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Original Article

Influence of Pre-operative Cognitive Status on Propofol Requirement to Maintain Hypnosis in the Elderly: A Study of 50 Cases

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Abstract

Introduction: In elderly patients decrease in cognitive function after anesthesia has been reported in the literature for over a century. Various studies have implicated agents such as propofol and sevoflurane in the development of post-operative cognitive dysfunction. We evaluated the effect of pre-operative cognitive status by mini–mental state examination (MMSE), on consumption of propofol during anesthesia in the elderly.

Materials and Methods: In this prospective observational study, we included 50 patients (65-99 years) undergoing elective abdominal surgeries under general anesthesia. Propofol infusion was adjusted to the bispectral index (BIS) and was maintained within 40-60. Multiple linear regression analysis determined if body mass index (BMI), age, baseline BIS, gender, and pre-operative MMSE score were related to the consumption of propofol.

Observation: MMSE and BMI scores were significantly related to the mean value of consumption of propofol. A decrease in propofol requirement in patients >65 years of age was associated with a low MMSE score. Effect of age, gender, and baseline BIS on the propofol consumption was insignificant.

Conclusion: To maintain hypnosis propofol requirement during general anesthesia appears to decrease with deterioration in the cognitive status in elderly patients. Cerebral cholinergic dysfunction associated with cognitive dysfunction may influence propofol sensitivity in aged patients.

Key words: Cognition, General anesthesia, Mini-mental state examination, Propofol requirement

INTRODUCTION

In elderly patients decrease in cognitive function after anesthesia has been reported in the literature for over a century, there is still a lack of consensus as to whether anesthetic agents may directly cause permanent cognitive loss.[1] The general concern has been that while the potential neurotoxicity of anesthetics may be well tolerated by younger persons, age-related losses in cerebral reserve, increased permeability of the blood–brain barrier and slower drug elimination rates may lead to adverse effects and perhaps also precipitate neurodegenerative disorders.

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The causes of prolonged recovery of cognition and memory after anesthesia and surgery are multifactorial. Various studies have implicated agents such as propofol and sevoflurane in the development of post-operative cognitive dysfunction. Agents such as propofol, sevoflurane, nitrous oxide (N_2O), midazolam, and fentanyl act on various types of receptors in the brain and these, in turn, may lead to cognitive dysfunction.[2] The Folstein test or mini–mental state examination (MMSE) is a 30-point questionnaire test which is useful for screening briefly for impairment cognition.[3-6] MMSE is generally used for screening dementia in medicine. It is used in estimating the severity of impairment of cognition and following the changing course in cognition in an individual over time, thus making it an efficient way for documenting the treatment response in each individual. In this study, we evaluated the influence

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of pre-operative cognitive status using MMSE on propofol requirement to maintain hypnosis in the elderly and evaluated the influence of propofol on cognitive status.

MATERIALS AND METHODS

After obtaining individual informed consent and approval from the Ethical Committee 50 patients under ASA II and III, in the age group of 65-99 years, undergoing elective abdominal surgery under general anesthesia were included in this prospective, observational study. In this patient with ASA IV, increased levels of anxiety preoperatively (Hamilton Anxiety Scale [HAMA] >23), increased levels pain preoperatively (visual analogue scale > 4), severe impairment in cognition without responses to pain and anxiety score assessment and patients taking anticholinergic drugs were excluded in this study.

Assessment of the cognitive performance of patients was done using MMSE. The MMSE is a tool for screening cognitive performance, particularly in the elderly patients. The MMSE includes an instructions list, that examines: "Orientation in space (five points) and time (five points), registration (three points) and recall of words (short-term memory, three words), attention or calculation (five points), language naming (two points), repetition of a sentence (one point), following a three-stage command (three points), reading (one point), writing (one point), and copying a visual construction (one point). The maximum MMSE score is 30. Poor cognitive performance was defined by MMSE total score of 23 or less. The HAMA is a rating scale for quantifying severity of anxiety and is mostly used in evaluating patients under psychotropic drugs.[7] It consists of 14 items, each defined by a series of symptoms. Each item is rated on a five-point scale, ranging from 0 (not present) to 4 (severe). If the total score is 17 or less, the anxiety is deemed to be mild; in the range of 18-23, the person is deemed to have a mild-to-moderate anxiety, and a score of 25 indicates a severe anxiety. The Hamilton anxiety scale, MMSE score, and the visual analogue pain score were obtained during pre-operative assessment just before surgery. The MMSE score is measured preoperatively and postoperatively after 1 h.

Anesthetic management was standardized in all patients. Premedication was not given to any patient. An 18 G catheter was inserted in a forearm vein for fluid and drug administration. Monitoring with non-invasive blood pressure (BP), electrocardiogram, saturation of oxygen (SpO_2), end-tidal CO_2, and bispectral (BIS) (intraoperatively) were instituted during the procedure.

Infusion pump for propofol was kept ready. Anesthesia machine (dragger work station) was checked, and all emergency drugs kept ready. All patients were premedicated with glycopyrrolate 0.2 mg IM, 15-30 min before surgery. All patients were preoxygenated with 100% oxygen and induced with fentanyl 2 mcg/kg and propofol 2 mg/kg or till BIS drops to 40 and intubation facilitated with suxamethonium 2 mg/kg intubation done with ET tube size 8-8.5 mm for men and 7-7.5 mm for women. Anesthesia maintained with atracurium 0.5 mg/kg as loading dose followed by 0.1 mg/kg as maintenance dose every 20 min.

Following intubation anesthesia was maintained with N_2O:O_2 3:2 and propofol infusion at a rate of 120 mcg/kg/min for the first 10 min and then titrated according to the BIS value to be kept between 40 and 60. The patient was put on ventilator volume controlled mode with tidal volume 7-10 ml/kg, respiratory rate - 12-16 according to end-tidal CO2, positive end-expiratory pressure - 3-5 cm H_2O. Additional doses of Fentanyl given whenever the pulse rate or BP was 20% above the baseline with BIS between 40 and 60. Propofol infusion was decreased by 10 mcg/kg/min every 10 min. If the BIS value exceeds 60, propofol infusion was increased by 10 mcg/kg/min and maintained at that rate for the next 10 min.

The demographic parameters such as age, sex, weight (kg), and ASA classification II/III were recorded. Patient pulse rate, BP, SPO_2, and body mass index (BMI) were recorded. The study parameters such as Hamilton anxiety rating scale, MMSE score (pre-operative and post-operative at 1 h), and baseline BIS and BIS at extubation, total dose of propofol administered (mg), and total time of administration of propofol (min) were recorded. The total duration of anesthesia and complications of anesthesia during the procedure were noted.

RESULTS

A total of 50 patients were enrolled in this study. The demographic details of the patients such as age, sex, weight, and height were recorded (Table 1). The pre-operative and post-operative MMSE score, HAMA score, baseline BIS and post-operative BIS, propofol dose, infusion rate, and total consumption were recorded. The mean MMSE score was 24 before surgery, and the mean HAMA total score was 6 that reflects no or mild anxiety in the patients. The pre-operative MMSE score was 24.52 ± 2.08 and post-operative MMSE score was 23.88 ± 1.77, and there was no difference between pre-operative and post-operative MMSE score ($P > 0.101$). The mean propofol total dose administered and the mean propofol administration duration were 246.2 (±44.3) mg and 80.2 (±29.3) min, respectively (Table 2).

The linear regression values between age and propofol consumption, BMI and propofol consumption, baseline BIS and propofol consumption and pre-operative MMSE, and propofol consumption were calculated. The correlation coefficient between BMI and propofol consumption and pre-operative MMSE and propofol consumption show moderate and high correlation, respectively (Table 3).

DISCUSSION

MMSE is a quick and simple test for roughly assessing the status of cognition and for classifying elderly patients as "no cognitive impairment (score range, 24-30), mild cognitive impairment (18-23), and severe cognitive impairment (below 18). In this study, we evaluated the requirement of propofol in relation to MMSE score in the elderly patients. We have done multivariate analysis of the five factors that might potentially affect requirements of propofol. BMI and the MMSE score is related to the mean propofol dose per unit body weight per minute and also other variables such as age and gender versus propofol consumption. It was observed that the consumption of propofol during propofol infusion in maintenance of anesthesia was dependent on BMI. No significant effect of age and gender on propofol consumption was observed. The level of pre-operative cognitive status as assessed by the MMSE is revealed as on more factor by adjusting the infusion of propofol to the target anesthetic depth by assessing BIS monitor to maintain hypnosis in patients older than 65 years. MMSE score is affected by age in large epidemiological studies. However, it is considered to be a codependent variable which reflects more specifically the ageing of brain. However, our results clearly showed that the mean propofol consumption was related to the pre-operative MMSE score, in addition to BMI.

Table 1: Demographic details

Parameters	Mean±SD
Age (years)	67.68±2.32
Weight (kg)	61.6±7.84
Height (cm)	165.04±5.09
BMI (kg/m^2)	22.62±1.92
Gender (M/F)	18/32

SD: Standard deviation, BMI: Body mass index

Table 2: Mean and standard deviation of all measured parameters

Parameters	Mean±SD
Pre-operative MMSE	24.52±2.08
Base BIS	94.08±1.54
Propofol dose (mg)	246.24±44.3
Propofol infusion time (min)	80.2±29.33
Propofol consumption (mg/kg/min)	0.0535±0.014
Surgery duration (min)	105.2±36.71
Post-operative BIS	93.76±1.04
Post-operative MMSE	23.88±1.77
HAMA	6.64±0.8

MMSE: Mini–mental status examination, BIS: Bispectral index, HAMA: Hamilton anxiety scale

Table 3: Linear regression for age, BMI baseline BIS and pre-operative MMSE

Linear regression	Coefficient	Correlation
Age versus propofol consumption	0.033	Very low
BMI versus propofol consumption	0.48	Moderate
Base BIS versus propofol consumption	0.165	Low
Pre-operative versus propofol consumption	0.612	High
Gender versus propofol consumption	0.2415	Low

BIS: Bispectral index, BMI: Body mass index, MMSE: Mini–mental status examination

From our study, we cannot conclude if the relationship between requirement of propofol and MMSE score is because of differences in pharmacodynamics or pharmacokinetics, as we were not measured propofol concentrations. A previous study by Schliebs and Arendt has noted that a correlation exists between the MMSE score and the extent of the loss of cholinergic neurons in the basal forebrain in normal and pathological ageing in humans.[8] Thus, the MMSE score appears to reflect the cerebral cholinergic dysfunction sustaining cognitive impairment. Propofol has an inhibitory effect on acetylcholine release, in a dose-dependent manner (more pronounced with a higher dose of propofol), in rodents. We suggest that a cognitive dysfunction linked to a cerebral cholinergic dysfunction might have influenced the brain pharmacodynamics of propofol in this study. It is reasonable to suggest that less propofol may be needed in the presence of cognitive dysfunction. Thereby, the dysfunctional brain is more sensitive to further reductions of cholinergic activity such as those caused by propofol.[9] Furthermore, there is no significant difference between the pre-operative and post-operative MMSE score measured at 1 h. This shows that cognition remains unaffected after general anesthesia and with the use of propofol as an infusion for maintenance of anesthesia.[10] However, the timing of obtaining post-operative MMSE scores might affect the results. Therefore, further evaluation has to be done regarding the timing of post-operative MMSE.

CONCLUSION

Our results show that the pre-existing cognitive status of the elderly significantly affected the propofol requirement to maintain hypnosis, mainly the dose reduction of propofol in the presence of cognitive dysfunction. The cognitive function of the patient is preserved after anesthesia with propofol infusion titrated to maintain BIS values between 40 and 60. We suggest that the clinical pre-operative assessment of the cognitive status of the patient using MMSE could be an effective tool to improve the delivery of anesthesia regimen in patients over 65 years.

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