

Effect of Propofol, Sevoflurane, and Isoflurane on Postoperative Cognitive Function Following Laparoscopic Cholecystectomy in Elderly Patients

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Abstract

Cognition refers to the mental action or process through which an individual acquires knowledge solves problems and makes decisions for the future. In other words, cognition may be defined as the mental processes which account for the daily activities carried out by an individual. Deficits in these mental processes tend to affect the memory, attention, verbal and non-verbal learning, visual and auditory processing, and motor functioning of an individual, thereby resulting in cognitive impairment. Memory is classified into two types, that is, explicit memory and implicit memory. Explicit memory involves the conscious recall of the information received in the past while implicit memory refers to the information or knowledge which is unconsciously and effortlessly recalled.

Keywords: cognition, memory, mental, motor function.

Introduction

Cognition refers to the mental action or process through which an individual acquires knowledge solves problems and makes decisions for the future. In other words, cognition may be defined as the mental processes which account for the daily activities carried out by an individual. Deficits in these mental processes tend to affect the memory, attention, verbal and non-verbal learning, visual and auditory processing, and motor functioning of an individual, thereby resulting in cognitive impairment [1]. Memory is classified into two types, that is, explicit memory and implicit memory. Explicit memory

involves the conscious recall of the information received in the past while implicit memory refers to the information or knowledge which is unconsciously and effortlessly recalled [2].

It was described by Bedford for the first time in 1955 that some elderly patients suffered from post-operative cognitive dysfunction (POCD) after being subjected to anesthesia and surgery [3]. Later, several researchers carried out studies to determine the impact of the commonly used medications to induce anesthesia before operations such as propofol, sevoflurane, and isoflurane on the implicit and explicit memory of patients. Most of the studies indicated that these medications bring about a negative impact

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on the cognition or mental processes of elderly patients [4].

Sevoflurane came to be in use in surgical departments in the year 1970. Relatively insoluble in blood, sweet-smelling, fluorinated methyl isopropyl ether is highly effective in rapid induction and recovery from anesthesia [5]. Exposure to sevoflurane cause neurodegeneration, thus bringing about major changes in the behavior of an individual, causing anxiety and spatial memory deficits. On the other hand, propofol, which was introduced in surgeries in the late 1980s is a short-acting induction agent which offers patients a rapid recovery even after infusions a long period. The major impact of this agent is found to be the decreased level of consciousness in the patients. Isoflurane is another common inhalation anesthetic agent used which causes the relaxation of muscles and reduces pain in patients. Exposure to isoflurane may lead to respiratory issues, hypotension, nausea, and vomiting in the postoperative period. In this regard, it can be stated that the anesthetic medications used during induction and maintenance are most likely to affect their cognitive ability.

Material and Methods

The study was conducted after clearance from the Board of Studies and after the approval of the institution's Ethical Committee in the Department of Anaesthesiology as well as informed consent from all the patients in SGRRIM&HS, Patel Nagar, Dehradun during the period 2020-2023. A double-blinded, prospective study was conducted, involving 90 ASA (**American Society of Anesthesiologists**) I and II aged more than 60 years patients posted for laparoscopic cholecystectomy.

Methodology

Written informed consent was taken from all the patients. A detailed pre-anesthetic evaluation was carried out to rule out the presence of any significant co-morbidity. All patients were kept nil orally from 8 h before surgery and pre-medicated with tablet alprazolam 0.25 mg and tablet

ranitidine 150 mg orally on the night before. The selected patients were randomly divided into three groups by computer-generated randomized number and then by picking sealed envelope and divided into three groups of 30 patients each to receive Propofol infusion (Group A), Sevoflurane inhalation (Group B) and Isoflurane inhalation (Group C) for maintenance of anesthesia. A thorough pre-operative check-up, general and systemic examination, and routine investigations were done. Cognitive functions were assessed preoperatively (1 hour prior) by the Rivermead behavioral memory test, California verbal learning test, and by asking the name of the surgeon and anesthesiologist.

In the operating room, baseline heart rate (HR), electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO₂) were recorded in all patients. All patients were given an injection of glycopyrrolate 4 µg/kg and an injection of midazolam 0.025 mg/kg via the intravenous route. Injection fentanyl 2 µg/kg IV was given to all patients just before induction. In both groups, induction was done with the injection of propofol 2-2.5 mg/kg of body weight till initial loss of verbal contact, and after checking for ventilation injection of vecuronium 0.1 mg/kg IV was administered. Endotracheal intubation was done after 3 mins of intermittent positive pressure ventilation with an appropriate-sized cuffed endotracheal tube. Group A patients were maintained on N₂O/O₂ (60/40%) and propofol infusion at the rate of 50-100 µg/kg/min titrated to maintain adequate depth of anesthesia.

Group B patients were maintained on N₂O/O₂ (60/40%) and sevoflurane 1-1.5% to achieve adequate depth of anesthesia. In addition, 25-100µg of fentanyl was given when Mean Arterial Pressure (MAP) and HR were 20% higher than baseline. Group C patients were maintained on N₂O/O₂ (60/40%) and isoflurane 1- 1.5% to achieve adequate depth of anesthesia. In addition, 25-100 µg of fentanyl was given when Mean Arterial Pressure (MAP) and HR were 20% higher than baseline. After stopping Injection Propofol, sevoflurane, and isoflurane were.

Injection neostigmine 0.05 mg/kg IV and injection glycopyrrolate 0.008 mg/kg IV were used for the reversal of neuromuscular blockade. Extubation was done after the return of spontaneous breathing and adequate motor recovery. Postoperatively injection of tramadol 100 mg sos is given.

Hemodynamic parameters ((HR, SBP, DBP, and MAP) were recorded and compared every 15 mins till the completion of surgery.

Recovery characteristics were recorded as:

a) Time from discontinuation of anesthetic agents to spontaneous breathing and eye-opening.

b) Time from discontinuation of anesthetic agents to an adequate response to verbal commands.

c) Time to extubation after discontinuation of anesthetic agents.

d) Time from discontinuation of anesthetic agents to orientation (to time, place, and person).

e) Modified Aldrete scoring was recorded every 15 minutes for one hour postoperatively. Patients required nine or more points for eligibility to discharge from the recovery room.

f) VAS score for postoperative pain was recorded every 30 mins for two hours in the recovery room.

Cognitive functions were assessed both preoperatively (1 hour prior) and postoperatively (after 2 hours) as:

1. River mead Behavioural Memory Test (RBMT): An animal was shown preoperatively to all patients and patients were asked to identify this animal postoperatively.
2. California Verbal Learning Test (CVLT): To check verbal memory, patients were checked whether they could rename five fruits postoperatively which they told preoperatively
3. Digit span test(DST)- Patients were asked to repeat four, five, or six-digit numbers to assess numerical memory.
4. Patients were asked to recall the names of the anaesthesiologist and surgeon both preoperatively and postoperatively.

5. MMSE SCORE – evaluated before surgery to know if there was any pre-existing cognitive dysfunction. The same was evaluated after the reversal of anesthesia.

Inclusion Criteria:

1. ASA grade I and II, elective cases
2. Age group: more than 60 years
3. Both sexes.
4. Education till high school.

Exclusion Criteria

1. Age less than 60 yrs.
2. ASA grade III and higher.
3. Allergy to the used drugs.
4. Patients receiving treatment with anti-anxiety drugs, anticonvulsants, and antipsychotics, patients with known psychiatric illness, drug or alcohol abuse, patients having chronic pain syndrome, Alzheimer's disease or presenile dementia, pregnant and lactating women, history of jaundice in the past.
5. Patients refusal
6. The patient's education level is below high school.

Results

The frequency distribution of Age interval, where 70 subjects were found in 61-70 Years i.e., 67.70%, 17 subjects were found in 71-80Years i.e., 18.90%, and 3 subjects were found in >85 Years i.e., 3.30%.

The frequency distribution of **Sex**, where 62 subjects were found to be Female i.e., 68.90%, and 28 subjects were found in Male i.e., 31.1%.

The frequency distribution of cases concerning ASA grading, in ASA 30(33.33%), 60(66.66%) subjects were found in Grade-I and Grade II.

In the comparison of Sex between DRUGS-GROUP, the result was found not Significant as the P-value is >0.05.

In the comparison of AGE INTERVAL between DRUGS-GROUP, the result was found not Significant as the P-value is >0.05.

In the comparison of Variables between DRUGS-GROUP, the result of Mean Age, Mean Height, Mean Weight, and Mean BMI were found not Significant as the P-values are >0.05 .

The comparison of HR between DRUGS-GROUP, the result of Mean HR at PRE-OP, at T0, and T15 were found not Significant as the P-values are >0.05 and the result of Mean HR at T30 and at POST-OP were found statistically significant as the p-values are <0.05 .

In the comparison of HR between DRUGS-GROUP, the result of Mean HR at T30 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean HR at POSTOP between Group B with Group A was found statistically significant as the p-value is <0.05 and the result of Mean HR at POSTOP between Group A with Group C was found statistically significant as the p-value is <0.05 .

In the comparison of SBP between DRUGS-GROUP, the result of Mean SBP at PRE-OP was found not Significant as the P-values are >0.05 and the result of Mean SBP at T0, T15, T30, and at POST-OP were found statistically significant as the p-values are <0.05 .

In the comparison of SBP between DRUGS-GROUP, the result of Mean SBP at T0 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean SBP at T0 between Group B with Group C was found statistically significant as the p-value is <0.05 , the result of Mean SBP at T15 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean SBP at T15 between Group B with Group C was found statistically significant as the p-value is <0.05 , the result of Mean SBP at T30 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean SBP at T30 between Group B with Group C was found statistically significant as the p-value is <0.05 and the result of Mean SBP at POSTOP between Group B with Group A was found statistically significant as the p-value is <0.05 .

In the comparison of DBP between DRUGS-GROUP, the result of Mean DBP at PRE-OP was

found not Significant as the P-values are >0.05 and the result of Mean DBP at T0, T15, T30, and at POST-OP were found statistically significant as the p-values are <0.05 .

The comparison of DBP between DRUGS-GROUP, the result of Mean DBP at T0 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean DBP at T0 between Group B with Group C was found statistically significant as the p-value is <0.05 , the result of Mean DBP at T15 between Group B with Group A was found statistically significant as the p-value is <0.05 , the result of Mean DBP at T15 between Group B with Group C was found statistically significant as the p-value is <0.05 , the result of Mean DBP at T30 between Group B with Group C was found statistically significant as the p-value is <0.05 , the result of Mean DBP at POST OP between Group B with Group A was found statistically significant as the p-value is <0.05 and the result of Mean DBP at POST OP between Group B with Group C was found statistically significant as the p-value is <0.05 .

The comparison of Spo2 between DRUGS-GROUP,

The result of Mean Spo2 at PRE-OP, at T0, at T15, at T30, and POST-OP were found not significant.

The comparison of Variables between DRUGS-GROUP, the result of Mean Spontaneous breathing (min), Mean Eye opening (min), Mean Response to commands (min), and Mean Orientation to stating the name (min) were found statistically significant as the p-values are <0.05 .

Mean SPONTANEOUS BREATHING (MIN)

- Statistically significant between Group B and Group A as the p-value is <0.05 ,
- Statistically significant between Group B and Group C as the p-value is <0.05 ,
- Statistically significant between Group A and Group C as the p-value is <0.05 ,

Mean EYE OPENING (MIN)

- Statistically significant between Group B with Group A as the p-value is <0.05,
- Statistically significant between Group B with Group C as the p-value is <0.05,
- statistically significant between Group A with Group C as the p-value is <0.05

Mean RESPONSE TO COMMANDS (MIN)

- Statistically significant between Group B with Group A as the p-value is <0.05,
- Statistically significant Between Group B with Group C as the p-value is <0.05,

Mean EXTUBATION (MIN)

- Statistically significant between Group B with Group A as the p-value is <0.05,
- Statistically significant between Group B with Group C as the p-value is <0.05,
- Statistically significant between Group A with Group C as the p-value is <0.05,

Mean ORIENTATION TO state NAME (MIN)

- Statistically significant between Group B with Group A as the p-value is <0.05,
- Statistically significant between Group B with Group C as the p-value is <0.05
- Statistically significant between Group A with Group C as the p-value is <0.05

Mean RBMT - Statistically insignificant ($p>0.05$) between drugs-group postoperatively.

Mean CVLT - Statistically insignificant ($p>0.05$) between drugs-group postoperatively

Mean of DST - Statistically insignificant ($p>0.05$) between drugs group postoperatively.

Mean Recall test - Statistically insignificant ($p>0.05$) between drugs group postoperatively.

Mean MMSE test - Statistically significant ($p<0.05$) between drugs group postoperatively.

Mean MODIFIED ALDRETE SCORE - statistically significant ($p <0.05$) at 15 MIN postoperatively between drugs group.

Discussion

Laparoscopy surgeries are widely used due to their higher advantage in terms of less incisional pain, shorter incision length, early recovery, shorter hospital stay, and less incidence of ileus compared to open surgeries. However, Postoperative Cognitive Dysfunctions (POCD) such as impairments in recent memory, concentration, language, comprehension, and social integration curb the increased advantages of laparoscopy. Surgical trauma and general anesthetics are observed to be major determinants of post-operative impairments in attention, memory, reaction time, and consciousness. The factors such as glucocorticoid levels, pre-existing cognitive impairment, neuroinflammation, age, brain hypoperfusion, hypoxia, and genetic aspects also potentially cause post-operative cognitive dysfunction^[5] There are mainly three types of Cognitive dysfunctions post-surgery namely short-term cognitive disturbance, Delirium, and true Post-operative cognitive dysfunction (POCD) in which cognitive dysfunction may last for weeks, months, or even longer. The post-operative cognitive dysfunction causes a delay in functional recovery which in turn lead to a prolonged hospital stay. This is vital in the case of surgeries such as laparoscopic cholecystectomy where there is a short discharge time after anesthesia. Furthermore, it is evident from the previous literature that general anesthetics such as propofol and sevoflurane cause cognitive dysfunction. Although the effectiveness of anesthetics is extensively studied, there is scant literature on the effect of different types of anesthetic agents on postoperative cognitive dysfunction. Against this backdrop, our study was conducted to study the occurrence of POCD by using general anesthetic agents specifically Propofol, Sevoflurane, and Isoflurane, and to compare the effect of these agents on postoperative cognitive functions among the elderly.

Conclusion

The present study findings suggest the desirable outcome with the use of sevoflurane against propofol and isoflurane among elderly patients for laparoscopic cholecystectomy concerning postoperative cognitive

function. Hence, it is imperative to consider geographical and socio-demographic characteristics and target population in the choice of general anesthetic agent.

In conclusion, the use of sevoflurane in comparison to propofol and isoflurane among elderly patients for laparoscopic cholecystectomy had better outcomes concerning postoperative cognitive function.

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Informed Consent: written informed consent was taken from patients.

Ethical Approval: ethical committee approval was taken from the Institutional Committee Of Ethics, SMI (SMI/2021/10-99)

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Conflict of Interest: there was no conflict of interest

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