Early cognitive function changes after dexmedetomidine added to propofol-based sedation for gastrointestinal endoscopy

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Research article

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Abstract

Background: Propofol usually used for sedation for gastrointestinal endoscopy, result in short-term, reversible decline in cognitive function. This prospective cohort trial aimed to propofol plus dexmedetomidine can improve cognitive function for elective outpatient gastrointestinal endoscopy.

Methods: Patients undergoing gastrointestinal endoscopy were included. Patients were randomized allocation into group C (groupC30 and groupC60), and group D. The group D was The group D was a continuous intravenous pumping of dexmedetomidine at a dose of 0.3µg/kg within 10min before anaesthesia; the group C were given an equal volume of normal saline instead. Patients underwent a MoCA test before sedation and at discharge.

Results: The MoCA scores were similar at baseline in each group. Compared to baseline before gastrointestinal endoscopy, the MoCA scores were decreased each group (group C30: $p<0.001$; group C60: $p<0.001$; group D: $p=0.002$). Compared to group C30, the MoCA scores were better in group C60 ($p=0.03$) and group D ($p<0.001$), and those in group D were higher than those in group C60 ($p<0.001$). Incidence of cognitive impairment in group C30 is 56.6% which ranks the highest among the three groups, and those in group D is 7.8% which ranks the lowest among the three groups, the difference is significant statistically ($p<0.001$). The MoCA scores were similar between the genders in each group ($p>0.05$).

Conclusions: Dexmedetomidine added to sedation for gastrointestinal endoscopy can improve early cognitive function and reduce incidence of cognitive impairment.

Background

Sedated gastrocolonoscopy has been widely used in many countries. over 98% of American clinicians have adopted the practice for examination and treatment^[1]. Propofol-based sedation for gastrointestinal endoscopy has been widely carried out in China. Propofol usually causes respiratory depression, and in many cases, patients' cognitive function at discharge was worse than their performance at baseline^[2].

Dexmedetomidine is a α_2 -receptor agonist which provides sedation and analgesia, and it can also reduce heart rate and blood pressure without respiratory depression^[3]. Dexmedetomidine can improve postoperative cognitive function and reduce the incidence of early postoperative cognitive dysfunction^[4].

Effect of dexmedetomidine added to propofol-based sedation on early cognitive function for gastrointestinal endoscopy have not been determined. Therefore, we are aiming to determine if dexmedetomidine added to propofol can results in less cognitive dysfunction at discharge than the use of propofol alone in patients undergoing elective outpatient gastrointestinal endoscopy.

Methods

A prospective, randomized clinical trial according to the CONSolidated Standards Of Reporting Trials (CONSORT) statement was performed on patients undergoing elective outpatient gastrointestinal endoscopy requiring sedation. This study was approved by the Research Ethical Committee of the First Affiliated Hospital of Wenzhou Medical University, and written informed consent was obtained from all patients participating in the trial. The trial was registered before patients' enrollment at Chinese Clinical Trial Registry (<http://www.chictr.org.cn>, ChiCTR1900022639; principal investigator: L. C.; date of registration: April 19, 2019).

Patients

The study population comprised of 202 patients receiving elective outpatient gastrointestinal endoscopy between May and September 2019. Eligible patients were aged 30–65, and they were of ASA physical status I-II and were presenting for elective gastrointestinal endoscopy. Patients with any one of the following conditions were excluded from the study: inadequate Chinese comprehension; Montreal Cognitive Assessment (MoCA) score < 26 (A final total score of 26 and above is considered normal) [6]; body mass index > 25 kg/m²; renal insufficiency, liver dysfunction; atrioventricular block; significant cardio-respiratory instability; neurological disease; mental disorder; or dexmedetomidine allergy.

All patients received oral bowel preparation the night before endoscopy. Patients were randomly divided into groups by computer. Randomization results were concealed in opaque envelopes until after consent was obtained and the anesthesiologists, patients, endoscopists and postoperative observers were blind to the results.

Procedure

After consent was obtained, demographic and medical data were recorded. Patients completed the MoCA before gastrointestinal endoscopy (at least three weeks earlier). IV access was established and patients were not given IV fluids. Oxygen was administered at 5 L/min via a nasal tube when patients arrived at the endoscopy room. Routine patient monitoring included electro-cardiography, pulse oximetry, and noninvasive arterial blood pressure measurement in keeping the stability of hemodynamics.

Patients were randomized allocated into the control (C) or the Dexmedetomidine (D) group, and sedative drugs were administered IV. Patients were given 5 µg sufentanil and 0.5 mg atropine in both groups. The group D was a continuous intravenous pumping of dexmedetomidine at a dose of 0.3 µg/kg (this procedure was completed within 10 minutes) before the anaesthesia; the group C was given an equal volume of normal saline instead. The method of propofol administration was determined by the anesthesiologist. Anesthesiologists were advised to aim for a depth of sedation in modified observer's assessment of alertness/sedation (OAA/S) score = 0 (Does not respond to painful trapezius squeeze) [5] for the whole procedure (Table 1). Predefined complications (hypotension, bradycardia, hypoventilation, etc.) were managed by anesthesiologists. After the endoscopy, patients were transferred to the

postanesthesia care unit (PACU). MoCA were evaluated at 30min or 60min after patients reached an OAA/S score = 5 (responds readily to name spoken in normal tone) in group C (groupC₃₀ or groupC₆₀), and 30min in group D.

Measurements

Gender, age, amount of propofol, Sedation time (defined as the time from administration of the first drug and until removal of the endoscope), endoscopist and patient satisfaction, MoCA score (range, 0–30).

Cognitive test

The MoCA was a rapid assessment scale for mild cognitive dysfunction^[6]. It includes attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. The total possible score is 30 points; a score of 26 and above is considered normal (<https://www.mocatest.org/>). In order to reduce errors caused by learning benefits from short-term repetitive testing, patients did not test the MoCA on the same day.

Sample size calculation and randomization

The sample size was planned and calculated according to comparison of the MoCA among group C₃₀, group C₆₀ and group D. In a one-way ANOVA study, sample sizes of 16, 16, and 16 are obtained from the 3 groups whose means are to be compared. The total sample of 48 subjects achieves 96% power to detect differences among the means versus the alternative of equal means using an F test with a 0.05 significance level. The size of the variation in the means is represented by their standard deviation which is 0.60. The common standard deviation within a group is assumed to be 1.00. With a 10% dropout rate, 102 patients were studied to allow for minimize statistical errors. 202 patients were collected in our study, randomized to group C₃₀ (76 cases), group C₆₀ (62 cases) and group D (64 cases).

Statistical analysis

Data were tested for normal distribution using the Kolmogorov–Smirnov test. Continuous data were expressed as the mean ± standard deviation (SD) and categorical data were expressed as number (percentage). For comparison of demographic and operative data, quantitative data were compared with the one-way ANOVA, Bonferroni method and categorical data were compared with the χ^2 test. For repeated-measurement data, data were analyzed by repeated-measures analysis of variance using the Bonferroni method. All analyses were conducted using SPSS software, version 17.0 for Windows. A P value < 0.05 were considered to indicate statistical significance.

Results

Patient enrollment and characteristics

The study flow diagram is shown in Figure 1. A total of 202 patients completed the study. No significant differences were found in terms of the clinical characteristics, including gender, age, amount of propofol, sedation time, endoscopist and patient satisfaction ($p>0.05$) (Table 2).

MoCA analysis

The MoCA scores were similar at baseline in each group. Compared with baseline before gastrointestinal endoscopy, the post-operation MoCA scores were decreased in all the groups (group C₃₀: $p<0.001$; group C₆₀: $p<0.001$; group D: $p = 0.002$). Compared with group C₃₀, the MoCA scores were higher in group C₆₀ ($p = 0.03$) and group D ($p<0.001$), and those in group D were higher than those in group C₆₀ ($p<0.001$) (Table 3). Incidence of cognitive impairment in group C₃₀ was 56.6% which ranked the highest among the three groups. The incidence in group D was 7.8% which ranked the lowest among the three groups, the difference is significant statistically ($p<0.001$) (Table 4). The MoCA scores were similar between the genders in each group ($p>0.05$) (Table 5).

Discussion

At present, the MoCA and the Mini-Mental State Examination (MMSE) are the most commonly used neuropsychological tests. As a simple cognitive screening tool, the MoCA was used in this study has more sensitivity and specificity than the MMSE^[7], and the MoCA was used to facilitate the assessment of functional cognitive disorder (FCD) and mild cognitive impairment (MCI)^[8].

Propofol is a commonly used intravenous anesthetic agent for gastrointestinal endoscopy may lead to cognitive impairment^[2]. Mounting evidence from experimental models has demonstrated that propofol could induce a similar neurotoxic effect^[9–11]. Allampati et al.^[12] have reported that in humans, cognitive flexibility returns to baseline within 30–45 min after propofol sedation despite delayed return of psychomotor speed and reaction time. Similarly, Borrat et al.^[13] have reported that patients have cognitive impairment after propofol and remifentanyl sedation, especially in attention and psychomotor function. Our results have shown that although among all the groups the MoCA scores were significantly lower than baseline after propofol-based sedation for gastrointestinal endoscopy, the MoCA scores in group C₆₀ were higher than group C₃₀. However, patients in group C₆₀ were unable to return to baselines at 60min. The reason may be that we have adopt deep sedation(OAA/S score = 0) for the whole procedure and also that we have used the MoCA test, which has greater sensitivity.

Growing clinical and animal studies have indicated that dexmedetomidine can provide neuroprotective effects^[4]. Hence, we hypothesized that dexmedetomidine added to propofol-based sedation for gastrointestinal endoscopy could improve cognitive function. As shown in this study, even though the MoCA scores in group D decreased, they were still significantly higher than those in group C. These data

have implied that dexmedetomidine interventions may reduce the incidence of cognitive impairment and improve patients' cognitive function at discharge.

Several limitations of this study should be noted. First, sufentanil was used for sedation in order to reached an OAA/S score = 0, but the effect of opioids on cognitive function has not been considered in this study. Second, our study was designed to reduce the effects of other factors on cognitive function, the population is a remarkably healthy (ASA I-II status), essentially devoid of concomitant organ dysfunction.. As a result, the study results are applicable to only a very narrow segment of the actual patient population requiring endoscopy. We aim to address these issues in future studies. Third, our study has no long-term follow-up over 60min. Moreover, some additional factors, including dehydration, hunger, procedural anxiety, and external distractions noise should also be taken into consideration.

Conclusions

In conclusion, cognitive function proved to be impaired postoperatively in patients undergoing sedation for elective outpatient gastrointestinal endoscopy. Dexmedetomidine added to sedation for gastrointestinal endoscopy can improve early cognitive function and also reduce the incidence of cognitive impairment.

Abbreviations

ChiCTR = Chinese Clinical Trial Registry; CONSORT = CONSolidated Standards Of Reporting Trials; ERAS = enhanced recovery after surgery; FCD = functional cognitive disorder; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; MoCA = Montreal Cognitive Assessment; OAA/S = observer's assessment of alertness/sedation; PACU = postanesthesia care unit; SD = standard deviation.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethical Committee of the First Affiliated Hospital of Wenzhou Medical University, and written informed consent was obtained from all patients participating in the trial. The trial was registered before patients' enrollment at Chinese Clinical Trial Registry (<http://www.chictr.org.cn>, ChiCTR1900022639; principal investigator: L. C.; date of registration: April 19, 2019).

Consent to publish

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contribution

CL and LLN designed the study and supervised the work. JLD and LB collected the patient samples and provided the clinical data. WFY analyzed all the results and performed the statistical analyses. CL and ZXY wrote the manuscript. All authors were involved in data discussion and critical reviewing of the manuscript.

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Tables

Table 1 Responsiveness scores of the modified Observer's Assessment of Alertness/Sedation Scale (OAA/S)	
Responsiveness	Score
Responds readily to name spoken in normal tone	5 (Alert)
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and/or repeatedly	3
Responds only after mild prodding or shaking	2
Responds only after painful trapezius squeeze	1
Does not respond to painful trapezius squeeze	0

Table 2 Clinical Characteristics of Patients			
	group C ₃₀	group C ₆₀	group D
Gender(M/F)	32/44	24/38	27/37
Age(yr)	50±9	52±10	51±10
Amount of propofol(mg)	211±49	209±47	207±60
Sedation time(min)	16±6	17±7	16±7
Endoscopist satisfaction(%)	97.4	96.8	98.4
Patient satisfaction(%)	98.7	98.4	98.4
Data are presented as mean ± SD			

Table 3 Cognitive Function at Baseline and Discharge			
	group C ₃₀	group C ₆₀	group D
Before	27.2±1.12	27.4±1.04	27.2±1.06
After	25.2±1.83 ^c	25.8±1.40 ^{ac}	26.6±1.00 ^{abc}
^a Compared with the group C ₃₀ , P<0.05, ^b Compared with the group C ₆₀ , P<0.05, ^c Compared with the Baseline, P<0.05, Data are presented as mean ± SD			

Table 4 Incidence of cognitive impairment

	Number (%)
group C ₃₀	43(56.6%)
group C ₆₀ ^a	22(35.4%)
group D ^{ab}	5(7.8%)
^a Compared with the group C ₃₀ , P<0.05, ^b Compared with the group C ₆₀ , P<0.05, Data are presented as mean ± SD	

Table 5 Cognitive Function between male and female						
	group C ₃₀		group C ₆₀		group D	
	Male	Female	Male	Female	Male	Female
Before	27.4±1.04	27.0±1.15	27.7±0.96	27.2±1.05	27.2±1.05	27.2±1.08
After	25.5±1.82	24.7±1.75	26.1±1.21	25.6±1.48	26.7±0.92	26.6±1.07
Data are presented as mean ± SD						

Figures

CONSORT 2010 Flow Diagram

Figure 1

CONSORT Flow Diagram

Supplementary Files

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