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Post-Operative Cognitive Outcomes in Elderly Patients Undergoing General Anesthesia: A Comparison of Inhalational (Sevoflurane) and Total Intravenous (Propofol) Maintenance of Anesthesia

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ABSTRACT:

Objective: The anaesthetic agent used to maintain anaesthesia may have an effect on postoperative cognitive impairment, however this has not been demonstrated (POCD). The goal of this study was to determine the prevalence of cognitive outcomes postoperatively in patients who were maintained anaesthetized with sevoflurane or propofol throughout total hip replacement surgery.

Methods: To maintain general anaesthesia in patients following spinal anaesthesia, anesthesiologists used sevoflurane (n=121) or propofol (n=171) to keep the processed electroencephalogram (BIS) below 60. A neuropsychological test battery was administered on day 7, three months, and one year after surgery to measure postoperative cognitive disorders.

Results: There were no statistically significant variations in POCD incidence between sevoflurane and propofol at any time point. The mean BIS was considerably lower in the sevoflurane group than in the propofol group (mean BIS 44.3 [SD 7.5] in the sevoflurane group against 53.7 [SD 8.1] in the propofol group, P=0.0001). At any time point, no statistically significant association between BIS levels and the prevalence of POCD was identified.

Conclusion: The anaesthetic used appears to have minimal effect on the occurrence of POCD in older adults.

INTRODUCTION:

Elderly persons are more likely to experience postoperative cognitive dysfunction (POCD) following anaesthesia and surgery, particularly in the early postoperative period[1]. Due to the increasing use of alternative approaches such as target-controlled infusions (TCI) and total intravenous anaesthesia (TIVA), the question of whether POCD rates differ between the two methods has arisen. Elderly patients are already a growing proportion of the surgical population[2,3]; this presents severe issues, given the increased prevalence of POCD in the elderly. Due to the fact that inhalational anaesthetics are frequently favoured in cases where there is no compelling reason to switch, it is critical to consider the difference in cognitive results when choosing an anaesthetic approach. We do not know how long-term cognitive effects of these two surgical methods compare. In the few clinical trials that

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examined this issue, a small number of patients were included, and their cognitive capacities were measured with inadequate technology, generating inconsistent results. Sufficient maze navigation and fear training have been linked to enhanced blood-brain barrier permeability in older rats given sevoflurane rather than propofol during surgery. Propofol had no effect on the cognition of Wistar rats aged 18 months, however sevoflurane (1.5 MAC) for two hours had a stronger effect on the rats' cognition than lower and mid-doses of sevoflurane. We previously discovered a link between pre-existing cognitive impairment and POCD in patients who underwent elective hip joint replacement surgery and received spinal anaesthetic in addition to general anaesthesia[5]. We investigated whether patients who underwent hip arthroplasty under general anaesthesia with sevoflurane or propofol had a higher or reduced prevalence of postoperative cognitive impairment in this subanalysis (POCD).

METHODOLOGY:

The Anaesthesia, Cognition, and Evaluation (ACE) examination was founded on a secondary analysis of a previously published prospective observational study. The ethics committees of the pertinent institution Khyber teaching Hospital accepted the study protocol. Between June 2019 and November 2020, advertisements in suitable newsletters and senior citizens' centers were utilised to recruit controls for the cognitive impairment assessment.

Participants had to be 60 years or older, have had a first-time total hip replacement for osteoarthritis, and live within a reasonable distance of a hospital. Pre-existing neurological or clinically evident neurovascular disease, as well as an MMSE score of less than 26 or a Clinical Dementia Rating Scale score of greater than 1, as well as the expectation of difficulty with neuropsychological assessment, such as limited English/Urdu proficiency, inability to perform neuropsychological testing, blindness or deafness, and critical medical problems, such as an ASA physical status IV or higher score, were all exclusion criteria.

Permission was obtained and patients were enrolled from a tertiary care hospital waiting lists in the week preceding the surgery. Patients performed baseline cognitive testing during their initial appointment. All patients and control subjects underwent an eight-item battery of neuropsychological tests performed by professional interviewers. The tests were repeated three days following surgery, on day 7, and three and a half and a half months afterwards to rule out any issues. The control group administered cognitive assessments at times that corresponded to those of the surgical patients. The CERAD Auditory Verbal Learning Test (A and B), the Digit Symbol Substitution Test, the Controlled Oral Word Association Test, the CERAD Semantic Fluency Test (animals), and the Grooved Pegboard Test were all included in the battery (dominant and non-dominant hands).

Two or more neuropsychological tests with a standard deviation (SD) greater than one standard deviation (SD) below population norms 5 indicated pre-existing cognitive impairment (PreCI). The dependable change index 6 was used to define POCD. This was determined as when two or more of the eight baseline tests resulted in a mean score that was at least 1.96 SD lower than the mean score of the matching control group after accounting for predicted change over time using controls. According to this assessment, POCD also had a total Z-score of less than -1.967. Multiply the 'Z total score' by the SD of the 'Z total score' in the control group to obtain the combined Z-score. To obtain this 'Z total score,' the eight Z-scores from all eight tests are added together and divided by the combined Z-score standard deviation in the control group (denominator). During the procedure, a standard clinical practise was followed. The orthopaedic surgeon performed a standard femoral neck osteotomy using anterolateral or posterior incisions. Following the acetabular component insertion,

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prosthetic femurs were placed into the intramedullary canal. All patients had spinal anaesthesia. Subarachnoid bupivacaine was administered (0.5 percent isobaric or strong bupivacaine). Intravenous fentanyl and midazolam were given as needed during the procedure for sedation and comfort. Prior to the operation's positioning, general anaesthesia was achieved using either a propofol infusion (TIVA) or inhalational sevoflurane, and the anaesthesiologist was able to maintain it using either way. In both situations, bispectral index (BIS) values were taken manually every five minutes. The airway was managed as needed using a Hudson mask, laryngeal mask, or endotracheal tube.

All patients were positioned lateral to the operating table for surgery, which aided patients who had been given propofol in maintaining their airways open while receiving oxygen via a Hudson mask, whereas patients who had been given volatile were initially given a laryngeal mask or endotracheal tube. BIS and vital signs were recorded every five minutes. In our analysis, we employed the operative time-averaged BIS value. The anesthesiologist used metaraminol, ephedrine, or phenylephrine to alleviate hypotension (systolic blood pressure less than 100 mmHg or greater than 20 percent below baseline). On a routine basis, a coronary artery line was inserted. Patients got deep vein thrombosis prophylaxis and standard postoperative analgesia with fentanyl or morphine and oral oxycodone during the postoperative phase. Orthopaedic and anaesthetic follow-up were done and recorded in-hospital according to normal procedure.

Statistical Analysis:

For dichotomous data, independent t-tests or logistic regression were used, as well as chi-square or Fisher's exact tests. Statistical significance was defined as a P-value less than 0.05 and 95 percent confidence intervals were calculated. SPSS version 25 was used for all statistical analyses.

RESULTS:

As previously reported5, 300 patients were chosen from a total of 1,537 who were screened; eight individuals were given merely sedation, leaving 292 patients under general anaesthetic. Sevoflurane was given to 121 patients, while propofol was given to 171. At each postoperative testing interval, there was a minor loss to follow-up. 279 of the 292 patients were examined after seven days, 276 after three months, and 265 after a year. In the sevoflurane group, 98 patients had their airways covered using a laryngeal mask, whereas 23 had to be intubated. In the propofol group, 153 patients were able to keep their airways open and receive oxygen using a Hudson mask, 17 patients received a laryngeal mask, and one patient was intubated. With considerable sedation and anaesthetic, all patients were in a lateral posture, enhancing airway control. The baseline data are given in Table 1, and the baseline cognitive test results are shown in Table 2 for both the sevoflurane and propofol groups. At the onset, there were no significant variations in neurocognitive test results or MMSE scores between groups. The length of anaesthesia did not differ significantly between groups. The sevoflurane group had a mean (SD) length of 141.5 (30.8) minutes, while the propofol group had a mean (SD) duration of 140.1 (29.1) minutes (P=0.68). The cumulative incidence of POCD was 48/279 (17.2 percent) at seven days, 27/276 (9.8 percent) at three months, and 7/265 at twelve months (2.6 percent). Table 3 illustrates the prevalence of POCD in each group. There was no statistically significant difference in the incidence of POCD between the sevoflurane and propofol groups at any timepoint in univariate analysis (Table 3). POCD was discovered in 44 patients (23 sevoflurane vs 21 propofol) at day 7, and 10 (4 sevoflurane versus 6 propofol) also showed POCD at

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three months, and one (propofol) at 12 months. The BIS of the sevoflurane group, at 44.3 (7.5), was substantially lower than that of the propofol group, with a significant difference between the two groups (P=0.0001). Even when BIS was taken into consideration, there was no statistically significant difference in the incidence of POCD (Table 3).

Table 1:

Demographic Characteristics	Inhalation (N=121)	Intravenous (N=171)	P value
Age, years, mean (SD)	69.9 (6.3)	70.1 (6.7)	0.8
Male, n (%)	77 (63.6%)	114 (66.7%)	0.59
Body mass index, kg/m2 , mean (SD)	28.5 (5.1)	28.1 (4.7)	0.52
PreCI, n (%)	38 (31.4%)	55 (32.2%)	0.89
Hypertension, n (%)	64 (53.3%)	91 (53.2%)	0.98
Diabetes, n (%)	12 (10.2%)	13 (7.7%)	0.46
Cancer, n (%)	26 (21.7%)	29 (17.4%)	0.36
Transient ischemic attack, n (%)	4 (3.5%)	4 (2.5%)	0.63
Smoker, n (%)	63 (52.1%)	77 (45.0%)	0.37

Table 2:

	Inhalation (N=121)	Intravenous (N=171)	P value
MMSE score	28.1 (1.2)	28.2 (1.3)	0.63
CERAD AVLT, n	17.4 (3.7)	17.6 (3.9)	0.60
TMTA, s	51.3 (23.1)	51.7 (20.3)	0.89
TMTB, s	111.4 (50.8)	120.7 (65.3)	0.18
DSST, n	38 (11.5)	38.0 (10.3)	0.99
COWAT, n	34.4 (11.2)	35.7 (13.2)	0.39
CERAD semantic fluency, n	17.6 (4.6)	18.0 (4.6)	0.42
GPBd, s	96.7 (34.7)	98.2 (37.2)	0.74
GPBnd, s	108.5 (43.6)	110.4 (58.2)	0.75

Table 3:

Time period	Inhalation (N=121)	Intravenous (N=171)	P-value	P-value(adjusted for BIS)
Day 7, 279	24/119 (20.2%)	24/160 (15%)	0.26	0.41
Month 3, 276	10/15 (8.7%)	17/161 (10.6%)	0.61	0.62
Month 12, 265	1/111 (0.9%)	6/154 (3.9)	0.23	0.23

DISCUSSION:

There was no statistically significant difference in the incidence of POCD between patients whose anaesthesia was maintained with sevoflurane or propofol, though the percentage incidence appeared to be higher in the sevoflurane group at seven days and lower at three and twelve months following total hip joint replacement. The rate of cognitive impairment following volatile medicine or propofol anaesthesia is unknown. However, assessing cognition at this early stage is difficult due to the

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presence of residual anaesthetic medicines and the stress associated with surgery. These early changes in cognition should not be classified as neurocognitive dysfunction, but as delayed neurocognitive recovery, to indicate that they may be transient, as recommended by the Nomenclature Consensus Working Group for the nomenclature of anaesthesia and surgery-associated cognitive changes [8].

According to two studies, sevoflurane patients demonstrated greater cognitive damage than propofol patients after seven days [9,10]. Even though sevoflurane and propofol demonstrated early differences in cognition, these differences vanished after ten days, consistent with the notion that early cognitive abnormalities following anaesthesia and surgery are temporary, as Cai et al. reported. Few studies have examined cognition three months or more after comparing anaesthetic medications, implying that the early effects of anaesthesia and surgery, as well as any postoperative complications, had disappeared. Two studies analysed different anaesthetic methods using a battery of cognitive tests three to twelve months after anaesthesia and surgery. Micha et al. randomly assigned 80 patients to receive sevoflurane or propofol as a maintenance anaesthetic. Sevoflurane considerably impairs cognitive performance when compared to propofol, implying that propofol may sustain cognitive function better than sevoflurane after nine months[12]. Egawa et al[13] investigated cognition three months after randomising 148 patients for lung surgery in a study aimed at determining cerebral oxygenation. Anaesthesia with propofol or sevoflurane had no statistically significant effect on patients' cognitive capacity. Liu et al. discovered that sevoflurane generated higher cognitive decline than propofol in Chinese patients with amnestic moderate cognitive impairment two years following anaesthesia and surgery.

Egawa et al. discovered that sevoflurane or propofol anaesthesia had no effect on postoperative cognition. Our findings corroborate this conclusion. At three and a half and twelve months, the sevoflurane group had a reduced percentage of persons who deteriorated, indicating that sevoflurane may give some cognitive protection during these times. This, however, cannot be substantiated due to the study's insufficient statistical power. Despite the decreased mean BIS, there was no statistically significant difference in the incidence of POCD between the sevoflurane and propofol groups. However, we discovered that BIS-guided anaesthesia, which maintained a higher BIS than standard anaesthesia, significantly decreased the incidence of POCD three months after surgery, regardless of the kind of general anaesthetic employed (Chan et al[15]) (10.2 percent in BIS-guided group versus 14.7 percent in non BIS-guided group; P-value 0.02). Each group received a BIS score of 53.2 (SD 8.9) and 38.6. (SD 6.5). Although the mean BIS was substantially higher in the propofol group than in the sevoflurane group (44.3 (SD 7.5), this difference in BIS was not related with an increased incidence of POCD at any time point.

Apart from the large sample size (292) and the use of a control group to establish the prevalence of POCD, this study contains a number of distinguishing characteristics that set it apart from similar studies. This study has certain drawbacks. Because this was an unplanned secondary analysis, no one was randomly assigned to the propofol or sevoflurane groups. If the BIS of a patient was maintained at or below 60 regardless of the anaesthetic employed, the anesthesiologist was free to choose the mode of anaesthesia. Second, all patients had a spinal anaesthetic prior to being placed under anaesthesia, which was aided by an intravenous dosage of midazolam. Additionally, the sevoflurane group received a single propofol induction dosage. Midazolam and sevoflurane-induced intravenous induction may have influenced the outcomes. The findings, however, are applicable because to the frequent use of these medications in combination.

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CONCLUSION:

When propofol and sevoflurane anaesthesia were administered in conjunction with spinal anaesthetic, there was no significant difference in POCD incidence. This research demonstrates that sevoflurane and propofol both cause POCD at three and twelve months, however sevoflurane had a somewhat lower incidence of POCD at these intervals (albeit not statistically significant). Due to the small sample size, there was insufficient data to evaluate if the prevalence of POCD varied by anaesthetic group. To detect a significant difference between the two groups (=0.05, 1=0.8), we required 3,791 patients in each group, based on the three-month incidence of POCD. To address this question, we would recommend a large prospective clinical trial involving thousands of patients, given the potential long-term consequences of cognitive decline and the fact that thousands of patients have already been studied in several large randomised controlled trials in anaesthesia[16,17].

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