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Effect of the using a pupillometer on recovery and early cognitive functions in anesthesia management for endoscopic retrograde cholangiopancreaticography in geriatric patients

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Ethics Committee Approval
The study was approved by the Local Ethical Committee of Necmettin Erbakan University, Meram Faculty of Medicine (Number: 126-2021/3107). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Endoscopic retrograde cholangiopancreatography (ERCP) is an invasive procedure used for the diagnosis and treatment of pancreaticobiliary pathologies. Because it is an invasive procedure that is difficult to tolerate by the patient and takes a long time, it is preferable to use it under deep patient sedation and even under general anesthesia in some cases. This study aimed to evaluate the effects of using a pupillometer versus the Ramsey sedation scale (RSS) during anesthesia management for ERCP on recovery and return of cognitive functions in the geriatric patient population.

Methods: A mini-mental test was applied to evaluate the pre-operative cognitive functions of the cases before the intervention. The included patients were divided into groups using the sealed-envelope method. Management of the depth of anesthesia was evaluated by Ramsey sedation scale; in group R and was evaluated by pupillometer in group P. The infusion dose of dexmedetomidine was changed to 0.1 µg/kg/h according to the results of the evaluation.

Results: Sixty cases were included in the study. No difference between the groups in terms of age (P=0.246), gender (P=0.797), American Society of Anesthesiologists (ASA) score (P=0.197), comorbidity (P=0.748), anesthesia duration (P=0.397), midazolam doses (P=0.561), propofol doses (P=0.677), and intra-operative hemodynamic values (P=0.668) were found. Intra-operative dexmedetomidine dose was statistically significantly lower (P=0.004), and recovery was faster in group P (P<0.001). While no differences between the groups in the pre-operative mini-mental test scores (P=0.140) were found, the post-operative scores were statistically significantly lower in group R (P=0.025).

Conclusion: In this study, it was observed that the pupillometer led to a reduction in the use of dexmedetomidine and cognitive functions were better during the post-operative recovery period. As a result, depth of anesthesia can be monitored with a pupillometer. Although the use of pupillometer in endoscopic interventions in the geriatric patient group does not make a hemodynamic difference when compared with the RSS, the pupillometer leads to accelerated recovery from anesthesia, improvement in the return of cognitive functions, and reduction in drug consumption.

Keywords: geriatric anesthesia, endoscopic retrograde cholangiopancreatography, pupilometer, mini-mental test, post-operative cognitive dysfunction

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Introduction

Endoscopic retrograde cholangiopancreaticography (ERCP) is an invasive modality used for the diagnosis and management of pancreaticobilliary pathologies. Due to procedure invasiveness and patient intolerance during conscious sedation, general anesthesia is usually preferred for this lengthy and complicated procedure. Adequate sedation and patient cooperation are essential for successful and safe ERCP. While deep sedation may result in airway obstruction, aspiration, respiratory depression, and hemodynamic instability, conscious sedation is associated with significant patient discomfort and intolerance during endoscopic procedures. Thus, achieving adequate and regular sedation without increasing the rate of cardiorespiratory depression is intended [1–4].

Evaluating the depth of anesthesia during induction and maintenance is a challenging issue [5]. The Ramsay sedation scale (RSS) is a simple and reliable scoring system that is frequently used today for the evaluation of sedation [6]. Technological advances and emerging modalities have facilitated anesthesia depth assessment. Pupil diameter measurement with a pupillometer can be used for the evaluation of intra-operative depth of Anesthesia [7,8]. Standardized measurement methods for a pupillometer have enabled objective comparisons of serial measurements [9]. Pre-operative evaluation of geriatric patients should include accurate assessment of their functional capacity, cognitive status, and comorbidity; finally, appropriate peri-operative management is essential.

In this study, we evaluated recovery of consciousness and cognitive functions using pupillometer when compared with RSS during anesthesia management for ERCP procedures in geriatric patients.

Materials and methods

Setting and participant

Ethical approval for this study was obtained from (Necmettin Erbakan University, Meram Faculty of Medicine, Ethics Committee) (Number: 126-2021/3107) according to the declaration of Helsinki. Power analysis was performed to determine the number of samples. A sample size of 60 was determined to be sufficient assuming that α was 0.05, effect size was 0.50, and power was (1 β) 0.80. G*power (Version 3.1.9.6) was used for this calculation. Sixty patients older than 65 years with American Society of Anesthesiologists (ASA) class II/III physical status who underwent ERCP procedures under deep sedation between April and December 2021 in the gastrointestinal endoscopy unit were enrolled in this study. Patients with orientation and cooperation disorders, severe psychiatric disorders, cardiac dysrhythmia and heart failure history, drug dependence, intra-operative inotropic drug use, emergent patients, and patients who refused to participate in the study were excluded. Informed consent was obtained from all patients before inclusion in the study.

Anesthetic management

Demographic data of the participants were recorded and randomized using the sealed envelope method. Patients were grouped as group R for patients managed with Ramsay sedation scale and group P for those managed with pupillometer device. Minimental test was applied for the evaluation of the preoperative cognitive functions of the participants before the procedure. Hemodynamic measurements, such as heart rate, echocardiographic (ECG) monitoring, non-invasive arterial blood pressure and pulse oximetry were recorded. All patients received bolus midazolam (0.15 mg/kg), propofol (1 mg/kg), and dexmedetomidine (0.5 µg/kg) infusion for anesthesia induction. Dexmedetomidine (0.2–0.7 µg/kg/h) was applied for maintenance. Dexmedetomidine dose was changed by 0.1 µg/kg/h after evaluating the depth of anesthesia at 5-min intervals.

While evaluating the depth of anesthesia, RSS scores of 3 to 4 were included in group R; serial measurements of pupil diameter were recorded and compared to first pupil diameter measurement after induction in group P. Dexmedetomidine infusion dose was changed to 0.1 µg/kg/h based on changes in pupil diameter.

Once the procedure was completed, infusion was terminated, and the patient was awakened. The time from infusion termination to an Aldrete score of 9 was recorded as recovery time. The mini-mental test was repeated 30 min after infusion termination to evaluate for the cognitive functions.

Statistical analysis

Data was analyzed using SPSS 18.00 (Statistical Package for Social Sciences, Inc., Chicago, IL). Continuous variables were presented as mean (standard deviation) and percentages (%). Categorical variables were presented as numbers and percentages. Kolmogorov–Smirnov test was used for testing normal distribution of the data. Mann–Whitney U test was used for analyzing continuous variables. A chi-squared test was used for comparison and analysis of categorical variables between groups. *P*-values <0.05 were considered statistically significant.

Results

A total of 60 patients with 30 patients in each group, were included in the study. 14 (46.7%) female and 16 (53.3%) male patients were included in group P while 16 (53.3%) female and 14 (46.7%) male patients were in group R. Five (16.7%) patients in group P and 7 (23.3%) patients in group R had no comorbidities. No significant differences between both groups in terms of age (P=0.246), gender (P=0.797) and comorbidities (P=0.748) were found.

No statistically significant difference between both groups in terms of anesthesia duration was found (P=0.397). No difference between intra-operative propofol application (P=0.677) was observed. Dexmedetomidine use in group P was significantly lower than group R (P=0.004), and recovery time in group P was significantly faster than group R (P<0.001) as shown in Table 1. Figure 1 shows hemodynamic follow-up the both groups. With regard to mini-mental test results, no significant difference was observed between both groups during the pre-operative period (P=0.140), while a statistically significant difference in the post-operative period (P=0.025) was found (Table 2).

Table 1: Administered drugs and administration durations

	Group P (n=30) Mean (SD)	Group R (n=30) Mean (SD)	*P*-value
Anesthesia duration (min)	39.20 (13.72)	41.70 (8.32)	0.397
Midazolam (mg)	1.93 (0.25)	1.97 (0.18)	0.561
Propofol (mg) (induction)	67.00 (25.88)	79.67 (23.56)	0.052
Propofol (mg) (total)	133.00 (61.42)	140.33 (73.79)	0.677
Dexmedetomidine (mg)	14.94 (7.49)	21.23 (8.90)	0.004*
Recovery time (min)	18.33 (6.74)	26.50 (7.79)	<0.001*

* *P*<0.05 statistically significant

Figure 1: Comparison of intra-operative parameters of heart rate (HR), peripheral oxygen saturation (SPO2), systolic (SPB) and diastolic (DPB) blood pressures between groups.

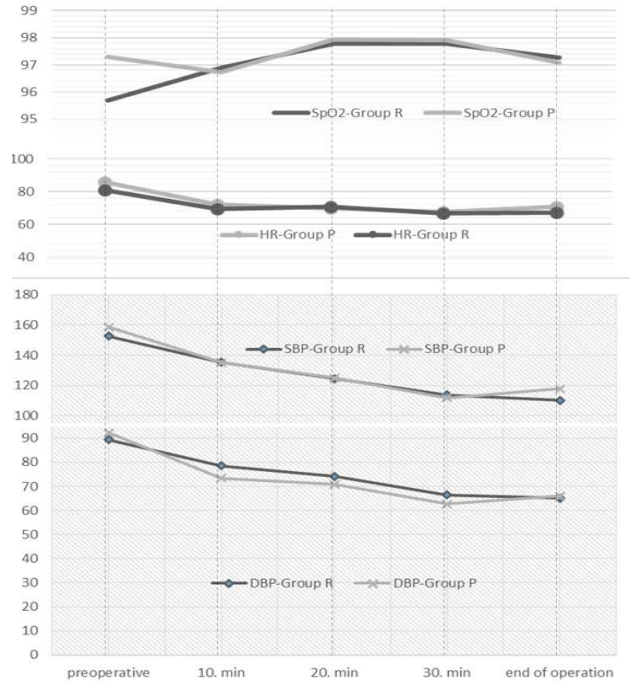

Table 2: Mini-mental test scores

	Group P (n=30) Mean (SD)	Group R (n=30) Mean (SD)	*P*-value
Pre-operative	19.37 (4.87)	21.10 (4.08)	0.140
Post-operative	18.90 (4.92)	16.23 (3.99)	0.025*

* *P*<0.05 statistically significant

Discussion

By applying pupillometer parameters and Ramsay scores as references in the management of intra-operative depth of anesthesia, we observed that pupillometer usage led to a reduction in the use of dexmedetomidine and resulted in better cognitive functions in the postoperative recovery period. There is an increase in the number of therapeutic endoscopic procedures in geriatric patients due to population aging. Development of a personalized sedation strategy that takes into account a patient's general condition, underlying disease, and estimated surgical difficulty during ERCP procedure in geriatric patients has important implications toward a patient's prognosis [10]. Although deep sedation increases patient's comfort during the procedure, this type of sedation is associated with airway obstruction, aspiration, respiratory depression, and hemodynamic instability; in contrast, patients may suffer from pain under inadequate sedation. The primary goal of sedation management is to maintain adequate and regular sedation without causing an increase in the risk of cardiac or respiratory depression. Thus, the dose of conscious sedation agents used should be titrated well and patients should be monitored closely [11]. Monitoring the depth of anesthesia reduces the dose and cost of the drugs used and accelerates recovery [12–15].

Nociception monitoring is one of the biggest current challenges in anesthesiology. Inadequate sedation can result in potentially harmful hemodynamic variations. Clinical parameters, such as heart rate and/or blood pressure changes, are frequently used to evaluate intra-operative analgesia. Since these parameters' reliability and specificity are questionable in most cases, other physiological indices and measurements may be useful for providing more accurate clinical feedback on depth of anesthesia.

Different physiological approaches and noninvasive modalities have been developed to monitor intraoperative nociception stimuli. Individualization of the intra-operative drug doses is the main goal to avoid both under and over dosing [16]. Among these modalities, a pupillometer appears to be a reliable tool. Pupillary diameter increase in patients under anesthesia after nociceptive stimuli is known as "pupillary dilation reflex". The amplitude of pupillary dilation reflex is proportional to the intensity of nociceptive stimulus and inversely proportional to the amount of administered drug [17–20].

Intra-operative pupillary diameter is a dynamic indicator of pain; however, no previous studies have evaluated the potential clinical benefits of pupillometry-guided ERCP. In our study, dexmedetomidine was preferred for induction, while propofol was used for maintenance. Propofol is preferred in ERCP and other endoscopic procedures due to its short duration of action, rapid awakening, and easy titration. Dexmedetomidine is desirable in procedural sedation as it induces cooperative sedation, analgesia and rapid recovery without causing respiratory depression [21,22]. In this study, RSS was used as an objective method to determine sedation level in our control group. Patients in the control group were maintained at a goal Ramsay sedation score of 4. Ceylan et al. [22] investigated the effects of propofol and dexmethodimidine sedation on the hemodynamic and cognitive functions of patients during ERCP procedures. Ramsay sedation scores of 3 to 4 were associated with adequate levels of sedation without producing any negative impact on recovery scores, hemodynamic, and/or respiratory parameters. These findings are compatible with our results regarding hemodynamic parameters. Bispectral index (BIS)-based depth of anesthesia monitoring was associated with improved early recovery in previous studies [23–25].

Although Adequacy of Anesthesia (AoA) monitoring did not lead to a reduction in the occurrence of unwanted events, it did produce a reduction in the amount of medications used and helped accelerate recovery [26,27]. Similarly, the use of Smart Pilot View (SPV) improved recovery and drug consumption [28,29]. Post-operative recovery time was significantly lower in the pupillometer group when compared with the RSS group.

The cognitive reserve of the brain decreases while sensitivity to stress and the risk of postoperative cognitive dysfunction increase with aging [30]. Careful evaluation and documentation of the cognitive status of geriatric patients before surgery is critical for the diagnosis of post-operative cognitive dysfunction (POCD), which is a common occurrence after surgery. Pre-operative cognitive impairment may be a key indicator of risk for postoperative delirium [31–33].

Many factors have a negative impact on early post-operative cognitive functions and time for recovery of

consciousness and cognition after anesthesia, including type of surgery, anesthetic agents, and anesthetic auxiliary drugs (such as steroids, anticholinergics), duration of anesthesia, level and duration of pre-operative hypotension, hormone levels (thyroid stimulating hormone [TSH], sex hormones), sedative and anxiolytic premedication, and patient's age and underlying diseases [34–37]. Post-operative cognitive dysfunction is associated with prolonged hospitalization, increased mortality, and functional decline. Peri-operative multidisciplinary and multi-modal approach, antipsychotic use, depth of anesthesia monitoring, and dexmedetomidine were found to be associated with a reduction in post-operative cognitive dysfunction in non-cardiac elective surgery patients [38]. Dexmedetomidine may alleviate POCD by producing a decrease serum tumor necrosis alpha and interleukin 6 (TNF-α and IL-6, respectively) levels [39]. In our study, dexmedetomidine was preferred for sedation maintenance in both groups. Besides, post-operative mini-mental test scores were higher in the pupillometer group.

Limitations

In this study, we compared anesthesia management by using the pupillometer and RSS methods. Lack of comparison with other monitoring methods and evaluation challenges due to undesirable/adverse post-operative events in our study can be considered as limitations.

Conclusion

Depth of anesthesia can be monitored with a pupillometer. Although no difference in hemodynamic parameters when compared with the RSS, pupillometer monitoring causes acceleration of anesthesia recovery, improvement in the return of cognitive function, and reduction in drugs used during endoscopic procedures in geriatric patients.

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