**	**100**	**118**	**78**	**91**	**78**	**100**	**116**	**76**	**89**	**80**	**100**	**118**	**72**	**87**	**76**	**100**	**120**	**78**	**92**	**78**	**100**	**1**
126	**84**	**98**	**70**	**100**	**124**	**82**	**96**	**82**	**100**	**122**	**84**	**97**	**86**	**100**	**124**	**88**	**100**	**84**	**100**	**126**	**84**	**98**	**82**	**100**	**2**
132	**94**	**107**	**80**	**100**	**112**	**81**	**91**	**79**	**100**	**122**	**87**	**99**	**85**	**100**	**127**	**91**	**103**	**125**	**100**	**116**	**83**	**94**	**82**	**100**	**1**
125	**83**	**97**	**70**	**100**	**130**	**90**	**103**	**82**	**100**	**133**	**89**	**104**	**70**	**100**	**122**	**85**	**97**	**68**	**100**	**125**	**83**	**97**	**63**	**100**	**1**
117	**84**	**95**	**87**	**100**	**120**	**81**	**94**	**80**	**100**	**117**	**80**	**92**	**79**	**100**	**123**	**81**	**95**	**81**	**100**	**115**	**77**	**90**	**84**	**100**	**1**
124	**83**	**97**	**84**	**100**	**118**	**80**	**93**	**84**	**100**	**117**	**78**	**91**	**82**	**100**	**118**	**80**	**93**	**84**	**100**	**118**	**78**	**91**	**86**	**100**	**1**
122	**74**	**90**	**74**	**100**	**126**	**72**	**90**	**76**	**100**	**124**	**74**	**91**	**72**	**100**	**128**	**72**	**91**	**72**	**100**	**126**	**72**	**90**	**74**	**100**	**1**
135	**102**	**113**	**77**	**100**	**119**	**95**	**103**	**71**	**100**	**114**	**86**	**95**	**69**	**100**	**111**	**88**	**96**	**67**	**100**	**103**	**79**	**87**	**65**	**100**	**1**
126	**82**	**97**	**69**	**100**	**122**	**82**	**95**	**72**	**100**	**110**	**72**	**85**	**70**	**100**	**118**	**80**	**93**	**68**	**100**	**116**	**78**	**91**	**66**	**100**	**1**
124	**72**	**89**	**68**	**100**	**126**	**78**	**94**	**66**	**100**	**122**	**70**	**87**	**68**	**100**	**120**	**78**	**92**	**70**	**100**	**122**	**74**	**90**	**68**	**100**	**1**
138	**88**	**105**	**68**	**100**	**134**	**82**	**99**	**66**	**100**	**133**	**80**	**98**	**67**	**100**	**131**	**82**	**98**	**66**	**100**	**130**	**80**	**97**	**66**	**100**	**1**
110	**72**	**85**	**68**	**100**	**108**	**70**	**83**	**64**	**100**	**107**	**68**	**81**	**62**	**100**	**108**	**68**	**81**	**62**	**100**	**108**	**70**	**83**	**64**	**100**	**1**
132	**82**	**99**	**64**	**100**	**128**	**80**	**96**	**62**	**100**	**127**	**78**	**94**	**60**	**100**	**128**	**78**	**95**	**58**	**100**	**126**	**80**	**95**	**60**	**100**	**1**
115	**78**	**90**	**86**	**100**	**112**	**76**	**88**	**78**	**100**	**110**	**74**	**86**	**74**	**100**	**110**	**74**	**86**	**76**	**100**	**111**	**76**	**88**	**74**	**100**	**1**
128	**80**	**96**	**76**	**100**	**124**	**78**	**93**	**66**	**100**	**122**	**76**	**91**	**64**	**100**	**123**	**76**	**92**	**64**	**100**	**122**	**76**	**91**	**64**	**100**	**1**

126	**82**	**97**	**78**	**100**	**122**	**80**	**94**	**70**	**100**	**120**	**78**	**92**	**68**	**100**	**119**	**71**	**87**	**67**	**100**	**117**	**70**	**86**	**66**	**100**	**1**
117	**80**	**92**	**68**	**100**	**118**	**78**	**91**	**62**	**100**	**115**	**77**	**90**	**60**	**100**	**118**	**77**	**91**	**62**	**100**	**118**	**76**	**90**	**62**	**100**	**1**
130	**88**	**102**	**88**	**100**	**128**	**86**	**100**	**76**	**100**	**127**	**86**	**100**	**70**	**100**	**128**	**84**	**99**	**72**	**100**	**128**	**86**	**100**	**70**	**100**	**1**
126	**72**	**90**	**74**	**100**	**124**	**70**	**88**	**72**	**100**	**122**	**70**	**87**	**70**	**100**	**120**	**72**	**88**	**68**	**100**	**120**	**72**	**88**	**68**	**100**	**1**

GROUP 2

SL NO	AGE(YRS)	SEX	ASA GRADE	DIAGNOSIS	SURGERY	BASELINE					T0					TP				
						SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2
1	46	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	128	78	95	72	100	110	74	86	68	100	124	82	96	78	100
2	43	M	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	132	90	104	76	100	100	70	80	78	100	124	88	100	80	100
3	48	F	2	APPENDICITIS	LAP APPENDICECTOMY	138	86	103	84	100	122	77	92	79	100	148	101	117	97	100
4	45	M	2	APPENDICITIS	LAP APPENDICECTOMY	144	99	114	82	100	125	84	98	79	100	145	98	114	86	100
5	62	M	2	INGUINAL HERNIA	LAP HERNIA REPAIR	150	90	110	76	100	134	82	99	68	100	147	99	115	79	100
6	57	M	2	CHOLELITHIASIS + UMBILICAL HERNIA	LAP CHOLECYSTECTOMY + HERNIA REPAIR	140	78	99	99	100	101	82	88	96	100	140	98	112	84	100
7	48	M	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	122	77	92	68	100	114	72	86	64	100	129	86	100	78	100
8	63	M	2	UMBILICAL HERNIA	LAP HERNIA REPAIR	142	90	107	77	100	114	78	90	64	100	132	88	103	74	100
9	21	M	1	APPENDICITIS	LAP APPENDICECTOMY	118	70	86	66	100	100	70	80	64	100	132	90	104	68	100
10	50	M	2	GALL BLADDER EMPHYSEMA	LAP CHOLECYSTECTOMY	131	77	95	74	100	122	76	91	70	100	142	92	109	88	100
11	40	F	1	UMBILICAL HERNIA	LAP HERNIA REPAIR	126	82	97	78	100	104	79	87	70	100	128	86	100	83	100
12	60	M	2	CALCULOUS CHOLECYSTITIS	LAP CHOLECYSTECTOMY	141	78	99	82	100	127	78	94	74	100	134	80	98	82	100
13	55	M	1	CALCULOUS CHOLECYSTITIS	LAP CHOLECYSTECTOMY	124	77	93	73	100	118	70	86	68	100	126	80	95	78	100
14	20	F	1	APPENDICITIS	LAP. APPENDICECTOMY	120	70	87	72	100	108	70	83	78	100	118	77	91	84	100
15	60	M	2	APPENDICITIS	LAP. APPENDICECTOMY	134	85	101	83	100	122	85	97	79	100	139	89	106	85	100
16	51	M	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	136	80	99	77	100	124	86	99	76	100	138	90	106	86	100
17	62	F	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	126	80	95	73	100	118	77	91	72	100	126	77	93	83	100

18	63	F	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	132	84	100	72	100	122	84	97	76	100	132	90	104	88	100
19	28	M	1	APPENDICITIS	LAP. APPENDICECTOMY	112	77	89	70	100	110	70	83	72	100	120	77	91	79	100
20	59	F	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	124	78	93	82	100	120	80	93	76	100	141	96	111	88	100
21	62	M	2	INGUINAL HERNIA + CHOLELITHIASIS	LAP CHOLECYSTECTOMY + HERNIA REPAIR	141	88	106	72	100	122	95	104	70	100	162	103	123	90	100
22	18	F	1	APPENDICITIS	LAP. APPENDICECTOMY	108	70	83	68	100	90	60	70	72	100	118	80	93	84	100
23	52	M	1	UMBILICAL HERNIA	LAP HERNIA REPAIR	127	76	93	80	100	122	80	94	84	100	133	94	107	94	100
24	34	M	1	PERFORATED APPENDIX	LAP APPENDICECTOMY	125	70	88	74	100	117	68	84	78	100	125	78	94	82	100
25	51	M	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	126	78	94	68	100	114	78	90	70	100	131	92	105	87	100
26	22	M	1	INGUINAL HERNIA + CHOLELITHIASIS	LAP HERNIA REPAIR	110	72	85	66	100	90	70	77	75	100	108	77	87	78	100
27	39	F	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	117	70	86	75	100	110	68	82	72	100	123	78	93	79	100
28	25	F	1	APPENDICITIS	LAP. APPENDICECTOMY	114	74	87	78	100	102	72	82	68	100	122	89	100	79	100
29	42	M	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	123	86	98	88	100	118	82	94	79	100	134	89	104	88	100
30	47	F	2	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	127	84	98	76	100	122	80	94	78	100	131	88	102	84	100
31	30	M	1	APPENDICITIS	LAP. APPENDICECTOMY	116	75	89	74	100	110	70	83	72	100	122	82	95	78	100
32	40	M	1	CHOLELITHIASIS	LAP CHOLECYSTECTOMY	127	85	99	89	100	114	80	91	80	100	131	89	103	91	100

T5					T10					T15					T20					T25					T30					RSS
SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	SBP	DBP	MAP	HR	SPO2	
148	100	116	99	100	148	101	117	108	100	147	99	115	96	100	130	88	102	82	100	131	90	104	78	100	127	86	100	74	100	1
144	98	113	96	100	151	102	118	101	100	138	90	106	89	100	130	82	98	78	100	132	88	103	79	100	129	84	99	80	100	1
152	99	117	104	100	139	90	106	97	100	121	86	98	84	100	115	80	92	78	100	118	82	94	77	100	123	80	94	76	100	1
154	104	121	101	100	148	98	115	97	100	132	90	104	83	100	128	86	100	79	100	131	86	101	78	100	130	87	101	76	100	1
162	114	130	98	100	158	102	121	109	100	144	99	114	107	100	138	90	106	100	100	146	90	109	94	100	144	90	108	86	100	1
175	126	142	98	100	165	134	144	99	100	161	105	124	90	100	137	101	113	83	100	94	74	81	73	100	93	72	79	71	100	1
142	94	110	92	100	142	90	107	88	100	134	89	104	85	100	129	84	99	80	100	128	84	99	75	100	128	82	97	74	100	1
146	94	111	85	100	152	98	116	90	100	140	92	108	88	100	135	84	101	82	100	136	80	99	77	100	132	80	97	77	100	1
127	88	101	64	100	120	77	91	60	100	118	70	86	56	100	112	70	84	55	100	110	68	82	56	100	110	66	81	58	100	1
159	112	128	103	100	166	110	129	110	100	147	99	115	98	100	134	90	105	84	100	122	86	98	76	100	121	85	97	76	100	1
136	90	105	92	100	134	88	103	94	100	122	88	99	90	100	122	80	94	86	100	126	79	95	83	100	126	80	95	82	100	1
149	90	110	98	100	151	99	116	103	100	139	90	106	94	100	129	88	102	82	100	131	88	102	79	100	130	86	101	80	100	1
141	90	107	90	100	144	92	109	95	100	136	88	104	88	100	130	86	101	79	100	134	85	101	74	100	131	85	100	74	100	1
128	78	95	95	100	129	80	96	98	100	127	79	95	90	100	122	78	93	86	100	124	80	95	82	100	122	77	92	80	100	1
148	100	116	103	100	154	102	119	104	100	140	98	112	94	100	129	90	103	88	100	130	88	102	80	100	130	90	103	81	100	1
151	102	118	108	100	158	102	121	102	100	147	96	113	95	100	130	88	102	87	100	132	90	104	79	100	131	88	102	78	100	1
145	99	114	97	100	147	99	115	95	100	138	90	106	88	100	130	87	101	84	100	126	84	98	80	100	126	85	99	76	100	1
148	96	113	96	100	140	90	107	89	100	136	90	105	80	100	131	86	101	83	100	127	82	97	76	100	127	82	97	75	100	1
131	88	102	87	100	131	86	101	84	100	125	80	95	79	100	122	79	93	73	100	120	77	91	72	100	120	76	91	72	100	1
149	100	116	92	100	147	96	113	88	100	136	90	105	81	100	136	88	104	76	100	131	83	99	77	100	131	80	97	78	100	1
156	103	121	102	100	171	101	124	93	100	158	94	115	86	100	139	91	107	80	100	139	85	103	78	100	124	94	104	78	100	1
122	78	93	90	100	124	80	95	92	100	118	78	91	87	100	117	78	91	82	100	118	78	91	78	100	118	76	90	76	100	1
144	98	113	100	100	140	90	107	98	100	131	88	102	90	100	132	88	103	85	100	132	87	102	84	100	128	88	101	79	100	1

137	90	106	89	100	136	90	105	94	100	130	88	102	92	100	126	84	98	89	100	124	84	97	83	100	124	86	99	80	100	1
142	98	113	94	100	144	98	113	89	100	136	90	105	82	100	130	84	99	80	100	130	82	98	76	100	131	80	97	75	100	1
124	86	99	85	100	128	87	101	88	100	120	82	95	80	100	121	81	94	79	100	122	84	97	76	100	121	82	95	72	100	1
135	88	104	83	100	128	86	100	79	100	120	84	96	74	100	121	82	95	72	100	120	80	93	69	100	121	80	94	68	100	1
129	90	103	88	100	126	90	102	97	100	128	96	107	90	100	122	88	99	86	100	118	77	91	76	100	110	70	83	74	100	1
146	97	113	99	100	140	96	111	94	100	137	92	107	90	100	128	88	101	87	100	131	80	97	82	100	128	78	95	79	100	1
148	99	115	96	100	144	102	116	114	100	145	100	115	107	100	136	97	110	100	100	134	92	106	91	100	132	90	104	88	100	1
136	88	104	86	100	130	94	106	88	100	124	88	100	80	100	120	80	93	78	100	122	78	93	78	100	121	77	92	76	100	1
149	99	116	102	100	140	102	115	108	100	138	98	111	99	100	131	90	104	87	100	130	86	101	80	100	128	87	101	78	100	1