The Comparison of Postoperative Recovery Characteristics Using Isoflurane and Sevoflurane in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract- Inhaled volatile anesthetic remain the most widely used drug for the maintenance of general anesthesia. This is because of the ease of administration and predictable intraoperative and recovery characteristics. Isoflurane and sevoflurane are in current practice for maintenance of anesthesia. Management of haemodynamic stability is the most important part of standardized balanced technique. Post operative recovery is the most important aspect to look for in standardized balanced anaesthesia technique with volatile anesthetics.

The study was done to evaluate post operative recovery characteristics (Early recovery and delayed recovery criteria using PACU discharge criteria) in laparoscopic cholecystectomy patients with two different volatile anesthetic agents namely isoflurane and sevoflurane into two group of patients–A(USING 0.6% ISOFLURANE) AND B(USING 1% SEVOFLURANE).

Based on our study results we can say both the volatile anesthetic agents can be used for maintenance of anesthesia in elective laparoscopic cholecystectomy operations of ASA I and II patients. Both maintains good hemodynamic parameters and airway intraoperatively and post operatively.

But sevoflurane has early recovery than isoflurane.

Hence, based on our study we can recommend that in elective laparoscopic cholecystectomy operations agent of choice for maintenance of anesthesia will be sevoflurane followed by isoflurane according to early recovery characteristics.

I. Introduction

Inhaled volatile anesthetic remain the most widely used drug for the maintenance of general anesthesia. This is because of the ease of administration and predictable intraoperative and recovery characteristics.

Over the past years, there have been three gases and thirteen volatile anesthetic agents made available for clinical use. The majority have fallen by the way side as a consequence of their various side-effects. Nitrous oxide, diethyl ether, and chloroform were the earliest inhalational anesthetics. Subsequently drugs still available for clinical uses are– Halothane, Isoflurane, Sevoflurane & Desflurane.

Nitrous oxide was first recognized as an analgesic in the early 19th century, but it’s low potency precludes its use as the sole anesthetic agent for most procedures.

Halothane was the first non-combustible halogenated volatile anesthetic and was introduced in 1956. Its role in anesthetic practice is declining as newer drugs with better safety profiles have been developed. The primary concern with halothane are– its arrhythmogenic potential and hepatotoxicity.

Isoflurane was first used clinically in 1981. It is a good, general purpose anesthetic and is probably the most widely used currently. Metabolism to other potential toxic substances is minimal. It produces less depression of the cardiovascular system than halothane and is fairly potent. However, as a sole agent it produces tachycardia and vasodilation, particularly in younger patients.

Sevoflurane was introduced in 1994. The low blood solubility provides more precise control over the delivery of anesthesia, and more rapid recovery at the end of anesthesia independent of their duration of administration. Its advantage over isoflurane is the pleasant odor which makes it the agent of choice for gas induction. Unlike other agents, however, concerns have been made about sevoflurane interaction with carbon dioxide absorbers.
Two volatile anesthetic namely isoflurane and sevoflurane are commonly in current practice for maintenance of anesthesia. Management of haemodynamic stability is the most important part of standardized balanced technique.

Post operative recovery is the most important aspect to look for in standardized balanced anaesthesia technique with volatile anesthetics.

The study was done to evaluate post operative recovery characteristics in laparoscopic cholecystectomy patients with two different volatile anesthetic agents namely isoflurane & sevoflurane.

II. Materials And Methods

STUDY DESIGN- Prospective and Randomized study was conducted in
STUDY LOCATION- Department of Anaesthesiology and Critical Care, Darbhanga Medical College & Hospital, Laheriasarai, Bihar
STUDY DURATION- October 2016 to April 2018
SAMPLE SIZE- A total of 60 adults

RANDOMISATION AND SAMPLE SELECTION- After obtaining Institutional Ethical Committee’s approval and informed consent from each patient 60 ASA status, scheduled for elective laparoscopic cholecystectomy under general anesthesia were randomly divided by random tables into two groups – group A & B with equal numbers (n=30).

Group - Study drug-
A    Isoflurane-0.6%
B    Sevoflurane-1%

Inclusion Criteria
1. AGE ≥ 18 yr
2. SEX – Either Sex (Male/Female)
3. WEIGHT – 40-75 Kg
4. ASA GRADE 1 & 2
5. MALLAMPTTI GRADE 1 & 2

Exclusions Criteria
Patients were excluded from the study, if they had:
1. History of allergic reaction to drugs,
2. Any evidence of major cardiovascular, pulmonary, hepatic, renal, endocrine, metabolic, neurologic and psychiatric diseases.
3. Patients chronically receiving sedative medication.
4. Pregnant females
5. Morbid obesity
6. Patient refusal

Preparation of patients
After fasting for at least 6 hours, patients received inj glycopyrollate 0.2 mg, inj perinorm and inj ceftriaxone 1 gm iv.

Anesthesia Technique
All operations were performed under general anesthesia with controlled ventilation.

In the operative room, a 18G I.V cannula was inserted and crystalloid started. Monitoring included pulse oximetry, non-invasive blood pressure, 3 lead standard electrocardiogram (ECG), end-tidal carbon dioxide (ETCO2) and end-tidal inhalational gas. After induction with Fentanyl 3μg/kg and Propofol 1-2 mg/kg IV in a titrated dose till loss of eye lash reflex, patients were intubated following vecuronium 0.1 mg/kg IV and connected to circle absorber system. For maintenance patients received either isoflurane 0.6% or sevoflurane 1% with nitrous oxide 60% in oxygen. ETCO2 was maintained between 35-40 mmHg. MAP and H.R within 20% of pre-induction baseline values. If MAP or H.R remained increased for 5 min; additional dose of fentanyl (0.5 mg/kg) was given. If H.R. dropped below 45 beats per minute, atropine 0.4 mg IV was given. Intraoperative hypotension was treated with intraoperative fluid loss replacement. If not responsive, then anesthetic concentration was decreased. Muscle relaxation was maintained with vecuronium 1/5th the intubating dose at 30 minute interval.

The time of discontinuation of anesthetic agent was considered time end for all measurements.
Assessment
The following parameters were noted intraoperatively:
A. Patient characteristics
• Age
• Weight
• Gender (male/female)
• ASA I / II

B. Following parameters are used as markers of post operative recovery:
1. Early recovery characteristics:
   • Eye opening.
   • Hand grip.
   • Tracheal extubation.
   • State name.
2. Delayed recovery characteristics:
   • PACU discharge criteria (fast tracking score)

Statistical Analysis
All data are reported as mean value with variability expressed as SD. F test and Kruskal Wallis Chi-square test has been used to compare the intraoperative parameters in between the three groups. Chi square test for independence of attributes was also used.

General comment: When P value is more than 0.05 there is no significant difference between mean values. P values less than 0.05 but more than 0.01 denotes that significant difference exist between mean values. P Value less than 0.01, denotes that highly significant difference exists between mean values. Demographic data of patients under study in each group were compared. Though HR, SBP, DBP and MAP were noted at baseline, after intubation, before incision and 5 minutes thereafter, but only HR and MAP at baseline, after intubation, before incision and 10 minutes thereafter till 50 minutes were considered for statistical analysis and comparison. This was done to make the study simple, technically easy, but reliable.

Though hypertension response to intubation had been included in statistical analysis and graphical representation, it is not the objective the study.

Statistical software used – SPSS ver.7.5.
F Test is usually use for parametric data & Kruskal Wallis chi sq. test is usually used for non-parametric

Criteria Used to Determine FAST TRACKING (PACU DISCHARGE CRITERIA)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of Consciousness</td>
<td></td>
</tr>
<tr>
<td>Awake and oriented</td>
<td>2</td>
</tr>
<tr>
<td>Arousable with minimal stimulation</td>
<td>1</td>
</tr>
<tr>
<td>Responsive only to tactile stimulation</td>
<td>0</td>
</tr>
<tr>
<td>Physical Activity</td>
<td></td>
</tr>
<tr>
<td>Able to move all extremities on command</td>
<td>2</td>
</tr>
<tr>
<td>Some weakness in movement of the extremities</td>
<td>1</td>
</tr>
<tr>
<td>Unable to voluntarily move the extremities</td>
<td>0</td>
</tr>
<tr>
<td>Hemodynamic Stability</td>
<td></td>
</tr>
<tr>
<td>Blood pressure &lt; 15% of the baseline MAP value</td>
<td>2</td>
</tr>
<tr>
<td>Blood pressure between 15% and 30% of the baseline MAP value</td>
<td>1</td>
</tr>
<tr>
<td>Blood pressure &gt; 30% below the baseline MAP value</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory Stability</td>
<td></td>
</tr>
<tr>
<td>Able to breathe deeply</td>
<td>2</td>
</tr>
<tr>
<td>Tachypnea with good cough</td>
<td>1</td>
</tr>
<tr>
<td>Dyspneic with weak cough</td>
<td>0</td>
</tr>
<tr>
<td>Oxygen Saturation Status</td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintains value &gt; 90% on room air</td>
<td>2</td>
</tr>
<tr>
<td>Requires supplemental oxygen (nasal prongs)</td>
<td>1</td>
</tr>
<tr>
<td>Saturation &lt; 90% with supplemental oxygen</td>
<td>0</td>
</tr>
</tbody>
</table>

**Postoperative Pain Assessment**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or mild discomfort</td>
<td>2</td>
</tr>
<tr>
<td>Moderate to severe pain controlled with IV analgesics</td>
<td>1</td>
</tr>
<tr>
<td>Persistent severe pain</td>
<td>0</td>
</tr>
</tbody>
</table>

**Postoperative Emetic Symptoms**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or mild nausea with no active vomiting</td>
<td>2</td>
</tr>
<tr>
<td>Transient vomiting or retching</td>
<td>1</td>
</tr>
<tr>
<td>Persistent moderate to severe nausea and vomiting</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total score**

14


A score over 12 with no individual score less than 1 is required for fast-tracking.

**III. Observations And Results**

**Demographic characteristics**

<table>
<thead>
<tr>
<th>Age Distribution(Table 1):</th>
<th>Isoflurane (A)</th>
<th>Sevoflurane (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>50.86±3.66</td>
<td>53.4±6.92</td>
</tr>
</tbody>
</table>

**Age Distribution**

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<table>
<thead>
<tr>
<th></th>
<th>Isoflurane (A)</th>
<th>Sevoflurane (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Male:Female)</td>
<td>14:16</td>
<td>18:12</td>
</tr>
</tbody>
</table>

### Sex Distribution

![Sex Distribution Chart](chart1)

### Weight Distribution

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane (A)</th>
<th>Sevoflurane (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (in Kgs)</td>
<td>54.5±3.93</td>
<td>56.8±7.07</td>
</tr>
</tbody>
</table>

![Weight Distribution Chart](chart2)
The Comparison of Postoperative Recovery Characteristics Using Isoflurane and Sevoflurane

Height Distribution (Table 4):

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane (A)</th>
<th>Sevoflurane (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cms)</td>
<td>157.2±6.74</td>
<td>158.3±7.46</td>
</tr>
</tbody>
</table>

ASA Classification (Table 5):

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane (A)</th>
<th>Sevoflurane (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA class (I:II)</td>
<td>14:16</td>
<td>13:17</td>
</tr>
</tbody>
</table>
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### Table 6: Early Recovery Time (sec) in two groups

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane (B)</th>
<th>Isoflurane (A)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Opening</td>
<td>122.87±22.5</td>
<td>181.33±2.07</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hand grip</td>
<td>179.2±18.07</td>
<td>242.07±1.93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tracheal extubation</td>
<td>323.07±3.93</td>
<td>483.67±5.56</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>State Name</td>
<td>425.73±8.78</td>
<td>546.53±9.55</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Kruskal-Wallis test is used because assumption of normality (for ANOVA) is violated in these variables.

### Early Recovery Time (sec) in both groups

![Bar chart showing early recovery time in both groups]

### Table 7: PACU Monitoring

<table>
<thead>
<tr>
<th>Fast tracking Score</th>
<th>Sevoflurane (B)</th>
<th>Isoflurane (A)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>4.07±0.58</td>
<td>2.33±0.75</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>15 min</td>
<td>5.8±0.8</td>
<td>4.23±0.77</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30 min</td>
<td>7.67±0.71</td>
<td>5.87±0.73</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>45 min</td>
<td>9.17±0.95</td>
<td>7.67±0.88</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>60 min</td>
<td>10.87±1</td>
<td>9.43±0.97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>75 min</td>
<td>12.43±0.82</td>
<td>11.47±0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>90 min</td>
<td>Score for all is 14</td>
<td>13.93±0.25</td>
<td></td>
</tr>
</tbody>
</table>

Kruskal-Wallis test is used because assumption of normality (for ANOVA) is violated in these variables.

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IV. Discussion

The study was prospective as all parameters were noted after the treatment was given. It was randomized by randomly allocating the patients in two groups. In our study, regarding age, height, weight, ASA physical status and sex there was no significant difference between the two groups (P>0.05) (ref. table I, II, III).

The number of patients in each group were equal (n=30), so impact of age, height, weight, ASA physical status and sex; if any, was equal in all the there groups. In our study we used isoflurane 0.6%, sevoflurane 1% and in 60% N₂O anesthesia. These are equipotent mixture and about 1 MAC in N₂O anesthesia. The percentage of sevoflurane and isoflurane is same as that used by S.Gergin et al in their study in 2005.

Bennett et al in 1992 in their study, showed that sevoflurane like isoflurane could maintain haemodynamic stability in concentration producing surgical anesthesia.

MH Nathanson et al in 1995 showed that HR and MAP were similar during maintenance period with either sevoflurane 3% to 6% or isoflurane, 1% to 2% with N₂O in O₂.

Torri G and Casati A in 2000, in their study using sevoflurane and isoflurane in 60% N₂O and O₂ mixture, showed that sevoflurane provided equally safe and cardiovasular homeostasis as isoflurane.

S. Gergin et al in 2005 showed that there was no significant difference regarding HR and MAP during maintenance of anesthesia, either with sevoflurane 1% or 1% isoflurane in N₂O anesthesia.


The findings of our study that there no significant difference in haemodynamic parameters between isoflurane and sevoflurane corroborates with the study of Patel SS in 1995.

In 1992 Frink EJ, Malan TP et al found that sevoflurane and isoflurane produced similar systolic and diastolic blood pressure changes, but HR before and after incision was faster in patients in the isoflurane group.
V. Summary And Conclusion

SUMMARY:
This was a randomised, prospective and double blinded study performed in 60 patients with 30 patients in each group undergoing elective laparoscopic cholecystectomy. Group A received Isoflurane & Group B received Sevoflurane as inhalational agent in elective laparoscopic cholecystectomy of ASA I and II patients.

The main parameters studied were Early and Delayed post operative recovery characteristics.

To summarise the findings of our study:
1. There was no statistically significant difference between the two groups in respect to demographic parameters like age, sex, weight and height.
2. On comparing early post operative recovery characteristics sevoflurane group has the early recovery followed by the isoflurane group.
3. On comparing the delayed recovery characteristics too Sevoflurane group has the early recovery followed by Isoflurane group. None of the patients have any intraoperative and post operative hemodynamic or airway related problems.
4. Both the drugs can be used for maintenance of anesthesia in laparoscopic cholecystectomy operations.
5. Baseline parameters in both the groups are same and comparable.

CONCLUSION:
Based on our study results we can say both the volatile anesthetic agents can be used for maintenance of anesthesia in elective laparoscopic cholecystectomy operations of ASA I and II patients. Both maintains good hemodynamic parameters and airway intraoperatively and post operatively.

But sevoflurane has early recovery than isoflurane.

Hence, based on our study we can recommend that in elective laparoscopic cholecystectomy operations agent of choice for maintenance of anesthesia will be sevoflurane followed by isoflurane according to early recovery characteristics.

References
[3]. Bunker JP. Final report of the National Halothane Study.
[20]. Schellard MS, Tatjeski A, Drummond C, Zornow MH. The effects of sevoflurane on cerebral blood flow, cerebral metabolic rate for oxygen, ICP & EEG are similar to those of isoflurane in rabbits.
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