



Anaesthesiology

A COMPARATIVE STUDY OF THE EFFICACY OF INTRAVENOUS PARACETAMOL AND DEXMEDETOMIDINE ON PERI OPERATIVE HEMODYNAMICS AND POST OPERATIVE ANALGESIA FOR PATIENTS UNDERGOING LAPAROSCOPIC SURGERY

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ABSTRACT Perioperative hemodynamic instability is one of the known complication of Laparoscopic surgeries. CO₂ insufflation causes increased abdominal pressure and hypercapnia which will contribute to undesirable hemodynamic changes. Dexmedetomidine when administered as a loading dose causes sedative, hypnotic, anxiolytic, analgesic and sympatholytic effect. In this study 60 Patients were randomised in two groups 30 each . Group 1/ Group P recieved 1gm paracetamol diluted in 100 ml 0.9% Normal saline IV over 10 minutes before induction. Group 2/Group D Bolus -1mcg/ kg diluted in 100 ml 0.9% Normal saline IV over 10 minutes before induction. Perioperative Hemodynamic parameters , post operative analgesia were compared. Increase in heart rate , blood pressure were found to be more in Group 1/Group P compared to Group 2/ Group 2/ Group D. Patients in both groups had moderated pain postoperatively and requires rescue analgesia after extubation. We observed the use of Dexmedetomidine is very effective in managing Perioperative Hemodynamic instability when compared to paracetamol

KEYWORDS : laparoscopic surgery, Dexmedetomidine, Hemodynamic instability, post operative analgesia

INTRODUCTION

Laparoscopic surgery is minimal invasive surgery that is associated with several advantages like smaller scar, reduced bleeding, reduced postoperative pain and infection which contributes to shorter hospital stay.CO₂ insufflation causes increased abdominal pressure and hypercapnia which may contribute to undesirable hemodynamic changes. Laparoscopy leads to ventilator changes as the pneumoperitoneum created decreases thoraco-pulmonary compliance by 30-50% in healthy and obese patients. Reduction in functional residual capacity and development of atelectasis due to elevation of the diaphragm and changes in the distribution of pulmonary ventilation and perfusion from increased airway pressure can be expected. However, increasing intra-abdominal pressure to 10-14 mm Hg with the patient in a 10-to 20-degree head-up or head-down position does not significantly modify either physiological dead space or shunt in patients without cardiovascular problems.

Goals of any anaesthetic technique are smooth onset of action, adequate intraoperative analgesia and amnesia, good surgical condition , rapid recovery and minimal adverse effects. Enhanced recovery is the outcome of applying a range of multimodal strategies that has been designed to prepare and optimize patients before, during and after surgery, ensuring prompt recovery and discharge. Stimulation of laryngeal and tracheal tissues during intubation causes catecholamine discharge, with an increase in sympathetic-adrenergic activity and also an increase in systemic arterial pressure and Heart rate. These increases begin with laryngoscopy.

Peritoneal insufflations to intra abdominal pressure >10 mm hg induces a significant alteration of hemodynamics such as increased intra abdominal pressure and hypercarbia. Hemodynamic insults secondary to increased intra abdominal pressure include increased afterload and preload and decreased cardiac output whereas ventilator consequences include increased airway pressures , hypercarbia and decreased pulmonary compliance.

AIMS AND OBJECTIVES OF STUDY

To study comparison of perioperative hemodynamic response and post

operative analgesia after loading dose of Paracetamol and Dexmedetomidine .Comparison of Paracetamol and Dexmedetomidine in terms of

- Hemodynamic response to Laryngoscopy and Intubation
- Intra operative hemodynamics
- Post operative analgesia

PHARMACOLOGY**PARACETAMOL**

Acetaminophen (Tylenol also known as Paracetamol ,N-acetyl -p-aminophenol) is a popular antipyretic and analgesic with little anti-inflammatory action. Acetaminophen has a central analgesic effect that is mediated through activation of descending serotonergic pathways .

Primary mechanism of action is still debatable and is thought to be inhibition of prostaglandin synthesis .At the spinal cord level ,it has been shown to antagonize neurotransmission by N-methyl-D-Aspartate (NMDA) ,substance P, and nitric oxide pathways.

Oral acetaminophen has excellent bioavailability .Used as first line analgesic in osteoarthritis and useful in patients in whom aspirin is contraindicated (peptic ulcer disease, aspirin hypersensitivity ,children with febrile illness).Conventional oral dose of acetaminophen is 325 to 650 mg every 4-6 hours total dose should not exceed 4 grams.[9]

An intravenous (IV) preparation provides analgesia for around 4 hours for 37% patients with acute postoperative pain . In clinical practice, paracetamol does not cause the side effects typically with other nonsteroid anti-inflammatory drugs (NSAID),which are thought to occur due to inhibition of peripheral COX-1 (gastric toxicity, antiplatelet activity).[6]



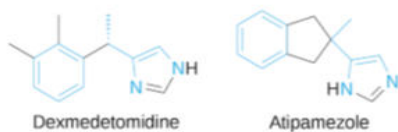
DEXMEDETOMIDINE

The alpha-2 adrenergic receptor agonists have sedative, anxiolytic, hypnotic, analgesic and sympatholytic effects.

Dexmedetomidine is a more selective alpha-2 agonist with a selectivity ratio for the alpha-2 receptor compared to alpha-1 receptor of 1600:1 as compared to a ratio of 220:1 for clonidine. It acts as a nonselective alpha 2 agonist on membrane bound G protein coupled alpha 2 adrenoreceptors. Three subtypes of alpha 2 adrenoreceptors have been described in humans: alpha 2A, alpha 2B, alpha 2C. The alpha 2A adrenoreceptors are primarily distributed in the periphery, whereas alpha 2B and alpha 2C are in the brain and spinal cord. Receptors located in the CNS and spinal cord are involved in sympatholysis, sedation, and antinociceptive effects of alpha 2 adrenoreceptors. The alpha 2 agonists have the advantage that their effects are readily reversible by alpha 2 adrenergic antagonist Eg: Atipamezole. Atipamezole is currently not approved for use in humans.[19]

PHYSIOCHEMICAL CHARACTERISTICS

Dexmedetomidine is the S enantiomer of medetomidine, a substance that has been used since many years in veterinary medicine for sedation and analgesia. The pKa is 7.1. It belongs to the imidazole subclass of alpha 2 receptor agonists.

**PHYSIOLOGICAL EFFECTS OF PNEUMOPERITONEUM CARDIOVASCULAR**

Increased IAP affects venous return (VR), systemic vascular resistance (SVR) and myocardial function. Because of autotransfusion of pooled blood from the splanchnic circulation initially there is an increase in venous return and cardiac output. Further increases in IAP result in compression of the inferior vena cava, reduction in venous return and subsequent decrease in cardiac output. SVR is increased due to direct effects of the IAP and because of release of circulating catecholamines especially epinephrine and norepinephrine. This change in SVR is greater than reduction of cardiac output maintaining or increasing blood pressure. The increasing SVR, systolic and diastolic blood pressures and tachycardia result in large increase in myocardial workload.

RESPIRATORY

The supine position and general anaesthesia decrease functional residual capacity (FRC). Pneumoperitoneum and the Trendelenburg position cause cephalad shift of the diaphragm, further decreasing FRC, possibly to values less than closing volume; this causes airway collapse, atelectasis, ventilation-perfusion (V/Q) mismatch, potential hypoxaemia and hypercarbia. There is an increase in airway resistance and reduction in compliance which potentiates the risk of barotrauma with positive pressure ventilation.

RENAL

Markedly increased IAP reduces renal function and urine output owing to an increase in renal vascular resistance and reduction in Glomerular Filtration Rate (GFR)

GASTROINTESTINAL

Increased IAP may cause regurgitation of gastric contents with associated risk of pulmonary aspiration which is particularly significant in the obese patient.

NEUROLOGICAL

Intracranial pressure (ICP) is increased by the rise in IAP, which may result in a decrease in the cerebral perfusion pressure (CPP), especially if there is a reduction in cardiac output.

COMPLICATIONS OF GAS INSUFFLATION ARRHYTHMIAS**SUBCUTANEOUS EMPHYSEMA, PNEUMOMEDIASTINUM AND PNEUMOTHORAX****VENOUS GAS EMBOLISM****MATERIAL AND METHOD**

After obtaining institutional ethical committee approval and written informed valid consent, a study in 60 patients of either sex, ASA I/II in the age group of 18-66 years was conducted.

STUDY DESIGN:

This is a prospective, randomised, observational, single blind study. It was done at Civil hospital Ahmedabad from December 2019 to June 2021. The study involved use of Dexmedetomidine and Paracetamol which were available in Government supply at Civil Hospital. Randomization was performed using a computer generated programme to allocate patients to various study groups using method of random number. Patients who were undergoing Laparoscopic surgeries under General Anaesthesia were divided into two groups, 30 patients in each group.

1. GROUP 1 OR GROUP P (PARACETAMOL)

1 gram Paracetamol diluted in 100 ml 0.9 percent Normal Saline IV over 10 minutes before induction.

2. GROUP 2 OR GROUP D (DEXMEDETOMIDINE)

Bolus: 1 mcg/kg diluted in 100 ml 0.9 percent Normal Saline IV over 10 minutes before induction.

Inclusion Criteria:

Patients in the age group of 18-66 years

- ASA-I/II
- Scheduled for Laparoscopic surgeries under General Anaesthesia

Exclusion Criteria:

- Patient refusal
- Patient with history of cardiac, respiratory, renal or hepatic failure
- Coagulation disorders
- Allergy to study medications

Source of Data:

Patients were screened for eligibility to participate in the study. Written informed consent was obtained who would be scheduled for laparoscopic surgeries in Civil hospital, Ahmedabad attached to B.J Medical College, Ahmedabad, Gujarat. Pre-operative evaluation was carried out a day before the surgery.

A thorough history was taken and examination was carried out in all patients. Patients were advised for routine and relevant investigations like CBC, renal and liver function tests, Random blood sugar, Chest X-Ray, 12 lead ECG and reports were reviewed. Patients were kept nil per oral (NPO) for 6 hours before surgery.

PROCEDURE

The procedure was explained to the patient and taken inside the operation theatre. All the minimum mandatory monitors, ECG, NIBP (non invasive blood pressure), pulse oximetry, end tidal CO₂ were applied, baseline hemodynamics were recorded and intravenous cannula of proper size was inserted into the largest vein on the forearm and an infusion of lactated ringer's solution was started at a rate of 5 ml/kg/hr.

PRE-MEDICATION-

All the patients were pre medicated with
Inj. Glycopyrrolate 0.004mg/kg IV
Inj. Ondansetron 0.15 mg/kg IV
Inj. Fentanyl 1mcg/kg IV

Now patients were randomly divided to one of the following two groups 30 patients each as per study drug injected.

Group 1 : Patient receiving loading dose of Paracetamol 1 gram IV in 100 ml 0.9% NS

Group 2 : Patient receiving loading dose of dexmedetomidine of 1mcg/kg IV in 100 ml 0.9% NS

Preoxygenation with 100% O₂ for 3-5 minutes. Induction was achieved with Inj Propofol 3mg/kg and Inj Succinylcholine 2mg/kg iv to facilitate intubation. Patient was intubated with appropriate sized endotracheal tube. After checking bilateral air entry, cuff was inflated and tube was fixed. Maintenance with 100% O₂ mixture with

Sevoflurane traces 1.5-2% and inj. Atracurium 0.5mg/kg. All patients were mechanically ventilated with tidal volume of 6ml/kg body weight and frequency of 12 cycles per minute using ventilator. PEEP of 3-5 cm H₂O 36 was applied. Ventilation Parameters were adjusted to maintain ETCO₂ 30-35 mm hg. Creation of pneumoperitoneum was allowed to maintain intraabdominal pressure 10-12 mmHg. After completion of surgery, neuromuscular blockade was reversed with Inj Glycopyrrolate 8mcg/kg and Inj Neostigmine 50mcg/kg IV. After thorough Oral and Endo-tracheal suction, extubation was done.

STATISTICAL ANALYSIS

Data were coded and recorded in MS Excel spreadsheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were expressed in terms of means and standard deviations for continuous variables. Data were presented in a graphical manner wherever appropriate for data visualization. Group comparisons for continuously distributed data were made using independent sample „t test when comparing 2 groups. If data were found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon Test were used. Chi squared test was used for group comparisons for categorical data.

P value was applied as follows:

- If $p > 0.05$, it means that there is no significant difference between means of two groups studied.
- If $p = 0.05$, it indicates that there is a significant difference at 5% level of significance (i.e out of 100, in 95 cases there is a significant difference)
- If $p < 0.05$, it indicates that the data is significant at 5% level of significance (i.e out of 100, in 95 cases there is a significant difference).

DISCUSSION

Laparoscopic surgeries allow for early mobilization, shorter hospital stay and are minimally invasive which makes these surgeries very popular these days. Main disadvantage can be said to be intra-operative hemodynamic instability due to pneumoperitoneum. Hence, as anaesthesiologists we must choose drugs which provide hemodynamic stability and aid in rapid recovery.

We chose Laparoscopic surgeries which have a short procedure time at our institute and minimal tissue handling which decreases intensity of postoperative pain and thus less potent analgesic like Dexmedetomidine can be compared to paracetamol. [10] We compared 60 patients of ASA physical status I-II undergoing laparoscopic surgery under General Anesthesia for intraoperative hemodynamic stability and post operative analgesic efficiency of intravenous Paracetamol and intravenous Dexmedetomidine.

In the two groups, the recorded values were tabulated for age, sex, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and VAS score post operatively. The result of the study was compared with the observation of other workers in the field of work taking into account for the differences as far as possible. The discussion of the study is as follows:

AGE AND SEX

Both the groups were comparable for age. The mean \pm SD of Age (Years) in the Group: 1 group was 37.87 ± 14.85 . The mean \pm SD of Age (Years) in the Group: 2 group was 36.33 ± 13.76 . The Age (Years) in the Group: 1 ranged from 18 - 66. The Age (Years) in the Group: 2 ranged from 18 - 65.

There was no significant difference between the groups in terms of Age (Years) ($p = 0.680$). Participants in the group Group: 1 had the larger proportion of Gender: Male. Participants in the group Group: 2 had the larger proportion of Gender: Female. There was a significant difference between the various groups in terms of distribution of Gender ($p = 0.037$).

HAEMODYNAMIC PARAMETERS

HEART RATE

The two groups differed significantly in terms of Heart Rate (BPM) at the following time points: During Laryngoscopy, During Intubation, 0 Minutes, 5 Minutes, 10 Minutes, 25 Minutes, 40 Minutes, 55 Minutes, 70 Minutes, 85 Minutes, 100 Minutes, 115 Minutes, 130 Minutes. There was a significant difference in the trend of Heart Rate (BPM) over time between the two groups ($p < 0.001$).

In our study we found that after giving loading dose of Inj. Dexmedetomidine in patient of Group 2 Heart Rate decreased significantly as compared to heart rate of patients in Group 1 who received Inj. Paracetamol. We also observed in our study that sympathoadrenal response to Laryngoscopy and intubation was significantly attenuated in the dexmedetomidine group (Group 2). Sarbari Swaika et al (2013) [6] found out in their study that the bolus of 1 mcg/kg Dexmedetomidine initially results in a transient increase of the blood pressure and a reflex fall in HR, especially in younger, healthy patients. Gowrishankar Reddy Manne et al (2014) [7] observed in their study that after starting dexmedetomidine infusion, the PR decreased highly significantly below the pre-infusion level. The effective attenuation of sympathoadrenal response to Intubation and Laryngoscopy with minimum side effects noted with 0.4mcg/kg/hour infusion.

Manjula Sarkar et al (2016) [10] observed that there was decreased heart rate and blood pressure during the bolus infusions suggesting that initial 1mcg/kg loading infusion for 10 minutes may not cause large blood concentrations of dexmedetomidine as dexmedetomidine can cause an increase in blood pressure and a decrease in heart rate with large concentrations or with rapid infusion rates. Activation of alpha 2 adrenoceptors on vascular smooth muscle is thought to result in vasoconstriction, increased blood pressure and probable reflex decreased heart rate. Quin Ye et al (2021) [23] concluded in their study that administration of 0.6 mcg/kg Dexmedetomidine before anaesthesia induction can attenuate the stress response during intubation, pneumoperitoneum and extubation, maintain hemodynamics more stable and relieve postoperative pain.

SYSTOLIC BLOOD PRESSURE

The two groups differed significantly in terms of Systolic BP (mmHg) at the following time points: Premedication, During Laryngoscopy, During Intubation, 0 Minutes, 5 Minutes, 10 Minutes, 25 Minutes, 40 Minutes, 55 Minutes, 70 Minutes, 85 Minutes, 100 Minutes, 115 Minutes, 130 Minutes. There was a significant difference in the trend of Systolic BP (mmHg) over time between the two groups ($p < 0.001$). We found in our study that after giving loading dose of Inj Dexmedetomidine in patients of Group 2 the systolic blood pressure reduced significantly and by the end of the surgery did not exceed the baseline values as compared to patients of Group 1 who received Inj Paracetamol where Systolic BP readings remained the same or increased during laryngoscopy, intubation and at the time of creation of pneumoperitoneum due to sympathoadrenal response as compared to baseline values. Sarbari Swaika et al (2013) [6] observed in their study that the intra-operative hemodynamic changes were similar in both the groups in respect to Heart Rate (HR), diastolic blood pressure, Mean arterial Blood Pressure except in the Systolic Blood Pressure where Dexmedetomidine significantly reduced it in comparison to Paracetamol ($P = 0.014$). Manjula Sarkar et al (2016) [10] observed in their study that incidence of hypotension was more in the Group D (Dexmedetomidine).

DIASTOLIC BLOOD PRESSURE

The two groups differed significantly in terms of Diastolic BP (mmHg) at the following time points: During Laryngoscopy, During Intubation, 0 Minutes, 5 Minutes, 10 Minutes, 25 Minutes, 40 Minutes, 55 Minutes, 70 Minutes, 85 Minutes, 100 Minutes, 115 Minutes, 130 Minutes. There was a significant difference in the trend of Diastolic BP (mmHg) over time between the two groups ($p < 0.001$). In our study we found higher fall in DBP in Group 2 (Group D) than Group 1 (Group P). Ridhima Sharma et al. (2017) [12] observed in their study that hemodynamic parameters remained stable in both the groups and did not show any comparative differences when analyzed statistically.

MEAN ARTERIAL PRESSURE

The two groups differed significantly in terms of MAP (mmHg) at the following time points: During Intubation, 0 Minutes, 5 Minutes, 10 Minutes, 25 Minutes, 40 Minutes, 55 Minutes, 70 Minutes, 85 Minutes, 100 Minutes, 115 Minutes, 130 Minutes. There was a significant difference in the trend of MAP (mmHg) over time between the two groups ($p < 0.001$). In our study we found significant fall in MAP readings in patients of Group 2 who received Inj Dexmedetomidine than patients of Group 1 who received Inj Paracetamol. Manne, et al. (2014) [7] observed in their study that MAP decreased significantly in Dex 0.2 group and highly significantly in Dex 0.4 group.

VAS SCORE

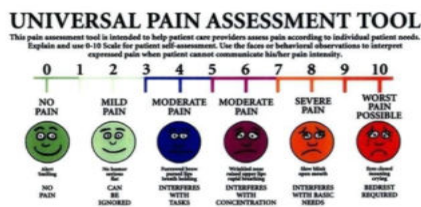
The two groups did not differ in terms of VAS at any of the time points. There was no significant difference in the trend of VAS over time between the two groups. In our study patients of both groups complained of moderate pain post extubation and were given either Inj. Diclofenac 75mg IV or Inj. Tramadol 100 mg IV in 100 ml 0.9% NS. From this we can conclude that loading dose of Dexmedetomidine and Paracetamol given before induction in our study was not adequate for post operative analgesia and patients required rescue analgesia in forms of other analgesics immediately after extubation. VAS scores were monitored for 6 hours post-operatively which showed progressive decline of VAS score over time. Manjula Sarkar et al. (2016)[10] concluded that there was no significant difference in VAS score but rescue analgesia requirement was more in the Dexmedetomidine group while Paracetamol consistently showed less VAS score without requiring frequent rescue analgesia. Ridhima Sharma et al.(2017)[12] observed in their study that mean value of VAS was more in PCM group compared to dexmedetomidine group at all time intervals. Time to administration of the first dose of rescue analgesia for the PCM group was lower as compared to the dexmedetomidine group. Sarbari Swaika et al. (2013)[6] found in their study that there was significant lower VAS score in Paracetamol group than Dexmedetomidine group and there was minimum requirement of rescue analgesia.

SUMMARY AND CONCLUSION

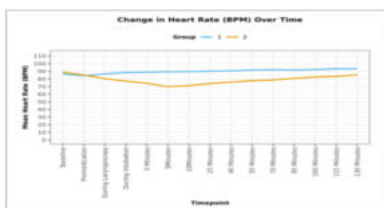
This study was designed to study and compare the efficacy of intravenous Paracetamol and Dexmedetomidine on intraoperative hemodynamics and post operative analgesia in patients undergoing laparoscopic surgeries under General Anaesthesia.

1. Patients in group 2 who received loading dose of Dexmedetomidine proved to be a better drug for attenuating sympathoadrenal response to laryngoscopy and intubation as compared to patients in Group 1 who received loading dose of intravenous Paracetamol.
2. Patients in Group 2 had significant fall in Heart rate , SBP ,DBP and MAP after loading dose of dexmedetomidine was given and had better intraoperative hemodynamic stability as compared to patients in Group 1 who received loading dose of Paracetamol.
3. Patients in both groups had moderate pain postoperatively and required rescue analgesia immediately after extubation
4. No serious side effects or complications were found in any of the study groups.

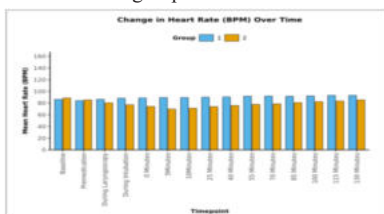
VAS (VISUAL ANALOG SCALE)



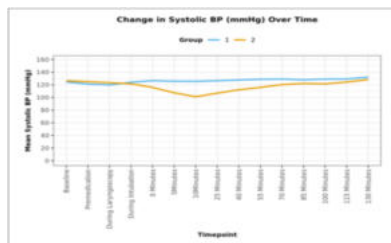
The following is a line diagram depicting the change in Heart Rate (BPM) over time in the two groups.



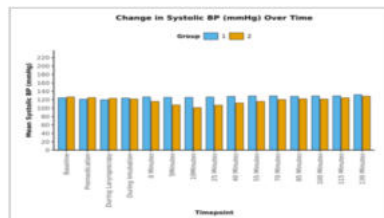
The following is a bar diagram depicting the change in Heart Rate (BPM) over time in the two groups.



The following is a line diagram depicting the change in Systolic BP (mmHg) over time in the two groups.



The following is a bar diagram depicting the change in Systolic BP (mmHg) over time in the two groups.



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