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EVALUATION OF SEVOFLURANE AND PROPOFOL'S EFFECT ON COGNITION AND MEMORY IN PATIENTS UNDERGOING LAPROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

General anesthesia (GA) may cause post-operative impairment of cognition and memory. This is of importance where time to discharge after anesthesia is short as after laparoscopic cholecystectomy. This study was conducted to compare the effects of propofol and sevoflurane on cognitive function in the post-operative period. Methods: After approval of the Ethical Committee, 70 female patients posted for laparoscopic cholecystectomy to be performed under GA were randomly divided into two groups. Propofol was used in Group P and sevoflurane in Group S. Data analysis was done with California verbal learning test (CVLT), digit span test (DST), Rivermead behavioural memory test (RBMT), mini mental state examination (MMSE) score Results: Cognition and explicit memory were affected more in the propofol group in the immediate post-operative period. Conclusion: Propofol was associated with significant impact on cognitive functions in comparison to sevoflurane in the immediate post-operative period. Sevoflurane anesthesia might be a better option in day care surgeries.

KEYWORDS: Anesthesia, Propofol, Sevoflurane, Cognitive function, Daycare surgery.

INTRODUCTION

Anaesthetic agents are prone to affect brains function in post operative period especially the General anaesthetic agents. Impairment of attention, memory, reaction time, and depressed level of consciousness are often reported.[1] Delayed functional recovery as a consequence of

cognitive dysfunction would lead to prolonged hospital stay in patients undergoing GA. This is of great importance where time to discharge after anaesthesia is short as after laparoscopic cholecystectomy. Daycare surgeries are becoming more and more popular to cater to the needs of patients with tight work schedules and delayed recovery due to cognitive dysfunction is definitely not warranted. When providing GA, the goal is to achieve optimal surgical conditions while ensuring an early recovery. The causes of prolonged recovery of cognition and memory after anaesthesia and surgery are multifactorial. Various studies have implicated agents such as propofol and sevoflurane in the development of post-operative cognitive dysfunction (POCD).[2,3] Agents such as propofol, sevoflurane, nitrous oxide act on various types of receptors in the brain and these in turn may lead to POCD.[4,5] Sevoflurane and propofol are two most commonly used anaesthetic agents in day care cases. The present study was to compare the effects of sevoflurane with that of propofol on cognition and memory in patients.

METHODS AND MATERIALS

This study was designed as prospective randomized comparative study, conducted after obtaining approval of the Ethical Committee of the Institution. A total of 70 female patients posted for elective laparoscopic cholecystectomy to be performed under GA were included, after getting informed consent and they were divided into two groups of 35 patients each The endpoint was to compare early post-operative cognitive functions between the two groups. Propofol was used in Group P and sevoflurane in Group S. All patients underwent a thorough pre-anaesthetic check-up. Inclusion criteria were female sex, American Society of Anaesthesiologists (ASA) I physical status, age group between 18 and 40 years, education >8th and pre-operative mini mental state examination (MMSE) score >23. Exclusion criteria included male patients, age >40 years or <18 years, ASA Grade-II or higher, allergy to the drugs to be used, 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 pre senile dementia, pregnant and lactating women, history of jaundice in the past, patient refusal, patient's education level below 8th and pre-operative MMSE score <23. Pre-operative data were collected 1 h prior to surgery. In the operation theatre, baseline hemodynamic parameters heart rate, electrocardiography, non-invasive blood pressure, pulse rate and pulse oximetry were recorded in all patients.

After securing the intravenous line, injection fentanyl 2 µg /kg IV, injection glycopyrrolate 5 µg/ kg IV were administered to the patients. In Group P, anesthesia was induced with injection propofol 2 mg/kg IV slowly till BIS value 40 – 60 was achieved and maintained with propofol infusion at the rate of 100 to 300 µg /kg/min and inj. Atracurium at titrated doses. NM blockade was reversed with inj. Neostigmine 0.04 mg/kg and inj.Glycopyrolate 0.01 mg/kg. Trachea was intubated with an appropriate sized cuffed endotracheal tube. Maintenance of anaesthesia was done using oxygen: N2O at the ratio of 33:67. In Group S, anaesthesia was induced with inhalation of O2 and sevoflurane (5%) till BIS value of 40–60 was reached and maintenance of anaesthesia was with oxygen: N2O 33:67, sevoflurane and atracurium 0.5mg/kg. Rest of the procedure was kept uniformly same as in Group P.

Data collection and analysis were done as per following tests both pre-operatively (1 h prior) and post-operatively (at 5 min; 1, 2 and 4 h) California verbal learning test (CVLT).[6] – Patients were asked to remember the names of five fruits so as to check verbal memory. Digit span test (DST).[7] – Patients were asked to repeat four, five or six digit numbers to assess numerical memory. Rivermead behavioural memory test (RBMT).[8] – Patients were shown a picture of an animal pre-operatively and asked to identify this animal post-operatively and also asked if the location of the animal was same so as to check the recall of day today items by picture recognition. RBMT.[8] was used to check the semantic memory through recall of date of birth post-operatively. MMSE[9] score – evaluated prior to surgery in order to know if there was any pre-existing cognitive dysfunction. Same was evaluated after reversal of anaesthesia. The results were entered into excel spread sheet and analyzed using students t test for normally distributed data.

RESULTS

Demographic data were comparable between the two groups. There was no statistical difference in mean duration of anaesthesia /surgery between two group and the *P* value was 0.79. Cognitive functions and memory assessed by various tests and questionnaires after reversal of anaesthesia at 5 min, 1, 2 and 4h post-operatively showed following results. The comparison of MMSE between the two groups at 5 min Post operatively was significant p value <0.05 (p=0.01), the MMSE at 1 hour post operatively was significant p value < 0.05 (p=0.02) while the 2 hour postoperative value and the 4 hour post operative result comparison showed non significant values.

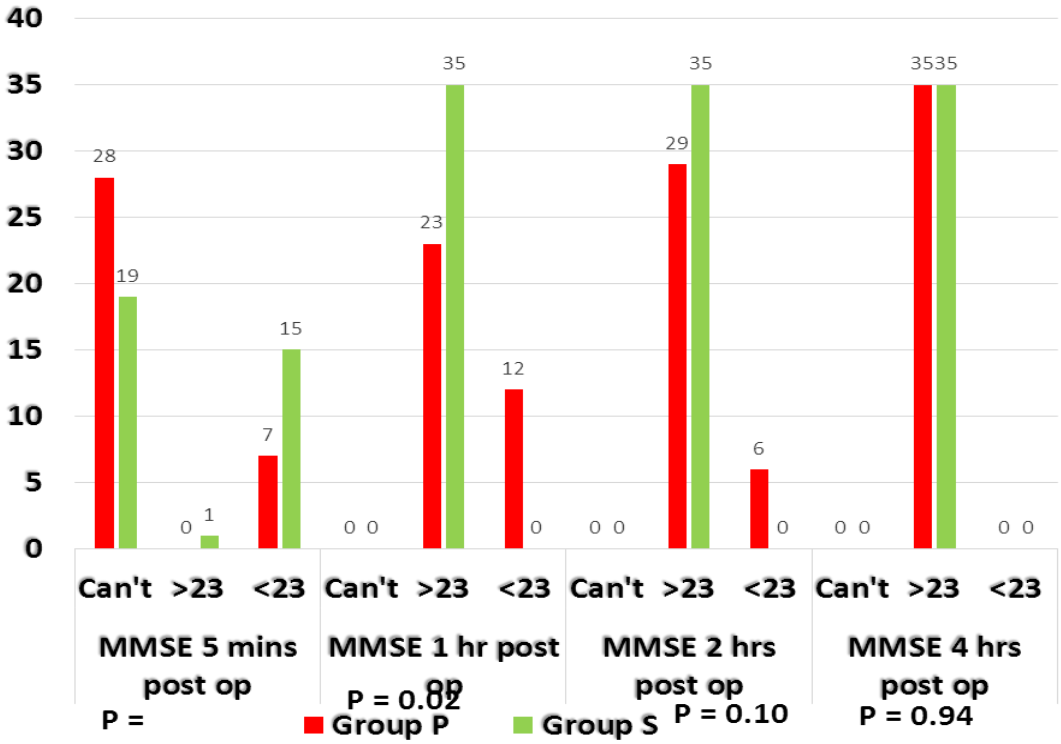

Figure 1: Post - Operative Mini Mental State Examination.

The comparison of MMSE between the two groups at 5 min Post operatively was significant p value <0.05 (p=0.01), the MMSE at 1 hour post operatively was significant p value < 0.05 (p=0.02) while the 2 hour postoperative value and the 4 hour post operative result comparison showed non significant values.

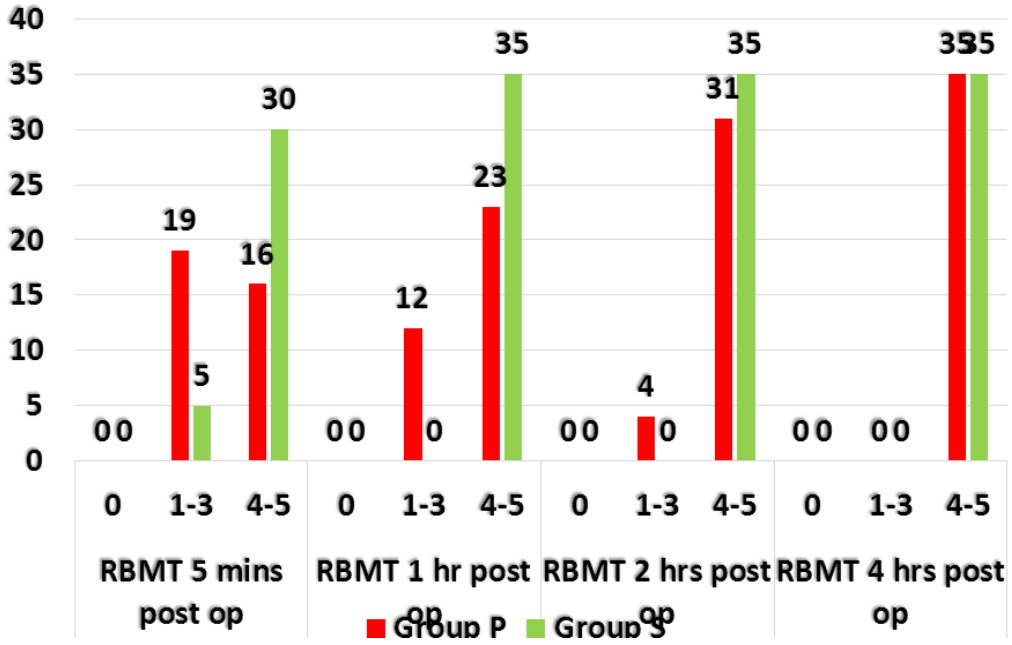

Figure 2: Rivermead Behavioural Memory Test

The RBMT showed significant results between the two groups at 4 min post operative and one hour postoperatively p value =0.002 ,p=0.004. The second hour and the fourth hour values were non significant

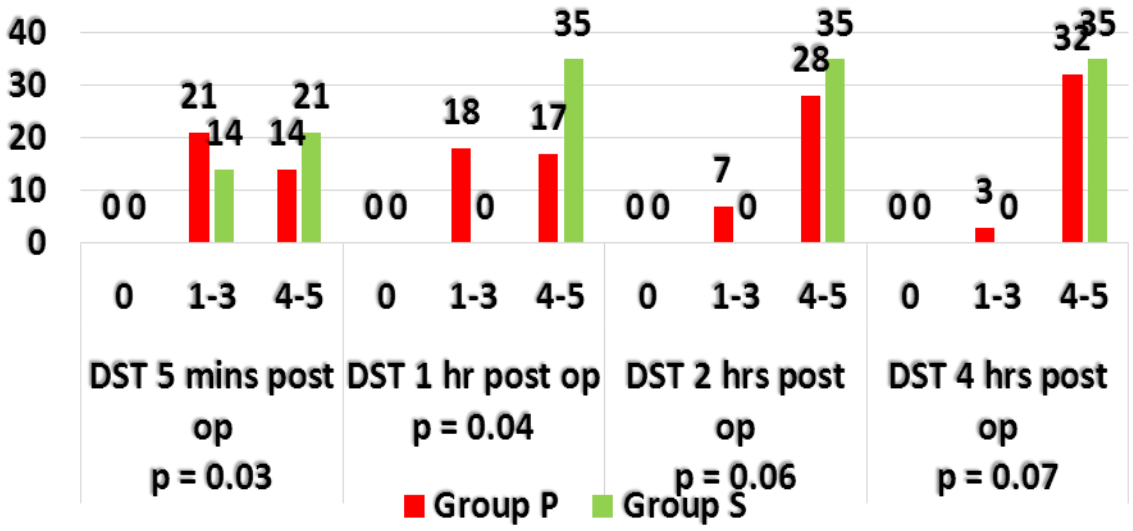

Figure 3: Digit Span Test.

The results of DST were found to be significant for the 5 min postoperative period and 1 hour post operatively p= 0.03,p=0.04 respectively. The second hour and fourth hour postoperative recording were statistically non significant.

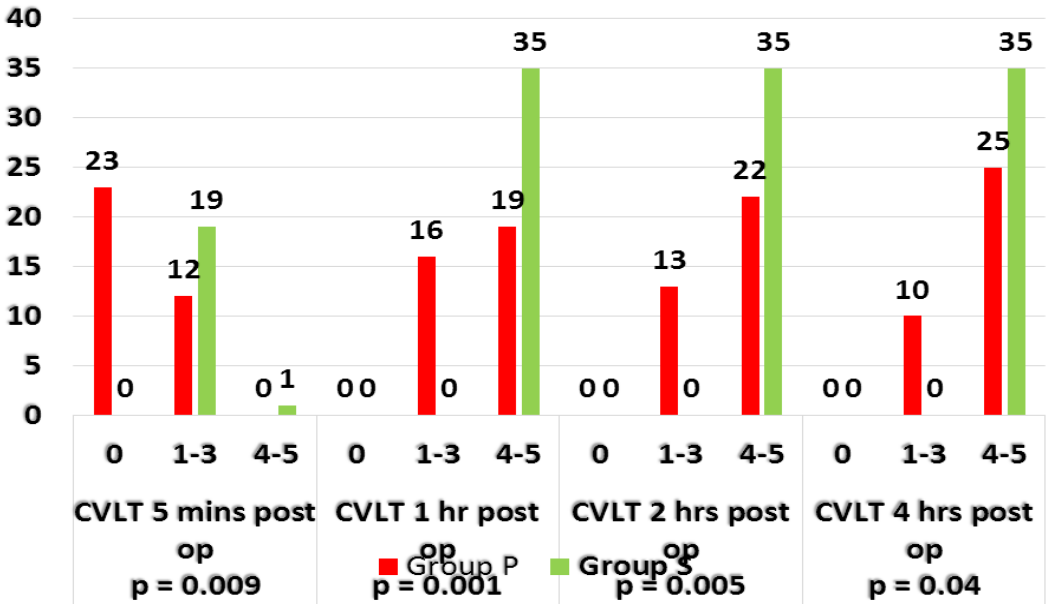

Figure 4: California Verbal Learning Test.

The record of CVLT showed statistical significance in all the four postoperative period 5 min=0.009, one hour p=0.001, second hour p=0.005 and the fourth hour comparison showed significance with p value = 0.04

DISCUSSION AND CONCLUSION

Cognition refers to all the mental activities involved in receiving, comprehending, storing, retrieving and using the information. Post operative cognitive dysfunction is impairment of mental process of perception; memory and information processing which allows the individual to acquire knowledge solve problems and plan for the future. Post-operative cognitive dysfunction is characterized by impairment of memory and cognitive function, reduced ability to concentrate and deterioration in emotional or social behavior. Three types of cognitive deterioration after surgery are delirium, short-term cognitive disturbance and true POCD which is a subtle deterioration in cognitive function lasting for weeks, months or longer.[1] It has been subjected to extensive research. Apart from anaesthetic agents, various other suspected factors are glucocorticoid levels, pre-existing cognitive impairment, neuro inflammation, age, brain hypoperfusion, hypoxia, and genetic aspects.[10,5] One study by Terri[11] however, offered firm evidence that commonly used inhaled anaesthetic agents do not increase the incidence of cognitive problems such as delirium in the early post-operative period. Anaesthetic drugs may act by causing long-term receptor changes, apoptosis, changes in cholinergic binding and gene expression.[12,13] The incidence of POCD which is reported in various studies involving the same form of surgery and anaesthesia varies immensely. The mechanistic pathways through which an anaesthetic drug could cause amnesia is enormous, most of which are still under evaluation. Propofol is said to be an archetypal amnestic drug though it encodes information robustly, it fails to consolidate and hence causes accelerated decay in memory processing. It is found to attenuate the hippocampal activation in response to various stimuli and also inhibits NMDA receptor dependent/independent long term potentiating in the memory model. On the other hand sevoflurane has not only been shown to precondition the brain to inflammatory changes and ischemia, but also to reduce the release of pro inflammatory cytokines. It is also found to attenuate acetylcholine induced phosphorylation of tau protein which is a proposed cause for POCD. Sevoflurane also causes up regulation of NMDA receptors which help in the enhancement of long term potentiating in the memory model.

In the present study, short-term POCD is evaluated. Traditionally, intelligence tests or tests developed for clinical neuropsychology have been used mostly in the geriatric age group. Post-operative delirium in elderly is one of the most under diagnosed clinical entities in anaesthesiology practice, which enhances the morbidity and mortality on this subset of the population.[14] There was no benefit of using total IV anaesthesia with propofol and opioid over the conventional balanced volatile technique in terms of recovery and cognitive functions.[15] Emergence and return of cognitive function were significantly faster after propofol compared with sevoflurane when assessed 60 min post-operatively in anotherstudy.[16] In our study, propofol has been shown to affect explicit memory and other cognitive functions more in the immediate post-operative period. Sevoflurane, an inhalational anaesthetic of the ethereal origin with low solubility in blood and body tissue is characterised by rapid induction and recovery and has been found to have less cognitive impairment than propofol.[17] Sevoflurane with a blood gas partition coefficient of 0.65 might, therefore, be a better drug as far as short-term preservation of cognitive functions are concerned and hence a better option in day care surgeries.

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