A COMPARATIVE EVALUATION OF ISOFLURANE VS HALOTHANE TO ATTENUATE HAEMODYNAMIC RESPONSE DUE TO CO_2 PNEUMOPERITONEUM DURING LAPAROSCOPIC CHOLECYSTECTOMY

Chavi Sethi, Anshul Jain, Pradeep Sahi, Roopesh Kumar, Amit Sehgal, Ajai Vikram Singh, Paras Gupta, Rachna Chaurasia

1. Lecturer. Department of Anaesthesiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.
2. Lecturer. Department of Anaesthesiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.
3. Professor. Department of Anaesthesiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.
4. Assistant Professor. Department of Anaesthesiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.
5. Consultant Orthopaedician. M. L. B. Medical College, Jhansi, Uttar Pradesh.
6. Lecturer. Department of Anaesthesiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.
7. Lecturer. Department of Orthopaedics, M. L. B. Medical College, Jhansi, Uttar Pradesh.
8. Lecturer. Department of Radiology, M. L. B. Medical College, Jhansi, Uttar Pradesh.

CORRESPONDING AUTHOR:
Dr. Chavi Sethi,
Lecturer,
J-41 Ajay Enclave, Jhansi
E-mail: dr_chavi@yahoo.com
Ph: 0091 9935370472.

ABSTRACT: BACKGROUND: Laparoscopic cholecystectomy is a relatively new surgical procedure which is enjoying ever increasing popularity and presenting new anesthetic challenges. Volatile anesthetics play an important role in the management of haemodynamic changes due to CO2 pneumoperitoneum during laparoscopic surgeries. The aim of the study is to evaluate Isoflurane Vs Halothane as an adjunct to obtund haemodynamic response due to CO2 pneumoperitoneum. **MATERIALS & METHODS:** 50 patients aged 20-60 yrs of either sex belonging to ASA grade I & II scheduled for elective laparoscopic cholecystectomy admitted in MLB Medical College, Jhansi were randomly divided into two group.

Group I – O_2: N_2O + Inhalational agent (Isoflurane 1.5-2%)

Group II – O_2: N_2O + Inhalational agent (Halothane 1.5-2%)

RESULTS : Hypertensive response due to CO_2 pneumoperitoneum was well suppressed by Isoflurane (1.5-2%) {Group-I} which maintained pulse rate at a relatively higher side than halothane, (1.5-2%){Group II} decreased mean arterial pressure more significantly than halothane without any difference in arterial oxygen saturation (SPO_2) and end tidal CO_2 concentration (E_TCO_2). **CONCLUSION**: This can be concluded from the study that Isoflurane (Group-I) more effectively attenuated the haemodynamic response due to CO_2 pneumoperitoneum during laparoscopic cholecystectomy as compared to Halothane (Group-II) under balanced anesthetic technique.
KEYWORDS: Inhalational agent, CO_2 pneumoperitoneum, Isoflurane, Halothane.
MESH TERMS: Haemodynamic changes, Isoflurane, Halothane.

INTRODUCTION: Laparoscopic cholecystectomy is a relatively new surgical procedure which is enjoying ever increasing popularity and presenting new anesthetic challenges. Though they are

visually minimally invasive to the patient, the intraoperative requirement of laparoscopic surgery produces significant physiological changes, unique to the procedure. So far no anesthetic agent has been used successfully to blunt these changes produced due to CO_2 pneumoperitoneum. Volatile anesthetics now a days play an important role in the management of haemodynamic stability during a standardized balanced technique because of their ease of administration and predictable intraoperative characteristics.

The extent of haemodynamics changes associated with laparoscopic cholecystectomy depends on the interaction of factors viz. exogenous gas insufflation, patient position, and results of increased intraabdominal pressure,

(i) Patient position – for initial trocar insertion patient is placed in trendelenburg position ($10\text{-}20^0$) which results in increase in-central blood volume, decreased vital capacity. Then patient is placed in supine reverse trendelenburg ($20\text{-}30^0$) which improves diaphragmatic function, decrease venous return, right atrial pressure and pulmonary capillary wedge pressure, right atrial pressure, mean arterial pressure (MAP) and cardiac output (CO).

(ii) Neurohormonal effect of exogenous insufflating gas viz- CO_2, N_2O, helium. Absorption of CO_2 from the peritoneal cavity is the potential mechanism for hypercarbia and a rise in end tidal carbon dioxide concentration (E_TCO_2), Haemodynamic alternation occurs only if $PaCO_2$ is increased by 30% above normal levels which causes rise in pulse rate (PR), systemic vascular resistance (SVR), blood pressure (BP), central venous pressure (CVP).

(iii) Different mechanism viz. pooling of blood in legs, inferior venacaval compression, decrease venous resistance decrease venous return and cardiac output. On the other hand increased intrathoracic pressure, vascular resistance of intraabdominal organs increases systemic vascular resistance (SVR) and hence mean arterial pressure (MAP). Release of neurohormonal factors viz. vasopressin, catecholamines also play a role in increasing mean arterial pressure (MAP).

AIM OF THE STUDY: To evaluate Isoflurane Vs Halothane as an adjunct to obtund the haemodynamic response due to CO_2 pneumoperitoneum during laparoscopic cholecystectomy under balanced anesthetic technique.

MATERIALS & METHODS: 50 patients aged 20-60 yrs of either sex belonging to ASA grade I and II scheduled for elective laparoscopic cholecystectomy under balanced general anesthesia admitted in MLB Medical College, Jhansi.

After premedication with intravenous glycopyrrolate (0.2mg) and I/V midazolam (.03mg/kg), I/V fentanyl (1-2µg/kg), the patients were induced by I/V propofol (1.5-2mg/kg). Intubation was carried out with the help of suxamethonium (1.5-2mg/kg). Volatile anesthetic was then switched on and surgeon was asked to proceed with surgery. Intermittent positive pressure respiration was carried out to maintain normocarbia. The patients were randomly divided into two groups.

Group I – O_2 : N_2O + Isoflurane (1.5-2% vaporizer concentration) + nondepolarizing muscle relaxant (Atracurium 0.5 mg/kg)

Group II – O_2 : N_2O + halothane (1.5-2% vaporizer concentration) + nondepolarizing muscle relaxation (Atracurium 0.5 mg/kg).

For maintenance of anesthesia inhalational agent was delivered by Fluotec mark IV vaporizer. End tidal carbon dioxide concentration (E_TCO_2) was maintained between 35-40 mmHg with Bain circuit to maintain intra abdominal pressure 12-14 mmHg. Haemodynamic parameters like changes in mean pulse rate, mean arterial pressure, arterial oxygen saturation(SpO2),end tidal carbon dioxide(EtCO2) were recorded before induction (control value),at induction ,at5min ;15min;30min;45min after volatile anesthetic is switched on after CO2 pneumoperitoneum is created, after CO2 removal{deflation}, at the end of surgery and postoperatively at 15min;30 min.

OBSERVATION S: The following parameters were observed and recorded. All the observations were analyzed using SPSS statistical software and the results were compared (via paired T test) to determine the 'p' value. A 'p' value of less than 0.05 was considered significant whereas 'p' value of <0.01 was taken as highly significantly.

Table-1: Shows group wise distribution of age, sex and weight. There was no significant difference between the two groups.
Table-2 : Shows 48% of patients in Group I and 56% in Group II had indication of chronic cholecystitis with cholelithiasis.

Table-3 : Shows changes in mean pulse rate (bpm) in both groups.

1. In Group I (Isoflurane) the mean pulse rate increased gradually from the control value. This rise in pulse rate was statistically insignificant ($p > 0.05$) at 15 min (90.84 ± 5.66/min), at 30 min (90.93 ± 6.69 / min) and at 45 min (88.21 ± 6.67 / min) after the volatile anesthetics is switched on.
2. There was a gradual fall in mean pulse rate in group II (Halothane 5 minutes after the volatile anesthetics were switched on. The pulse rate decreased from 84.62 ± 8.42/min (control value) to 77.46 ± 9.78/min at 15 min, 72.80 ± 8.22 at 30 min and 68.60 ± 8.12/min at 45 min. This change was statistically significant ($p < 0.05$) at 15 min and highly significant ($p < 0.001$) at 30 min and 45 min intraoperatively.
3. Volatile anesthetics were switched off 10 minutes before the end of operation. Isoflurane (Group I) maintained the pulse rate towards higher side as compared to halothane (Group II).

Table-4 shows changes in mean arterial pressure at various time intervals in the two groups. Before induction i.e. 5 min after premedication the mean arterial pressure in Group I was 92.88 ± 6.41 mmHg and in Group II was 94.03 ± 6.34 mmHg (Control value). In group I (Isoflurane), 5 min after the volatile anesthetics was switched on, the mean arterial pressure (MAP) increased from 92.88 ± 6.41 mmHg to 108.01 ± 6.62 mmHg at 15 min, 110.66 ± 5.41 mmHg at 30 min and 103.33 ± 5.11 mmHg at 45 min. This change in MAP was statistically insignificant ($p > 0.05$) when compared to control value.

In Group II (Halothane), the MAP increased from 94.03±6.34mmHg (control value) to 130.33 ± 6.42 mmHg at 15 min, 128.61 ± 4.31 mmHg** at 30 min, 126.31 ± 6.44** mmHg at 45 min. The increase in mean arterial pressure was statistically significant at 15 min ($p< 0.05$) and highly significant ($p< 0.01$) at 30 min and 45 min, when compared to control value.

Thus isoflurane (Group I) lowered the mean arterial pressure more as compared to halothane (Group II). The MAP which increased after CO_2 pneumoperitoneum decreased

gradually after volatile anesthetics was switched on in both groups but Isoflurane (Group I) more effectively attenuated the response due to CO_2 pneumoperitoneum keeping MAP at significantly lower levels when compared to halothane (Group I).

Table-5: Shows changes in arterial oxygen saturation (SPO_2) in both groups. After the volatile anesthetic was switched on there was no significant change ($p < 0.05$) in arterial oxygen saturation (SPO_2) in both the groups at any time interval intraoperatively.

Table-6: Shows ECG changes in lead II. Sinus bradycardia ,ST segment changes and ectopics were observed in Group II (Halothane) which were transient and disappeared on withdrawal of inhalational agent.

Table-7: Shows changes in (E_TCO_2) end tidal carbon dioxide concentration in the two group. There was no significant ($p > 0.05$) change in E_TCO_2 in both the groups.

Table-8: Shows the complications in postoperative period. Nausea and vomiting was observed in 3 patients in Group I (Isoflurane) while 2 patients in Group II (Halothane) .Shoulder pain was reported in 1 patient in Group I while in 3 patients in Group II. Injection fentanyl (1-2µg/kg) was given in post operative period. 16 patients in Group I (Isoflurane) while 19 patients in Group II (Halothane) required immediate postoperative analgesia.

Degree of awareness was assessed by the degree of intraoperative sweating and lacrimation, abrupt changes in pulse was blood pressure (PRST Score). The PRST score was 2 in Group I (Isoflurane) and 4 in Group II (Halothane). Thus there was no significant difference in the degree of awareness present during surgery in both the groups.

Table-9 also shows the recovery pattern in both the group. Recovery from anesthesia was judged after extubation by asking the patients to open eyes on command, recall of name, response to painful pinch, spontaneous movement and handgrip. This was done at intervals of every one minute after discontinuing the inhalational anesthetic. It was seen that recovery times are factors with isoflurane (Group I).

DISCUSSION: For the past four decades halothane has been, by far the most commonly used volatile anesthetic agent. However, as Smith (1981) has pointed out, Halothane possesses some properties which fall short of the properties which an ideal anesthetic agent should have. First it sensitizes the heart to endogenous and exogenous catecholamines and secondly, there is a rare but potentially lethal association with hepatitis. After about a quarter of a century, during which halothane remained virtually unchallenged as the safest and most versatile volatile anesthetic, to agents enflurane and isoflurane have been induction which are said to be free from the two adverse effects. This study is confined to compare the haemodynamic response of both the agents which have a particularly wide role to play in contemporary hospital anesthetic practice in attenuating response to CO_2 pneumoperitoneum during laparoscopic cholecystectyomy.

There is no co-relation of age, sex and type of surgical procedure. Rise in pulse rate was observed in both the groups because of CO_2 pneumoperitoneum. Halothane lowered it significantly due to its negative chronotropic effect on SA node. Isoflurane maintained it towards a higher side due to its beta sympathomimetic activity but at clinically acceptable levels.

Skovsted, Seagard et al., Kotrly[1,2,3] et al., have reported that Isoflurane is more often associated with an increase in heart rate than Halothane. Two factors may be involved. Firstly, isoflurane may have less effect on the rate of spontaneous discharge on the SA node than Halothane. Secondly, isoflurane appears less depressant than Halothane as changes in heart rate mediated by baroreceptors.

Kissin, Morgan and Smith[4], suggested that isoflurane provides a greater margin of heamodynamic safety than Halothane. The more favourable cardiac index of Isoflurane is likely to result from the fact that, although isoflurane decreases myocardial contractility, it does less than either Halothane or enflurane (Basch, Beapure[5] et al.,).

Hypertensive response was well suppressed with Isoflurane (1.5-2%) which decreased the mean arterial pressure (MAP) due to its vasodilating property (↓ SVR). Halothane at a similar concentration could not suppress the mean arterial pressure significantly.

Eger[6], speculated that both the volatile agents decrease systemic arterial pressure in a dose related fashion but by different underlying mechanism. Isoflurane reduces systemic vascular resistance (SVR) more than contractility, in contrast to Halothane which reduces cardiac output (CO). Mckinney MS, Fee JPH[7] investigated that haemodynamic changes like cardiac performance was depressed by Halothane more than that by isoflurane. It was postulated by Ciofolo MJ and Reiz S[8] that both the agent produces a dose dependent decrease of systolic and diastolic function. Raventos, J. and Lemo P.G.[9] concluded that isoflurane preserved both cardiac index and ejection fraction, had less suppression of mean arterial pressure than Halothane and increased heart rate.

Findings of the present study are very much in accordance to those carried out by the above authors and observers.

No significant difference in arterial oxygen saturation (SPO_2) was found in both the groups. Only patients in halothane group (Group II) exhibited specific ST segment changes. These finding are in accordance with the observations of Bosnjak and Kampine[10] who demonstrated that volatile anesthetics alter the heart rhythm by influencing the rate of discharge of SA node. Atlee and Peterson[11] suggested that halothane and not isoflurane markedly reduce conduction within the myocardium. There was no statistically significant change ($p > 0.05$) in E_TCO_2 in both the groups intraoperatively. These findings are in accordance to that observed by Goldberg, M. Stephen and Wein Heiss[12].

Post operatively Isoflurane (Group I) offered a transient advantage compared with halothane with respect of early recovery and faster emergence from anesthesia. These findings are in accordance with those carried out by Pandit, Leach and Stende[13] who compared induction and recovery characteristics of the two agents. PONV, degree of awareness and requirement of postoperative analgesia was reported more with halothane. The low solubility of Isoflurane, its low blood/gas and tissue/blood partition coefficient ensures more rapid adjustment of the depth of anesthesia as compared to Halothane and makes it a suitable agent for day care laparoscopic surgery.

Most of the patients were in the age group 40-50 years, with male predominance over females. Most of the patients were in the range of 50-60 kgs.

CONCLUSION: On completion of the study after carefully analyzing the observations made, it was concluded that Isoflurane (Group I) more effectively attenuated the haemodynamic response due to CO_2 pneumoperitoneum during laparoscopic cholecystectomy as compared to Halothane (Group II) under balanced anesthetic technique along with faster recovery time. However there is no significant difference in arterial oxygen saturation (SPO_2) and end tidal

carbon dioxide concentration. E_TCO_2 with halothane and Isoflurane when administered with controlled ventilation.

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Table-1 : Demographic profile.

Variable	Group I Isoflurane (n=25)	Group II Halothane (n=25)
Age (yrs)) Mean	41.58	42.58
Range	20-60	20-60
Sex ratio		
M/F	1.78:1	2.11:1
Body weight (kg)	51.92	53.35
Range	30-60	30-60

Most of the patients were in the age group 40-50 years, with male predominance over females. Most of the patients were in the range of 50-60 kgs.

Table-2 : Indications for laparoscopic cholecystectomy.

Operative procedure	Group I Isoflurane (n=25)	Group I Halothane (n=25)
Chronic cholecystitis with cholethiasis (CC with CL)	12	14
Chronic cholecystitis with cholelithiasis with obstructive jaundice	8	8
Acute cholecystitis with cholelithiasis	3	2
Mucocele of gall bladder	2	0
Empyema of gall bladder	0	1

Table 2 shows 48% patients in group I and 56% in Group II had indication of CC with CL.

Table-3 : Changes in mean pulse rate (bpm) in both groups at various time intervals.

Groups	Group I Isoflurane (n=25)	Group II Halothane (n=25)
Before induction (control value)	86.80 ± 8.24	84.62 ± 8.42
Induction	106.84 ± 8.52	104.41 ± 9.21
Volatile Anesthetic switched on (incision)		
5 min (CO_2 insufflated)	97.71 ± 7.50	88.70 ± 9.30
15 min	90.84 ± 5.66	77.46 ± 9.78*
30 min	90.83 ± 6.69	72.80 ± 8.22**
45 min	88.21 ± 6.67	68.60 ± 8.12**
After CO_2 removal (Deflation)	86.70 ± 1.99	82.14 ± 1.78
End of surgery	104.84 ± 2.14	106.47 ± 2.18
Postop 15 min	97.6 ± 2.11	98.12 ± 1.12
30 min	84.77 ± 2.10	82.41 ± 2.10

Isoflurane (Group I) maintained the pulse rate towards the higher side as compared to Halothane (Group II)

* p value < 0.05 statistically significant

** p value < 0.01statistically highly significant

Table-4 : Changes in mean arterial presence (mmHg) in both the group.

Groups	Group I (Isoflurane (mean±SD)	Group II (Halothane n=25)
Before induction (control value)	92.88 ± 6.41	94.03 ± 6.34
Induction	116.33 ± 7.61	114.84 ± 7.41
Volatile Anesthetic switched on (incision)		
5 min (CO_2 insufflated)	114.66 ± 5.42	132.01 ± 5.91
15 min	108.01 ± 6.62	130.33 ± 6.42*
30 min	110.66 ± 5.41	128.61 ± 4.31**

45 min	103.33 ± 5.11	126.31 ± 6.44**
After CO_2 removal (Deflation)	114.02 ± 1.14	116.04 ± 1.78
End of surgery	112.00 ± 1.24	126.07 ± 3.12
Postop 15 min	96.00 ± 1.20	114.16 ± 1.12
30 min	92.00 ± 4.26	98.00 ± 11.21

Isoflurane (Group I) lowered the mean arterial pressure more than Halothane (Group II)

* p value < 0.05 statistically significant

** p value < 0.01statistically highly significant.

Table -5: Change in Arterial O_2 saturation (SPO_2) in both groups.

Groups	Group I Isoflurane (mean±SD)	Group II Halothane (n=25)
Before induction (control value)	98.00 ± 2.10	98.40 ± 1.98
Induction	99.00 ± 1.98	99.00 ± 1.46
Volatile Anesthetic switched on (incision)		
5 min (CO_2 insufflated)	99.40 ± 1.35	97.80 ± 1.22
15 min	99.06 ± 1.42	98.60 ± 1.32
30 min	98.8 ± 1.40	97.80 ± 1.22
45 min	98.6 ± 1.47	98.80 ± 1.21
After CO_2 removal (Deflation)	98.4 ± 1.37	98.60 ± 1.88
End of surgery	98.8 ± 1.35	98.20 ± 1.24
Postop 15 min	99.00 ± 1.58	99.00 ± 1.97
30 min	98.4 ± 1.47	99.20 ± 1.71

No significant difference in SPO_2 was found in both the groups (p> 0.05).

Talbe-6 : ECG changes in lead II.

	Group I Isoflurane (n=25)		Group II Halothane (n=25)	
	No. of patients	%	No. of patients	%
Sinus Bradycardia	-	-	4	16%
Sinus Tachycardia	2	4%	-	-
ST Segment changes	-	-	2	8%
Ectopic changes	-	-	1	4%

Sinus Bradycardia ,ST Segment changes ,ectopics were observed in Group II (Halothane) which were transient and disappeared on withdrawal of inhalational agent.

Table-7 : Changes in End Tidal carbon dioxide concentration (E_TCO_2) in both the group (mmHg).

Time Interval	Group I Isoflurane (n=25)	Group II Halothane (n=25)
Induction	36.74 ± 1.37	35.83 ± 1.21
5 min after volatile anesthetic switched on	39.76 ± 1.08	39.94 ± 1.24
15 min after volatile anesthetic switched on	39.14 ± 1.04	39.25 ± 1.30
30 min after volatile anesthetic switched on	38.36 ± 2.06	38.54 ± 2.04
45 min after volatile anesthetic switched on	40.24 ± 2.37	40.61 ± 1.81

After reversal	35.67 ± 2.34	37.64 ± 1.24

The above table shows the changes in E_TCO_2 in the two groups at various times interval intraoperatively. It is evident from the table that there was statistically insignificant ($p > 0.05$) change in E_TCO_2 in both the groups at any time interval intraoperatively. Patients were kept on IPPR to maintain E_TCO_2 between 35-40 mmHg.

Table-8 : Postoperative period : Complication and Recovery pattern in both the groups.

S. No.	Complication	Group I Isoflurane (n=25)	Group II Halothane n=25
1.	Nausea / vomiting	3 patients	2 patients
2.	Shoulder pain	1 patient	3 patients
3.	Postoperative analgesic requirement I/V fentanyl (1-2µg/kg)	16 patients	19 patients
4.	Degree of awareness PRST Score (0-8)	PRST-2	PRST-4
5.	Recovery pattern	Time(min)	Time(min)
I	Opening eyes on command	4.42 ± 1.48	7.59 ± 1.50
II	Recall of name	5.10 ± 1.44	6.30 ± 3.01
III	Response to painful pinch	4.25 ± 1.97	5.25 ± 2.24
IV	Handgrip	6.90 ± 1.52	8.20 ± 3.01
V	Spontaneous movement	3.60 ± 1.66	4.40 ± 2.16