**Latest Trends in Medical Science - “Single Institutional Comparative Study on the Impact of the Standard Pressure and Low Pressure Pneumoperitoneum on Post - Operative Pain following Laparoscopic Cholecystectomy - A Stratified Randomized Controlled Trial”**

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**Brief Introduction**

There are no Stratified RCT studies conducted before on this topic. Therefore, we conducted a stratified randomization in this pilot study to compare the impact of the Standard Pressure and Low- Pressure pneumoperitoneum technique on post-operative pain following conventional laparoscopic cholecystectomy

Gastro-Intestinal surgery has undergone a revolution in the recent years by the introduction of laparoscopic techniques. The most common complaint following laparoscopic surgery, initially being recognized by gynaecologists during early experience with laparoscopic sterilization is shoulder pain.2 the incidence varies but is common and is being seen in nearly 30% of patients undergoing laparoscopic cholecystectomy. The concept of “Keyhole Surgery” created an immediate disparity between the potential of the new technique and training of surgeons to perform it. Now modern surgical methods are aimed at giving cure along with minimal invasive techniques with patient in mind and safety never being compromised.

The pain that occurs after laparoscopic cholecystectomy can be categorized into 3 types:

1. Visceral Pain
2. Parietal Pain
3. Shoulder Pain.
4. **Visceral Pain:**

Visceral Pain happens due to the surgical dissection and tissue stretching due to the handling of gallbladder at its bed. This type of pain is transmitted by the neurons of the visceral peritoneum that covers the majority of the abdominal viscera through the same nerve supply as the neighbouring visceral organs.

1. **Parietal Pain:**

Parietal also called as somatic pain occurs due to the trauma caused to the anterior abdominal wall by the insertion of the trocars for manipulation.

1. **Shoulder Pain:**

Shoulder tip pain occurs due to the diaphragmatic irritation and stretching caused by the CO2 insufflation.5,6

Cholelithiasis, which is one of the most common Gastrointestinal disorders seen, was traditionally treated by conventional or open cholecystectomy. Currently laparoscopic cholecystectomy is the standard procedure as it is less painful, needs shorter recovery period and short hospital stay.

Recovery after laparoscopic cholecystectomy depends upon several factors such as: Abdominal pain, Shoulder tip pain, Nausea, Vomiting and Fatigue. These side-effects are due to peritoneal stretching and diaphragmatic irritation caused by high intra-abdominal pressure and by CO2. Among the causes for shoulder pain are: Stimulation of the sympathetic nervous system by hypercarbia, the residual pneumoperitoneum after the surgery, and rapid distention of the abdomen by carbon dioxide. Keeping this in mind, it was assumed that lower intra-abdominal pressure will decrease these complications. Traditionally, the pressure used to create pneumoperitoneum is around 15mm Hg. There are a few studies done using low pressure pneumoperitoneum (less than 12 mm Hg) and showed decrease in pain post-operatively. But, all the studies are not equivocal in this respect. Further, the safety of low-pressure pneumoperitoneum is not established.



Figure 1: Operative image of a laparoscopic cholecystectomy. Laparoscopic forceps (arrow) are used to dissect “Calot’s triangle”. 16

**Materials and Methods:**

Primary Objective:

* Assessment of intensity and frequency of post-operative pain using VAS score (Visual Analog Scale).

Secondary Objectives:

* Assessment of the Duration of the Surgery.
* To measure the number of bile spillage in both the Standard and Low Pressure pneumoperitoneum technique.
* Post-operative Opioid consumption.
* To Assess Time for Patient Mobilization Post Surgery

Methodology:

Study Area:

* The present study was carried out in the Department of General and Minimal access Surgery, Manipal Hospital, Bangalore.

Study Population – Age Group:

* Patients admitted in the Department of General Surgery, Manipal Hospital for laparoscopic cholecystectomy between 18 and 70 years were eligible for the study.

Study Duration:

* 24 Months (January 2018 to December 2019).

Study Design:

* Stratified Randomized Controlled Trial

Sample Size:

* From a pilot study conducted among the patients attending to OPD of Department of General and Minimal access Surgery, Manipal Hospital, it has been observed that on an average 11 out of every 18 patients with cholelithiasis were operated. Thus proportion of patients operated for cholelithiasis was 61.11% in this hospital.

Formula: n = zα2 \* pq / d2
Where, n is the required sample size.
Z α is the standard normal deviate, which is equal to 1.96 at 95% confidence interval.
p is the prevalence in the population of the factor under study

q = 100-p
d = Absolute precision taken in between 5 to 10%
p = 61%
q = 39%
n = number of samples is to be studied
So,
n = zα2 \* pq / d2
= (1.96)2\* 61\* 39 / (8)2

=9139.1664/64

= 142.79 = 143

Randomization was done by a computer-generated sequence, with the help of the software www.randomization.com, and stored in sealed opaque envelopes. The subjects were chosen for 2 groups undergoing laparoscopic cholecystectomy repair, at different pneumoperitoneal pressures.

Inclusion Criteria:

* Patients between 18 to 70 Years were included in this study.
* Elective surgery for gall stone disease.
* Normal common bile duct (on pre-operative ultrasound).
* Patients with cholelithiasis proven by USG with at least one attack of upper abdominal pain and considered fit for elective cholecystectomy were included in the study.

Exclusion Criteria:

* Patient’s age above 70 years.
* Patients with endocrine, renal, hepatic, or immunological disease and pregnant patients.
* ASA grade III or IV.
* Conversion to open cholecystectomy.
* Patients with portal hypertension, uncorrectable coagulopathies, suspected gallbladder carcinoma, cirrhosis and generalized peritonitis.
* History or investigations suggesting CBD stones.
* History of prior abdominal surgery.
* Patients who have not given written consent are not included in this study

A stratified randomization study to compare impact of the Standard Pressure and Low-Pressure pneumoperitoneum technique on post-operative pain following conventional laparoscopic cholecystectomy was performed 143 patients during the period of Jan 2018- Dec 2019. Individuals fulfilling the inclusion and exclusion criteria were assigned to 2 groups as per methodology.

1. Group - A patients underwent laparoscopic cholecystectomy with low pressure pneumoperitoneum –LPP (7-8 mm Hg) while,
2. Group – B underwent laparoscopic cholecystectomy with standard pressure pneumoperitoneum -SPP (12-14 mm Hg).

The duration of surgery was carefully recorded using the wall mounted OT timers. The time of arrival in the postoperative ward was defined as 0 h postoperatively. Presence of shoulder pain, port site pain and / or diffuse abdominal pain was measured at 2, 4, 6, 12, 24, and 48 hours, respectively. Pain score VAS (Visual Analogue Score) according to scale was used to detect the intensity of the pain postoperatively

World Health Organization (WHO) analgesic step ladder was used as a framework for providing symptomatic pain relief to the patients. Statistical analysis was done using standard tools. Mean of two groups were compared using independent t-test. Chi square test was used to analyse the significance of difference between frequency distribution of the data. P value < 0.05 was considered as statistically significant.

**Observations and Result Analysis:**

A total of 143 patients satisfied the study criteria in this Stratified RCT study. The contents of each table are explained during discussion. Graphs are made to portray the relation existing among data wherever necessary.

**Study Process Flow Diagram:**



**Pre-Operative Parameters:**

**Pressure of pneumoperitoneum:**

* Standard Pressure Pneumoperitoneum (SPP) was done in 51% patients and Low Pressure Pneumoperitoneum (LPP) was done in 49% patients.

**Distribution according to Patient Age Group:**

* Majority of the patients belong to the age group of 28-37 years (39.2%) followed by 38-47 years (18.2%), 18-27 years (16.1%), 48-57 years (15.4%) and >58 years (11.2%). Mean age in SPP is 39.34+12.015, and mean age in LPP is 38.73+12.41. Overall mean age was 39.04+12.171.
* In patients receiving Standard Pressure Pneumoperitoneum, majority belong to the age group of 28-37 years (38.4%) and in patients receiving low pressure Pneumoperitoneum, majority belong to the age group of 28-37 years (40%). The association was found to be statistically not significant.

**Intra-Operative Parameters:**

**Surgeon visibility:**

* Surgeon visibility was good in 98.6% patients and poor in 1.4% patients. In patients receiving Standard Pressure Pneumoperitoneum, surgeon visibility was good in all the patients (100%) and in patients receiving Low Pressure Pneumoperitoneum, surgeon visibility was poor in 2.9% patients only. The association was found to be statistically not significant.

**Bile spillage:**

* Bile spillage was seen in 7.7% patients. In patients receiving Standard pressure Pneumoperitoneum, bile spillage was seen in 4.1% patients and in patients receiving Low Pressure Pneumoperitoneum, bile spillage was seen in 11.4% patients. The association was found to be statistically not significant.

**Post-Operative Parameters:**

**Post- operative Pain Score:**

* When comparing the means of pain score between the two groups at different time intervals, there was a statistical significance at 2nd hr, 4th hr, 6th hr, 12th hr, 24th hr & 48th hr.

**Post Operative Patient Mobilization Time**

* It was noted that patients belonging to LP group exhibited early post-operative mobilization with a mean of 8.39 + 0.967 Hrs as compared to patients belonging to SP group in whom the mean duration of postoperative mobilization was 9.67 + 1.001 Hrs.
* Further, on analysis it was noted that postoperative mobilization in patients belonging to LP group was earlier and statistically significant.

This can attributed to the fact that early postoperative pain relief is associated with early mobilization and increased patient satisfaction.

**Post- Operative Opioid Consumption:**

* It was noted that post-operative opioid consumption was significantly lower in the LP group as compared to SP group. The Analgesia was given to the patients according to WHO Pain Stepladder Approach. Opioids ( Inj Tramadol 50mg ) was given when the VAS Score was more than 5.
* It was noted, that there was a fall in the use of opioid in LP group in the 2nd and 4th hr and no additional use of opioid in the LP group in 6th , 12th and 48th hr.
* When comparing the Post- Op Opioid Consumption between the two groups, there was a statistical significance at 2nd, 4th, 6th, and 12th hour.

**Table 1: Group Statistics showing Pressure of Pneumoperitoneum & Pain score**

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| --- |
| **Group Statistics** |
| **Pressure of Pneumoperitoneum** | **N** | **Mean** | **SD** | **T test** | **P value** |
| Pain Score-2nd hr | SP | 73 | 5.42 | 0.644 | 12.32 | 0.001\* |
| LP | 70 | 4.11 | 0.627 |
| Pain Score-4th hr | SP | 73 | 4.56 | 0.850 | 7.69 | 0.001\* |
| LP | 70 | 3.60 | 0.623 |
| Pain Score-6th hr | SP | 73 | 3.95 | 0.896 | 7.97 | 0.001\* |
| LP | 70 | 2.89 | 0.671 |
| Pain Score-12th hr | SP | 73 | 3.10 | 1.120 | 4.10 | 0.001\* |
| LP | 70 | 2.43 | 0.791 |
| Pain Score-24th hr | SP | 73 | 2.41 | 0.998 | 4.58 | 0.001\* |
| LP | 70 | 1.73 | 0.760 |
| Pain Score-48th hr | SP | 73 | 1.73 | 0.786 | 3.86 | 0.001\* |
| LP | 70 | 1.30 | 0.492 |

* When comparing the means of pain score between the two groups at different time intervals, there was a statistical significance at 2nd hr, 4th hr, 6th hr, 12th hr, 24th hr & 48th hr.

**Chart 1: Line Diagram – Scatter Plot of Pain Score at different intervals between LP and SP Group**

**Results and Conclusion:**

Standard Pressure Pneumoperitoneum was done in 51% patients and Low-Pressure Pneumoperitoneum was done in 49% patients. Majority of the patients belong to the age group of 28-37 years (39.2%). Surgeon visibility was good in 98.6% patients and poor in 1.4% patients. Bile spillage was seen in 7.7% patients. Post-operative mobilization was earlier in patients belonging to Low Pressure Pneumoperitoneum group. Post-operative opioid consumption was significantly lower in the Low-Pressure group. There is no statistical significance among age, surgeon visibility & bile spillage.

Recovery after laparoscopic cholecystectomy depends upon several factors such as: Abdominal pain, Shoulder tip pain, Nausea, Vomiting and Fatigue. These side-effects are due to peritoneal stretching and diaphragmatic irritation caused by high intra-abdominal pressure and by CO2 7. Among the causes for shoulder pain are: Stimulation of the sympathetic nervous system by hypercarbia8, the residual pneumoperitoneum after the surgery, and rapid distention of the abdomen by carbon dioxide 9. Keeping this in mind, it was assumed that lower intra-abdominal pressure will decrease these complications. Traditionally, the pressure used to create pneumoperitoneum is around 15mm Hg10. There are a few studies done using low pressure pneumoperitoneum (less than 12 mm Hg) and showed decrease in pain post-operatively 7,11,12. But, all the studies are not equivocal in this respect 13. Further, the safety of low-pressure pneumoperitoneum is not established.

The following are the conclusions derived from this study:

* Low pressure pneumoperitoneum is feasible and safe and results in reduced postoperative pain and early mobilization time compared with standard-pressure pneumoperitoneum.
* Patients who underwent laparoscopic cholecystectomy under low pressure pneumoperitoneum required less postoperative opioids. Hence there is a reduction of POOC and reduced opioid related complications like drowsiness, constipation. This will promote day case laparoscopic cholecystectomy and hence, leads to cost saving.

We conclude that low pressure pneumoperitoneum results in decrease in intensity and frequency of post-operative pain and fewer requisite of opioids as compared to standard pressure.

**Recommendation:**

* Low pressure pneumoperitoneum in laparoscopic cholecystectomy is effective and results in reduced postoperative pain and near early mobilization time compared with standard-pressure pneumoperitoneum.
* Low pressure reduces the postoperative opioid requirement thus reducing the associated side-effects of opioids.
* More stratified RCT studies to be made on this topic.
* More studies are required to investigate the potential benefits of the reduced length of hospital stay.
* More studies can be conducted by combining low pressure techniques with other techniques like local anaesthetic infiltration of wounds and intraperitoneal instillation of Ropivacaine or Bupivacaine to decrease post-operative opioid requirement.

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