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STUDY OF EFFECTS OF KETAMINE ON COGNITIVE FUNCTION IN ELDERLY PATIENTS UNDERGOING DAY CARE SURGERY

Anesthesiology

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ABSTRACT

INTRODUCTION: Acute postoperative cognitive dysfunction is characterized by neurocognitive dysfunction and confusion. In this study, we compared the cognitive status of a geriatric population undergoing cognitive dysfunction, as assessed by the Short Portable Mental Status Questionnaire (SPMSQ) before and after ketamine administration.

METHODS: Sixty patients were enrolled for the study and they were randomly selected for double-blind study to receive either ketamine (0.3 mg/kg dose) or physiologic solution (control group). Fifty seven(control, n = 29; ketamine, n = 28) patients completed the trial. Cognitive performance was assessed with an abbreviated version of the SPMSQ. Measurements of analgesia, sedation, and hemodynamic variables were recorded.

RESULTS: With respect to cognitive performance, the baseline evaluation was similar for the control and ketamine groups. Postoperative evaluation showed an improvement only in the ketamine group. The average dose of midazolam was higher in the control group, but the difference was not clinically significant. After surgery, analgesic behavior was better in the ketamine group than in the control group. There were no differences between groups in the sedation scale or in hemodynamic variables.

CONCLUSIONS: The administration of 0.3 mg/kg ketamine during day care surgery in geriatric patients changed their cognitive status as assessed by the SPMSQ, decreased the required dose of anesthetics, and in hemodynamic variables.

KEYWORDS

cognitive dysfunction , cognitive dysfunction, ketamine, sedation scale

INTRODUCTION

Main risk factor for aging is cognitive changes which affect the performance of older patients as well as their memory and speed of thought. Another significant risk factor is poor vision and the association between age-related degenerative diseases and age-related macular degeneration in older people. Anesthesia and surgery also contribute to cognitive changes ; a decline in cognitive status after surgery is called postoperative cognitive dysfunction (POCD). In this study, we compared the cognitive status of a geriatric population undergoing day care surgery, as assessed by the Short Portable Mental Status Questionnaire (SPMSQ) before and after ketamine administration

METHODS

After approval from ethical committee of Gouri Devi Institute of Medical Sciences and Hospital, Durgapur study was performed with written informed consent from all subjects included in the study.

Participants were patients scheduled for day care surgery (Hydrocelectomy, Anal fissurectomy, Hemorroidectomy, dermoid cystectomy, lipoma excision . The inclusion criteria were as follows: patients aged 60 years and older, and ASA physical status I to III. Patients with a history of psychosis, schizophrenia, nephropathy, difficult to control arterial blood pressure, uncontrolled hepatic disorders, or allergy to ketamine , moderate to severe depression, ketamin contraindicated patient. ketamine were excluded.

Evaluation of patient's cognitive status was conducted with the SPMSQ. Patients were randomly assigned to one of the study groups. Sealed and numbered envelopes (assigned using a table of random numbers) indicated the prepared solution to be applied as follows: ketamine was administered at a dose of 0.3 mg/kg in a physiologic solution at 0.9% (250 mL), whereas the control group received only physiologic solution at 0.9%, with the same physical characteristics of the ketamine solution. Placebo or ketamine was administered IV after initial sedation and throughout surgery. Infusion velocity was calculated using the routine time for a particular type of procedure.

Once sedatives were administered, Anaesthesiologist performed a regional block(low dose spinal anaesthesia using hyperbaric bupivacaine). Two hours after surgery, when patients were ready for discharge, their cognitive statuses were assessed again using the tools described earlier. Because delirium is described as an acute confusional state associated with disturbances in attention and decreased awareness of the environment, and patients are often disoriented after surgery, we used the confusion assessment method to exclude postoperative delirium.

MENTAL STATUS TEST

Pfeiffer designed the SPMSQ for the detection of cognitive deterioration in geriatric patients; it was validated and translated into Spanish in 1992 by Gonzalez Montalvo et al. It consists of 10 questions that explore short- and long-term memory, orientation, information about daily events, and the capacity to calculate. Assessed on a scale of 1 to 10, a patient is assigned to 1 of 4 categories according to the number of errors committed: intact cognitive function (0–2 errors), mild cognitive deterioration (3–4 errors), moderate cognitive deterioration (5–7 errors), or severe cognitive deterioration (8–10 errors). The questions are the following: What is the date today? What day of the week is it? What is the name of this place? What is your telephone number? What is your street address? How old are you? When were you born? Who is the President now (we asked about the Mexican president)? Who was the president just before him? What was your mother's maiden name? Subtract 3 from 20, and keep subtracting 3 from the result all the way down to 0. The Spanish version of the SPMSQ has 100% sensitivity and 90% specificity for patients with up to 5 errors. This screening tool has a correction factor for low levels of education.

The most stringent criterion for the diagnosis of POCD is a decline of at least 2 SDs in 2 cognitive domains or a decline of at least 2 SD in a composite cognitive score

In addition, we performed an evaluation of analgesia and sedation using the verbal numerical scale and Ramsey test, respectively. We recorded the vital signs of each patient, as well as any signs of respiratory depression, or hallucinations.

Patients were included in an analysis of mean change of the number of items incorrectly answered in the SPMSQ between the preoperative and the postoperative assessments using an analysis of covariance model, which considered baseline status as covariate and the treatment group as the effect of interest.

RESULTS

Demographic and Clinical Characteristics of the Sample Sixty patients were recruited and randomly assigned. Three patients were excluded from analysis: 2 from the ketamine group because of hypertensive crisis (n = 1) and myocardial infarction (n = 1); 1 from the control group because of hypertensive crisis (n = 1). The remaining 57 patients were assigned to the control (n = 29) or ketamine (n = 28) groups.

Cognitive Performance

Before surgery, similar SD in the results of the SPMSQ were reported for the control and ketamine groups (1.9, SD = 1.6, and 2.1, SD = 2.0, respectively) ($t = -0.60$, $df = 63$, $P = 0.54$

According to the scoring scale, in the preoperative assessment, 68.96% (n = 20) of patients in the control group and 67.85% (n = 19) in the ketamine group performed within the normal range, whereas the remaining patients performed within the mild/moderately impaired range ($\chi2 = 0.03$, df = 1, P = 0.85). After surgery, an increased number of patients in the ketamine group performed within the normal range (n = 23, 82.14%; P = 0.03), whereas the percentage of patients in the control group with a normal cognitive performance remained almost unchanged (n = 22, 75.86%; P = 0.62).

Hemodynamic Measurements, Oxygen Saturation, Sedation and Analgesia Significant decreases over time were observed independently in both groups in hemodynamic variables and respiratory rate (P < 0.001), whereas oxygen saturation and sedation level increased (P < 0.001). No significant changes over time × group were observed in these variables in the general linear model

Conversely, significant changes were observed in analgesia, which was evaluated using a numerical verbal scale, followed by a Likert scale for statistical analysis. After anesthesia, 79.3% (n = 23) of patients in the control group reported mild/moderate pain, compared with 64.28% (18) of patients in the ketamine group ($\chi2 = 4.8$, df = 3, P = 0.18). After surgery, a significantly smaller proportion of patients reported mild/moderate pain in both groups, although it was less in ketamine group patients (n = 3, 10.71% vs n = 16, 55.17% of the control group; $\chi2 = 18.5$, df = 3, P < 0.001).

Table 1. Demographic, Coexisting condition Surgica Variables Between Groups

	Control (n=29)	Ketamin (n=28)	Statistics
Sex (n)			$\chi2 = 0.03$, df = 1, P = 0.54
Male	14	14	
Female	15	14	
Coexisting condition			
Hypertention	24	19	$\chi2 = 2.20$, df = 1, P = 0.13
Diabetes	19	22	$\chi2 = 0.37$, df = 1, P = 0.54
Type of surgery			
Hydrocelectomy,	12	13	
Anal fissurectomy,	06	04	
Hemorroidectomy,	04	03	
dermoid cystectomy,	03	04	
lipoma excision,	04	04	

Table 2. Hemodynamic Measurements, Respiratory Rate, and Oxygen Saturation

	Control (n=29)	Ketamin (n=28)	Statistics (time x group)
Heart rate (bpm)			F=2.56,P=0.12
Base line	70.1	77.2	
After SAB	66.5	71.5	
90 min in to surgery	64.2	67.8	
Systolic blood [pressure			F=1.1,P=0.26
Base line	165.3	160.2	
After SAB	156.3	158.2	
90 min in to surgery	154.5	152.9	
Diastolic blood pressure			F=0.94,P=0.33
Base line	89.2	90.3	
After SAB	85.6	85.4	
90 min in to surgery	83.4	82.3	
Oxygen saturation			F=0.20,P=0.65
Base line	93.6	93.8	
After SAB	96.3	95.9	
90 min in to surgery	99.2	99.2	
Respiratory rate(bpm)			F=1.7,P=0.18
Base line	18.6	18.3	
After SAB	16.5	16.4	
90 min in to surgery	14.1	14.2	
Ramsay scale total score			F=0.46,P=0.49
Base line	1.26	1.34	
After SAB	2.32	2.16	
90 min in to surgery	2.13	2.00	

DISCUSSION

In this study, we found statistical differences between the errors committed in the postoperative SPMSQ compared with the baseline evaluation. More studies should be conducted on day care surgery, because common age related diseases associated with the changes in cognition, with aging as a major preoperative risk factor. Some studies suggest that the NMDA receptor has a direct role in short-term and recognition memory through anti-inflammatory mechanisms, whereas other reports assign the effect to increased cerebral blood flow or to the binding of the drug to NMDA receptors. Consequently, ketamine attenuates the systemic inflammatory response to tissue injury and maintains cerebral perfusion pressure by activating the sympathetic nervous system.

In the control group, the number of baseline errors recorded in the SPMSQ was 1.91, whereas the number was 1.73 after surgery. In the ketamine group, the number of baseline errors was 2.18, which decreased to 1.18 after surgery. Given the nature of the questions, it is difficult to know with precision if the difference reported really had anything to do with the effect of ketamine on cognitive changes or if it was a difference in learning, but this issue can be answered by comparing the cognitive performance between groups. Our aim was to detect minor changes in cognitive performance; this is why the baseline evaluation of cognitive function was compared with another evaluation immediately after surgery. By performing the study in this way, we sought to avoid confusion that could be introduced by a postoperative evaluation after a longer period of time.

Patients in the ketamine group required a significantly lower average dose of midazolam. There was a difference in the use of fentanyl, but no significant difference between groups with respect to the sedation required according to the Ramsey scale. This might be explained by the scale used and/or the inter observer variations. Ketamine was administered throughout the surgical procedure; therefore, the need for midazolam/fentanyl was reduced with potential benefits. It is possible to assume that the evaluation performed in the immediate postoperative period considered only the immediate effects of the administered drugs. Because patients not receiving ketamine received larger amounts of midazolam, it is not possible to exclude that the difference was because of the effect of the drug. However, we do not think it very probable that the statistically significant difference was produced by the effect of midazolam because of the minimally different doses between groups, which does not represent a clinical difference of interest with respect to patients' cognitive function or sedation.

Because of the design of this study, we can provide no evidence of pathophysiologic mechanisms and the neuroprotective effect on POCD attributable to ketamine. Because POCD may last longer than the immediate postoperative periods, further studies should be done to evaluate cognitive performance at least 24 hours after surgery using various validated tests.

The use of only 1 questionnaire has limited benefits, and further research using other instruments is needed. However, our study showed that 0.3 mg/kg ketamine may be useful for inducing better cognitive performance after ophthalmic surgery in elderly patients, enhancing the effect of analgesics with safety improvements in hemodynamics, oxygen saturation, and intraocular pressure. However, these results need to be replicated in future studies

CONCLUSIONS

The administration of 0.3 mg/kg ketamine during day care surgery in geriatric patients changed their cognitive status as assessed by the SPMSQ, decreased the required dose of anesthetics, and produced no increase in hemodynamic variables. However, because the evaluation only analyzed the immediate effects of the administered drug, further research will be required to examine the impact of ketamine on the postoperative cognitive performance of geriatric patients before the drug can be formally recommended for this purpose.

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