Original Article

Relationship among melatonin, postoperative delirium, and postoperative cognitive dysfunction

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Background: Postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) are the most common central nervous system dysfunctions during the perioperative period. Melatonin protects nerve cells and impacts cognitive functioning in patients after surgery.

Methods: A total of 120 patients undergoing elective non-cardiac surgery were evaluated with the confusion assessment method (CAM) for diagnosis of POD on the day before and the 1^{st}, 2^{nd}, 3^{rd}, and 7^{th} day after surgery. Also, a neuropsychological test for the diagnosis of POCD was performed on the day before and 1 week after surgery. Patients' urine was collected to examine the concentration of 6-sulfatoxymelatonin (6-SMT), the metabolite of melatonin, with the enzyme-linked immunosorbent assay method. Meanwhile, urine creatinine values were examined to calculate the 6-SMT/creatinine ratio (M/C).

Results: The incidence rates of POD and POCD were 7% and 44%, respectively. There were no statistically differences for the M/C on the 1^{st}, 2^{nd}, 3^{rd}, and 7^{th} day after surgery between the POD and the non-POD groups (P>0.05). However, there were statistically significant differences (P<0.05) in the rates of M/C change [(preoperative value-postoperative value)/(postoperative value) ×100%] on the 1^{st} and 7^{th} day after surgery between both groups. Patients were divided into Group I_1 (≥100%) and Group II_1 (<100%) based on the M/C rate changes on the 1^{st} day, Group I_7 (≥200%) and Group II_7 (<200%) based on the M/C rate changes on the 7^{th} day, and Group I_w (≥100%) and Group II_w (<100%) based on the M/C rate changes during the 1^{st} week after surgery. The incidence rates of POD for Group I_1 and Group II_1 were 21.1% and 3.7%, respectively; for Group I_7 and Group II_7 were 50% and 1.1%, respectively; for Group I_w and Group II_w were 17.2% and 2.8%, respectively. For 7 patients with POD had POCD, the occurrence of POCD was related to POD (P<0.05).

Conclusions: Increased melatonin after surgery may be a risk factor for POD. There may be no correlation between melatonin and POCD. POD may be a risk factor of POCD.

Keywords: Melatonin; creatinine; postoperative cognitive dysfunction (POCD); postoperative delirium (POD); 6-sulfatoxymelatonin (6-SMT)

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Introduction

Central nervous system dysfunction often occurs in elderly patients after anesthesia and surgery. Postoperative delirium (POD) and postoperative cognitive dysfunction (POCD) are more important and common complications.

POD is defined by an acute, transient, and nonspecific change in the level of consciousness, attention, cognition, perception and sleep-wake cycle (1,2). According to a report of the American Psychiatric Association, the incidence of POD is as high as 51% (3,4). And the incidence of the elderly is 15–53% (5). POCD is defined as nervous system complications after surgery in patients who had no mental disorders, such as anxiety, personality changes, or memory impairment before surgery. The incidence of POCD is 25.8% at 1 week after surgery and 9.9% at 3 months (6), and is up to 30% for orthopedic surgery (7). Melatonin can protect nerve cells through its antioxidant and anti-apoptotic effects. At the same time, melatonin can regulate the light-dark cycle, produce a hypnotic effect, and improve sleep quality.

Sleep disorders are common in patients after surgery. The lack of synchronization between sleep-wake cycle and melatonin secretion can lead to the occurrence of POD (8). However, related studies do not illuminate the relationship among melatonin, POD, and POCD. Therefore, this study aimed to assess the incidence of POD and POCD in patients undergoing non-cardiac surgery, who are 60 years old and over and to assess the concentration of melatonin by detecting its urinary metabolite (6-sulfatoxymelatonin, 6-SMT) before and after surgery. As such the study seeks to determine the relationships among melatonin, POD, and POCD, and to assess if melatonin can indicate postoperative cognitive impairment. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2001).

Methods

Subject enrollment

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of Beijing Chaoyang Hospital, Beijing, China, and informed consent was obtained from all the patients. Older patients, aged 60–82 years, who were scheduled for non-cardiac surgery that was expected to last 2 h or longer, were recruited sequentially to this study. Exclusion criteria included: a score of ≤23 on the Mini-Mental State Examination (MMSE) before surgery, ≤6 years of education, a current or past history of psychiatric or neurological disease, kidney dysfunction, visual or auditory disorders, alcohol or drug dependence, regular use of tranquilizers or antidepressants and a history of open cardiac surgery or intracranial surgery. Patients were also excluded if they were not available to complete the neurocognitive test 1 week after surgery.

Perioperative management

A preoperative evaluation was conducted 1 day before surgery and included the patient's age, gender, whether had regular schedule recently, past medical history, physical examination results, education level, recent medication history, surgical history, and the visual analog scale (VAS) score before surgery. The VAS score is in relation to the degree of pain.

All patients received general anesthesia or combined spinal-epidural anesthesia (CSEA). General anesthesia was induced by using 1–2 mg/kg of midazolam, 15–25 µg of sufentanil, 1.5–2.5 mg/kg of propofol, and 0.6 mg/kg of rocuronium and was maintained with 0.01–0.02 mg/kg/h and 6–15 mg/kg/h of propofol during the operation. Patients were extubated in the operating room after surgery. Combined spinal-epidural anesthesia was administered at the L2–3 or L3–4 interspace using 1% ropivacaine, followed by insertion of an epidural catheter. Patients received patient-controlled analgesia (PCA) for postoperative pain control of their own accord. None of the patients received atropine before surgery nor were any inhalation anesthetics administered during the operation.

Intraoperative and postoperative observations included the way the operation was conducted, the anesthesia that were administered, duration of the operation and anesthesia, intraoperative and arterial blood gas analysis, blood pressure, blood loss, fluid infusion, blood products, urine output, medicines used intraoperatively and their dosage, the use of PCA, VAS score, and postoperative complications. Patients were assessed daily during their hospital stay to review their medical records.

Patients were tested 1 day before the operation and on the 1st, 2nd, 3rd, and 7th day after surgery with the confusion assessment method (CAM) for the diagnosis of POD. They were also tested 1 day before the operation and 1 week after surgery with a neuropsychological test for the diagnosis of POCD. In total, 10 neuropsychological tests (9-12) were used to assess the memory and executive functions of the patients. The 10 tests included The Mini-Mental Stage Examination (MMSE), Hopkins Verbal Learning Test (HVLT), HVLT (Delayed Recall), Brief Visual-spatial Memory Test (BVMT), BVMT (Delayed Recall), Trail Making Test (TMT), Digit Span Test (DST), Benton Judgment of Line Orientation, Digit symbol-coding Test and List Delayed Recognition (13). Before testing, the Beck Depression Inventory Test was used to exclude depressed patients.

Diagnostic criteria

The definition of POD was based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria (14). We used the American Psychiatric Association's CAM (15) to screen for cases of possible delirium and then confirmed if DSM-IV criteria were met. Mental health status information was also collected from nursing reports.

The diagnostic criteria from ISPOCD study were used for determining POCD of patient (6,12). Fifty age-matched adults who were not hospitalized and did not receive surgery (control group) were involved in the neuropsychological tests. The standard deviation (SD) value was obtained. A Z score was calculated by comparing differences between preoperative and 1-week postoperative score to control group (6,12). POCD was diagnosed when Z score >1.96 of more than 1 test.

Collection and detection of urine samples

Morning urine samples were obtained from the enrolled patients one day before surgery and on the 1^{st}, 2^{nd}, 3^{rd}, and 7^{th} day after surgery. Each urine sample was collected before breakfast. The urine supernatant was obtained using low-speed centrifugation, and the supernatant samples were stored in a sealed sterile container at −80 ℃ before testing. We tested the 6-SMT level in the supernatant samples using enzyme-linked immune sorbent assay (ELISA, Elisa kits: Immuno-Biological Laboratories, Minneapolis, MN, USA). In recognition that urine samples are highly diluted because of postoperative infusion, urine creatinine concentrations were utilized to adjust the urine samples' 6-SMT concentrations (16). The 6-SMT/creatinine ratio (M/C = 6-SMT/creatinine × 1,000) was used to provide a more objective estimate of urine 6-SMT concentration. For convenience, we will refer to this as the "6-SMT concentration" instead of the "adjusted 6-SMT concentration", unless otherwise stated. In addition, we detected the urine creatinine values in the same original urine samples. Assays of urine creatinine were carried out using a UniCel® DxC 800 Synchron® Clinical System (Beckman, Brea, CA, USA).

Statistical analysis

Statistical analyses were performed with SPSS for Windows (Version 16.0). Normally distributed measurement data were analyzed with independent-sample *t*-tests, while nonnormally distributed data were analyzed with a rank sum test. Categorical data were analyzed using chi-square tests (χ^2). A P value of <0.05 was considered as indicating a statistically significant difference.

Results

The incidence of POD and POCD

A total of 120 patients were recruited to this study, of whom 100 patients were assessed throughout. Seven patients were diagnosed with POD, and as such, the incidence of POD was 7%. Forty-four patients were diagnosed with POCD, and hence the incidence of POCD was 44%. The general characteristics of patients in the groups with and without POD are shown in *Table 1*. There were no significant differences among the groups.

The rates of M/C change

The patients were divided into the POD and non-POD groups based on the occurrence of POD. The M/C before surgery and on the 1^{st}, 2^{nd}, 3^{rd}, and 7^{th} day after surgery were compared between the two groups and there were no statistically significant differences (P>0.05). However, the rates of M/C change [the value of change = (preoperative value − postoperative value)/postoperative value × 100%] of the POD group compared to the non-POD group on the 1^{st} and 7^{th} day after surgery were significantly different (P values were 0.024 and 0.004, respectively; *Figure 1*); and there were no statistically significant differences for the other days. Each time point of M/C and the rates of change are shown in *Table 2*. The "rate of change" is defined as the maximum of the rate of M/C change on the 1^{st}, 2^{nd}, 3^{rd}, and 7^{th} day after surgery.

The incidence of POD in high fluctuations on the 1^{st} day after surgery

The patients were divided into Group I_1 and Group II_1 based on the magnitude of the M/C rate changes on the 1^{st} day after surgery (Group I_1 was defined as patients whose M/C change ≥100%, the rest were allocated to Group II_1). The incidence rate of POD of Group I_1 was 21.1%, which is higher than the 3.7% of Group II_1 (P=0.03). There was no statistically significant difference between the two groups (*Figure 2*).

Table 1 General condition of patients with and without postoperative delirium and patients with and without postoperative cognitive dysfunction

Variables	POCD group (n=44)	Non-POCD group (n=56)	P value (POCD)	POD group (n=7)	Non-POD group (n=93)	P value (POD)
Demographics						
Age	68.41±5.78	67.43±5.18	0.374	69.00±4.97	67.77±5.50	0.669
Gender (male)	63.6% (n=28)	62.5% (n=35)	0.907	28.6% (n=2)	65.6% (n=61)	0.121
Years of education	8.68±2.42	9.07±3.04	0.489	8.57±2.07	8.92±2.83	0.818
MMSE score before surgery	26.55±1.72	26.95±1.39	0.363	26.29±1.98	26.81±1.52	0.569
Medical history						
Hypertension	52.3% (n=23)	57.1% (n=32)	0.557	57.1% (n=4)	54.8% (n=51)	1.000
Coronary disease	20.5% (n=9)	14.3% (n=8)	0.439	28.6% (n=2)	16.1% (n=15)	0.757
Diabetes	22.7% (n=10)	14.3% (n=8)	0.742	42.9% (n=3)	19.6% (n=18)	0.33
Cerebrovascular disease	29.5% (n=13)	16.1% (n=9)	0.117	42.9% (n=3)	20.4% (n=19)	0.373
Cancer history	20.5% (n=9)	21.4% (n=12)	0.869	0.0% (n=0)	22.6% (n=21)	0.345
Past surgery	47.7% (n=21)	62.5% (n=35)	0.113	28.6% (n=2)	58.1% (n=54)	0.248
Surgery			0.099			0.305
Orthopedic surgery	86.4% (n=38)	67.9% (n=38)		100% (n=7)	74.2% (n=69)	
Abdominal surgery	9.1% (n=4)	21.4% (n=12)		0.0% (n=0)	17.2% (n=16)	
Thoracic surgery	4.5% (n=2)	10.7% (n=6)		0.0% (n=0)	8.6% (n=8)	
Anesthesia			0.423			1.000
GA	79.5% (n=35)	85.7% (n=48)		85.7% (n=6)	84.9% (n=79)	
CSEA	18.2% (n=8)	12.5% (n=7)		14.3% (n=1)	15.1% (n=14)	
Anesthesia time (min)	227.7±86.63	214.2±85.47	0.457	222.9±42.82	220.0±88.15	0.461
VAS (5 grade)						
1st day after surgery	4.27±0.82	3.89±1.14	0.108	4.57±0.79	4.02±1.03	0.112
7th day after surgery	2.52±1.05	2.54±1.16	0.934	2.71±1.11	2.52±1.11	0.622
Liquid management						
Intake (mL)	2,395±1,398.2	2,122±918.7	0.521	2,443±911.7	2,226±1,176.6	0.356
Output (mL)	935±807.7	787±565.3	0.623	1,249±846.0	820±663.4	0.087
Blood loss (mL)	331±546.5	233±307.8	0.675	541±883.3	254±372.4	0.622
Complications	75% (n=33)	69.6% (n=39)	0.554	85.7% (n=6)	71.0% (n=66)	0.688
PCA	100% (n=44)	98.2% (n=55)	1.000	100% (n=7)	98.9% (n=92)	1.000
Depression	0% (n=0)	0% (n=0)	1.000	0% (n=0)	0% (n=0)	1.000

P>0.05, no significant differences. MMSE, Mini-Mental State Examination; GA, general anesthesia; CSEA, combined spinal-epidural anesthesia; VAS, visual analogue scale; POD, postoperative delirium; POCD, postoperative cognitive dysfunction.

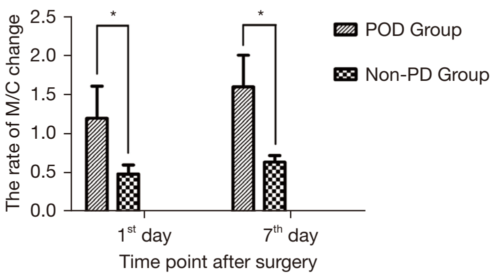

Figure 1 The rates of M/C in the postoperative delirium and non-postoperative delirium groups. *, P1=0.024, P7=0.004, there is a statistical significance. POD, postoperative delirium; M/C, the 6-SMT/creatinine ratio.

The incidence of POD in high fluctuations on the 7th day after surgery

If the M/C rate changed on the 7th day after surgery, the sample was divided into two groups analogously to the 1st day after the operation; however, there were statistically significant differences. Group I_7 was defined as patients whose M/C change ≥200%, and the rest were allocated to Group II_7. The incidence of POD of Group I_7 was 50%, which is much higher than the 1.1% of Group II_7 (P=0.000). There were no statistically significant differences between the two groups (*Figure 3*).

The incidence of POD in high fluctuations during the first week after surgery

Considering the occurrence of POD might relate to the overall change of 6-SMT across the 4 time points after surgery, the patients were divided into Group I_w and Group II_w based on the magnitude of M/C rate changes during the 1st week after surgery (Group I_w was defined as patients whose M/C change ≥100%, the rest were allocated to Group II_w). The incidence of POD of Group I_w was 17.2%, which is higher than the 2.8% for Group II_w (P=0.033). There was a statistically significant difference between the two Groups (*Figure 4*).

The incidence of POCD in the POD groups

Patients were divided into the POCD and non-POCD groups based on the occurrence of POCD. The M/C and the rates of change before surgery, and on the 1st, 2nd, 3rd, and 7th day after surgery were compared between the two groups, and there were no statistically significant differences (P>0.05, *Table 3*).

Seven patients with POD also had POCD. Patients were divided into the POD and non-POD groups based on the occurrence of POD. The incidence of POCD in the POD group was 100%, which is much higher than non-POD group's incidence of 39.8%. This suggests that the occurrence of POCD was related to POD (P<0.05, *Figure 5*).

Discussion

Past research has confirmed that the people over the age of 70 years have a significantly increased risk of POD (17,18). At the same time, advanced age is the only specific risk factor for POCD (19). The changes that accompany aging influence the individual's ability to withstand the stress of injury, surgery, and anesthesia. Therefore, we chose patients over 60 years old as research objects.

In total, seven patients met the diagnostic criteria of POD according to the CAM during the 1st to 7th day after surgery. The incidence of POD was 7%, which is lower than what is reported by previous studies. It may relate to the following factors. First, the patients recruited in this experiment were able to complete the neuropsychological assessments for POCD, and people with very low cognitive dysfunction were excluded from the study. Second, those who could not concentrate for a long time because of their low education levels, preoperative cognitive dysfunction and advanced ages were excluded from the study too. In addition, the reasons for the low incidence may be that CAM evaluations were conducted and diagnoses of patients with reduced activity types and mixed types of POD may have been missed.

The results of this study show that patients with high secretion level of melatonin after surgery were more susceptible to POD, especially on the 1st and 7th day. On the 1st day after surgery, the effects of surgery and anesthesia and postoperative pain are strongest in those most affected, and patients are susceptible to POD. During this period, as long as the increase of melatonin is up to two times or more of preoperative levels, patients have a higher risk of POD. On the 7th day after surgery the convalescence of the patients' physical condition and mental state is completed. During this period, the incidence of POD is reduced greatly compared to the 1st day after surgery, such that patients are susceptible to POD when the melatonin increases up to three times or more than the preoperative levels.

Shigeta and colleagues (20) studied the perioperative fluctuation of melatonin in 29 patients who underwent

Table 2 The 6-SMT/creatinine ratio and the rates of change at each time point in the postoperative delirium and non-postoperative delirium groups

Variables	POD group	Non-POD group	P value
M/C before surgery	11.57±5.62	17.11±10.15	0.131
M/C 1st day after surgery	22.86±8.40	22.17±16.11	0.314
M/C 2nd day after surgery	22.14±10.95	27.54±21.53	0.725
M/C 3rd day after surgery	21.43±13.45	27.82±16.89	0.331
M/C 7th day after surgery	29.43±15.67	25.04±15.10	0.462
Rate of change 1st day after surgery	1.20±1.09	0.49±1.13	0.02*
Rate of change 2nd day after surgery	1.21±1.36	0.88±1.52	0.418
Rate of change 3rd day after surgery	0.90±0.99	0.85±1.24	0.924
Rate of change 7th day after surgery	1.60±1.08	0.64±0.82	0.004*
Rate of change $_w$	0.71±0.49	0.26±0.44	0.989

*, P<0.05, there is a statistical significance. POD, postoperative delirium; M/C, the 6-SMT/creatinine ratio.

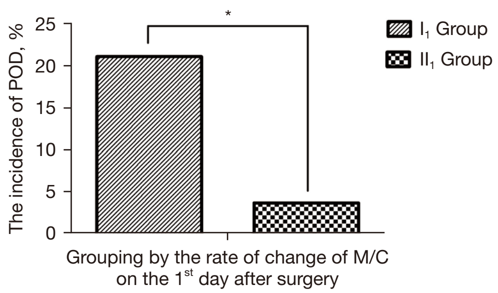

Figure 2 The incidence of postoperative delirium in high fluctuations on the 1st day after surgery. Patients were divided into Group I_1 (≥100%) and Group II_1 (<100%) based on the *M*/C rate changes on the 1st day. *, P=0.03, there is statistical significance. POD, postoperative delirium; *M*/C, the 6-SMT/creatinine ratio.

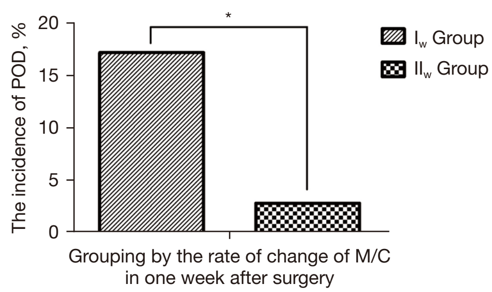

Figure 4 The incidence of postoperative delirium in high fluctuations during the first week after surgery. Group I_w (≥100%) and Group II_w (<100%) based on the *M*/C rate changes during the 1st week. *, P=0.033, there is a statistical significance. POD, postoperative delirium; *M*/C, the 6-SMT/creatinine ratio.

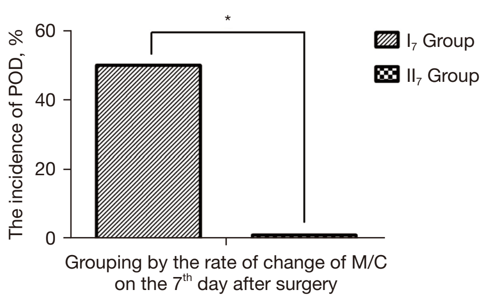

Figure 3 The incidence of post-operative delirium in high fluctuations on the 7th day after surgery. Group I_7 (≥200%) and Group II_7 (<200%) based on the *M*/C rate changes on the 7th day. *, P=0.000, there is a statistical significance. POD, postoperative delirium; *M*/C, the 6-SMT/creatinine ratio.

abdominal surgery. The results showed that melatonin levels after surgery were lower than before surgery in patients without complications, which was in contrast to patients with complications. Balan and colleagues' study (21) showed melatonin levels were related to the subtype of POD: and that patients with hyperactive POD had a significant decrease of melatonin during the acute period compared to during their convalescence, but that the mixed type showed no obvious changes. We attempted to further explore this, but too few patients with POD diagnosed were included in the sample to assess the effects of this subtype. A larger sample size would be required to prove this.

Some authors consider using melatonin to prevent and

Table 3 The 6-SMT/creatinine ratio and the rate of change in each time point in the postoperative cognitive dysfunction and non-postoperative cognitive dysfunction groups

Variables	POCD group	Non-POCD group	P value
M/C before surgery	16.96±9.94	16.51±10.10	0.811
M/C 1st day after surgery	21.89±17.21	22.51±14.33	0.417
M/C 2nd day after surgery	23.83±12.55	30.11±26.06	0.592
M/C 3rd day after surgery	24.19±11.91	30.19±19.70	0.073
M/C 7th day after surgery	25.72±13.16	25.02±16.76	0.289
Rate of change 1st day after surgery	0.54±1.31	0.53±0.97	0.220
Rate of change 2nd day after surgery	0.64±0.91	1.13±1.86	0.574
Rate of change 3rd day after surgery	0.65±0.85	1.04±1.45	0.106
Rate of change 7th day after surgery	0.71±0.86	0.71±0.89	0.994
Rate of change $_w$	1.59±1.94	1.78±1.50	0.167

P>0.05, no significant differences. POCD, postoperative cognitive dysfunction; M/C, the 6-SMT/creatinine ratio.

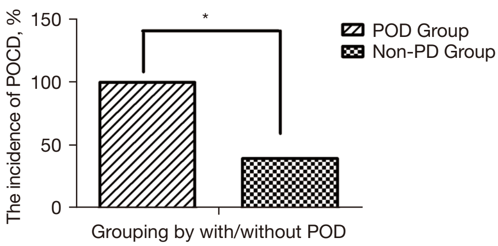

Figure 5 The incidence of postoperative cognitive dysfunction in the postoperative delirium and non-postoperative delirium groups. *, P=0.007, there is a statistical significance. POD, postoperative delirium; POCD, postoperative cognitive dysfunction.

treat POD in older patients, because of the relationship between melatonin and POD. So far, there was case report that confirmed melatonin was effective in preventing and treating POD (22). Campbell and colleagues' meta-analysis (23) also showed that perioperative melatonin reduced the incidence of delirium in older adults in the included studies. However, Ford and colleagues' randomized double-blind placebo-controlled trial in major cardiac surgery (24) did not support the use of melatonin to prevent delirium after major cardiac surgery. Also a meta-analysis (25) also showed there was no clear evidence that a melatonin agonist or melatonin reduced the incidence of delirium. Therefore, whether melatonin can be used to prevent POD remains to be investigated.

Forty-four patients were diagnosed with POCD on the 7th day after surgery. The incidence of POCD was 44%, which was a little higher than the occurrence reported by other authors (7). Our findings may relate to the type of surgery: 76% patients enrolled in this study had undergone orthopedic surgery. Maybe the following reasons can explain it: in orthopedic surgeries, the duration of operations is longer, the dosage of anesthetic is accordingly increased, the postoperative pain is serious, and the stress and inflammatory reactions are also more serious than in other non-cardiac surgery. The most important reason is that in orthopedic surgery can produce intracerebral adipose microembolus (26-28), which can lead to cerebral embolism. In addition, this study employed a widely used internationally validated neuropsychology test to assess patients. It decreased the occurrence of ceiling and learning effects brought by the MMSE assessment, thus increasing the detection rate of POCD.

This study showed that melatonin was not related to the occurrence of POCD. The relationship between melatonin and the occurrence of POCD has not been confirmed by previous research. In recent years, several animal experiments (29) revealed isoflurane might influence the plasma concentration of melatonin and the expression of melatonin receptors 1 and 2 (MT1/MT2), which could lead to memory function impairment in aged rats. Melatonin might reduce memory impairment in aged rats through regulating the plasma concentration of melatonin and melatonin receptor expression. The methods used in Wu and colleagues' study (13) are similar to the ones used in this study: urine samples were collected in the morning before surgery and on the 1st, 2nd, and 7th day after surgery to detect the concentrations of urinary 6-SMT, and patients were tested with neuropsychological assessments before surgery and 1 week after surgery to diagnose POCD. The results showed the incidence of POCD was significantly increased in the group whose concentration of urinary 6-SMT significantly fluctuated before and after surgery. However, the conclusions are opposite to each other. Gögenur and colleagues' study (30) showed that the concentration of 6-SMT exhibits the same changes after surgery compared with before surgery in all patients with high secretion during the daytime and low secretion during the nighttime. Although patients with POCD had poor quality of sleep and woke up more frequently during the night, their secretion of 6-SMT showed no significant differences, regardless of whether it was daytime or nighttime or the total 24 hours were included. The secretion of melatonin is affected by the rhythm of the sleep cycle. It is 5 to 10 times during the nighttime compared with the daytime and reaches a peak value at 2 AM to 3 AM in the morning (31). At the same time, the secretion is affected by the physical condition and external factors. Therefore, completely opposite results are not unexpected.

Because attention is important for all neuropsychology tests, delirium state and POCD are not two independent states. In some cases, POD might be an important risk factor for POCD (20). In addition, some studies have shown that the incidence of early POCD was higher in patients with POD (32). The statement above is consistent with this study. Seven patients with POD had POCD in our study, which shows that POD and POCD are closely related. The purpose of the treatment of POD and POCD is to quickly relieve the clinical symptoms and strive for the best long-term prognosis. The main treatment measures include non-drug treatment and drug treatment. Non-drug treatment is usually considered first, and drug treatment is suitable for patients with agitated delirium. An important step is to discover and clarify the pathogenesis of delirium patients, such as pain, sleep deprivation or disruption of sleep rhythm, malnutrition or sensory disorders, or infections. Generally, if these risk factors are found, the risk factors need to be treated. At the same time, check the patient's medication status on the day, screen out the drugs that may cause delirium, stop or use alternative medications. The limitation of this study is its insufficient sample size, which means the results are not very convincing. We should increase the sample size to get more accurate results.

Conclusions

The incidence of POD and POCD is 7% and 44%, respectively, in non-cardiac surgery patients. Melatonin increases after surgery may be a risk factor for POD. There may be no correlation between melatonin and POCD. POD may be a risk factor for POCD.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of Beijing Chaoyang Hospital, Beijing, China. Clinical records in our study were used with the informed consent of each participant.

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