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The influence of anaesthesia levels monitored by Narcotrend on haemodynamics and postoperative cognitive function of elderly patients

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Abstract

Objective. The aim of the study is to determine the appropriate level of anaesthesia for elderly patients when using Narcotrend for maintaining anaesthesia during surgery.

Materials and Method. A total of 135 elderly patients with intestinal tumours were randomly divided into 3 groups: A, B and C (during the surgery, the anaesthesia levels were maintained at D0, D2, and E1, respectively). Heart rate (HR) and Mean arterial pressure (MAP) were monitored at the following time points: T1 – before anaesthesia, T2 – before intubation, T3 – after intubation, T4 – during surgery, T5 – at the end of surgery, and T6 – at extubation. Additionally, cognitive function was evaluated through MMSE scores before and after the surgery.

Results. Compared with T1, group A showed a significant acceleration in HR at T3, T5 and T6. However, no significant fluctuations in HR were observed in Group B and Group C. Furthermore, in T2 and T4, the MAP of all groups decreased, and the change was most significant in group C. After the surgery, the MMSE scores of Group B and Group C were higher. However, compared with group C, the dosage of anaesthetic drugs in group B was lower and the extubation time was shorter.

Conclusions. Compared with D0, maintaining the anaesthesia level at D2 or E1 may be able to reduce the risk of postoperative cognitive dysfunction in elderly patients. Furthermore, compared to E1, the D2 level is more likely to maintain haemodynamic stability.

Key words

Narcotrend, anaesthesia, elderly patients, cognitive function, hamodynamics, cerebral oxygen metabolism.

INTRODUCTION

Cognitive decline or cognitive dysfunction is a common complication after surgery. Its main manifestations include disorders in memory, attention, information processing, and personality, which seriously affect the quality of life [1]. Age, diabetes, stroke, surgery, anaesthesia, and hypoxia are all risk factors that contribute to the decline in cognitive ability[2, 3]. Some scholars have proposed that the anaesthesia measures taken during surgery are closely related to postoperative cognitive function[4, 5]. It is worth noting that due to the decline in physical functions patients and reduced tolerance for surgery, the risk of cognitive decline is higher in elderly patients after undergoing general anesthesia surgery [6, 7]. Therefore, the impact of anaesthesia levels on postoperative cognitive dysfunction in elderly patients should be given sufficient attention by doctors.

In the past, anaesthesiologists determined the depth of anaesthesia based on clinical experience; however, the accuracy is relatively low, and the surgical risks are also relatively high. Currently, the main indicators used to monitor the level of anaesthesia include the bispectral index (BIS), the auditory evoked potential index (AEPi), and the Narcotrend index[8–10]. 'Narcotrend' as a new monitoring method, has gradually gained popularity in clinical practice due to numerous advantages. Similar to BIS, Narcotrend can reflect the entire process from brain electrical silence to wakefulness. Narcotrend classifies anaesthesia into six stages: A, B, C, D, E and F [11]. Studies have shown that Narcotrend can more accurately control the depth of anaesthesia [12, 13].

The aim of the study is to explore the appropriate anesthesia level for elderly patients when using Narcotrend during surgery, with the main focus on investigating the effects of different levels of anaesthesia (D0, D2, E1) on the postoperative cognitive function while using the Narcotrend system. Changes in haemodynamics parameters and cerebral oxygen metabolism rate were also monitored during the operation.

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MATERIALS AND METHOD

Patients. The research was approved by the Ethics Committee at The First Hospital of Xingtai, and has strictly followed the relevant requirements of the "Helsinki Declaration"

From May 2022 – May 2023, 135 elderly patients with gastrointestinal tumours who underwent surgery in the Xingtai hospital were selected for this study. Patients had to have a confirmed diagnosis through CT, MRI scans, or histopathological examinations with surgical indications. Inclusion criteria: 1) age ≥ 60; 2) American Society of Anesthesiologists class (ASA): I-II; 3) normal blood coagulation; 4) There is no severe heart or lung failure, and no liver or kidney dysfunction; 5) no history of drug abuse; 6) Be capable of cooperating with medical staff to complete the assessment of Mini-mental State Examination (MMSE) scale; 7) no similar neuropsychological tests have been taken before. Exclusion criteria: 1) There has been a history of brain trauma, stroke or some other diseases that may affect the cognitive function; 2) Those who have been using opioids or diazepines for a long time; 3) Patients with aphasia, hearing impairment or comprehension disorders; 4) The patient who was transferred to the ICU; 5) Patients who experienced adverse reactions during the perioperative period (e.g. massive bleeding or infection).

Experimental grouping. A total of 135 patients were randomly divided into three groups using a random number table: Group A, Group B, and Group C. During the surgery, based on the results shown by the Narcotrend, the anaesthesia levels of the three groups were maintained at D0, D2 and E1, respectively. Apart from the anaesthesiologists, neither the patients nor the data recorders were informed of the groupings.

Anesthesia induction. Clean the patient's scalp using Narcotrend skin cleansing cream, then place the electrodes and start using the Narcotrend single-channel monitoring system. Administer intravenous anaesthesia. After the heart rate and blood pressure have stabilized, oxygen was inhaled at a flow rate of 6L/min (for 3 minutes). During the induction of anaesthesia, Remifentanil, Propofol and Rocuronium were infused intravenously. When the patient loses consciousness, tracheal intubation is performed. During the surgery, Propofol and Remifentanil were used jointly to maintain the target depth of anaesthesia. The Narcotrend Index (NTI) of patients in group A was controlled between 64 – 57, in group B was controlled between 46 – 37, and in group C between 20 – 26. During the operation, it is essential to ensure that the changes in heart rate (HR) and mean arterial pressure (MAP) do not exceed ± 30%. If necessary, Ephedrine, Norepinephrine and Atropine can be used to maintain haemodynamic stability during the surgery. The infusion of muscle relaxants should be stopped 30 minutes before the end of the surgery. All patients underwent postoperative intravenous analgesia.

Observed indicators. After entering the operating theatre, the electrocardiogram (ECG), HR and pulse oxygen saturation (SpO2) were immediately monitored. Under local anaesthesia, an arterial puncture and catheterization were performed to measure the invasive blood pressure (IBP). HR and MAP were recorded at six time points: T1 – before anesthesia, T2 – before intubation, T3 – after intubation, T4 – during surgery, T5 – at the end of surgery, and T6 – at extubation. The operation time, extubation time, and incidence rates of adverse reactions, such as nausea, vomiting and restlessness, were recorded. The cumulative usage of Propofol and Remifentanil during the surgery was also calculated.

To reflect the effect of anaesthesia depths on cerebral oxygen metabolism rate, blood samples were collected from the radial artery and the bulb of the internal jugular vein at 5 time points from T1 – T5. An i-STAT portable clinical blood gas analyzer (Abbott Laboratories, USA) was used to analyze and calculate arteriovenous oxygen difference (Da-jv0_2) and cerebral oxygen extraction ratio (CER0_2).

Assessment of cognitive function. The MMSE scale is a widely used tool for assessing cognitive functions. In this study, the assessment moments of the MMSE scale were: t0 – one day before the operation, t1 – one day after the operation, t2 – 3 days after the operation, and t3 – seven days after the operation. The MMSE scale consists of 5 aspects: orientation, attention, memory, recall and language ability; total score – 30 points. The higher the score, the better the cognitive function.

Statistical analysis. The data were analyzed using IBM SPSS statistics 23.0 software. The differences were analyzed using the chi-square test and One-way ANOVA. When *P*<0.05, the difference is considered significant.

RESULTS

Comparison of the basic information. The basic clinical information of the patient is listed in Table 1. During the operation, under the guidance of Narcotrend, the anaesthesia depths of the 3 groups were maintained at D0, D2 and E1, respectively. There were no differences in age among these 3 groups of patients (*P*>0.05). Statistical results showed that there were no significant differences in the prevalence of hypertension and diabetes, educational levels, and ASA classification among the 3 groups (*P*>0.05). Therefore, in the subsequent experiments, these 3 groups were comparable.

Comparison of various indicators during the perioperative period. There were no significant differences in the operation

Table 1. Basic clinical information statistics of subjects

Index	Group A	Group B	Group C	P value
Sample size	45	45	45	-
Narcotrend stage	D0	D2	E1	-
Narcotrend Index	57–64	37–46	20–26	-
Gender (Male/Female)	21/24	23/22	18/27	0.567
Age (years)	67.51±9.50	66.44±9.89	64.51±11.15	0.371
BMI (kg/m²)	21.39±1.31	21.30±1.38	20.75±2.35	0.173
Smoker	5 (11.11%)	5 (11.11%)	6 (13.33%)	0.932
Hypertension	12 (26.67%)	13 (28.89%)	11 (24.44%)	0.893
Diabetes	10 (22.22%)	8 (17.78%)	7 (15.56%)	0.709
Educational level	6.78±2.51	7.13±3.32	6.29±2.05	0.327
ASA level (I/II)	17/28	20/25	20/25	0.761

BMI – Body Mass Index; ASA level – American Society of Anesthesiologists class. Values are shown as Number (percentage) or Mean ± SD and analyzed using Chi-square test or One-way ANOVA

Table 2. Comparison of anesthetic technique

Index	Group A (n=45)	Group B (n=45)	Group C (n=45)
Narcotrend Index	57–64	37–46	20–26
Duration of operation (min)	197±40	211±29	206±22
Fluid infusion volume (mL)	1843±294	1945±299	1907±282
Blood loss volume (mL)	316±42	297±42	308±44
Dosage of propofol (mg)	836±108	916±93[a]	1215±128[ab]
Dosage of remifentanil (mg)	2.62±0.49	2.75±0.50	2.68±0.91
Extubation time (min)	19.11±2.71	18.31±2.50	20.44±2.81[ab]

Values are shown as Mean ± SD and were analyzed using One-way ANOVA; [a]P<0.05 – significantly different from Groups A; [b]P<0.05 – significantly different from Groups B.

time, fluid infusion volume and blood loss among groups A, B and C (*P*>0.05) (Tab. 2). However, there were significant differences in the dosage of Propofol: with the increase in the depth of anaesthesia, the dosage of Propofol was also increased (*P*<0.05). Regarding the extubation time, the results show that maintaining the anaesthesia levels at D2 can significantly shorten the extubation time (*P*<0.05).

Influence of anesthesia depths on hemodynamic parameters and postoperative adverse reactions. As shown in Table 3, compared with T1, the HR in group A significantly accelerated at T3, T5 and T6 (*P*<0.05). Furthermore, at T3, T5, and T6, the HR of group A was significantly higher than that of group B and group C (*P*<0.05). At T2 and T4, the MAP of all 3 groups decreased (*P*<0.05). Furthermore, the MAP of group C was the lowest at T2 and T4 (*P*<0.05). It can be seen from this that when the depth of anaesthesia is maintained at D2, it is easier to maintain the stability of HR and MAP during the surgery.

Table 3. Comparison of hemodynamic indexes

Index	Group A (n=45)	Group B (n=45)	Group C (n=45)
HR (times/min)			
T1	77.29±8.94	78.51±8.61	76.89±7.92
T2	79.09±8.97	76.60±10.93	75.18±10.22
T3	86.89±10.83[a]	82.47±7.54[ab]	82.11±9.49[ab]
T4	75.24±8.74	75.60±11.15	79.40±9.79[b]
T5	85.98±10.94[a]	79.09±7.32[b]	78.71±6.27[b]
T6	87.31±8.67[a]	80.36±8.57[b]	80.60±9.91[b]
MAP (mmHg)			
T1	93.09±9.85	91.22±9.20	90.96±11.29
T2	83.33±10.24[a]	82.78±8.53[a]	72.69±7.34[abc]
T3	99.40±9.30[a]	90.31±12.24[b]	86.04±10.79[ab]
T4	82.71±13.35[a]	86.69±13.29[a]	75.62±12.62[abc]
T5	94.38±9.22	88.22±7.85[b]	86.64±9.92[ab]
T6	99.29±10.94[a]	91.38±11.04[b]	90.36±14.00[b]

HR – heart rate; MAP – mean arterial pressure; T1 (before anesthesia), T2 (before intubation), T3 (after intubation), T4 (during surgery), T5 (at the end of surgery), T6 (at extubation). Values are shown as Mean ± SD and were analyzed using One-way ANOVA. [a]*P*<0.05 – significantly different from T1. [b]*P*<0.05 – Significantly different from Groups A; [c]*P*<0.05 – Significantly different from Groups B.

The incidence of adverse reactions after anaesthesia were also recorded. The results show that the incidences of Nausea and Vomiting, Hypotension, Respiratory Depression, and Agitation are all relatively low, and there is no significant difference among the 3 groups (*P*>0.05) (Tab. 4).

Table 4. Probability of postoperative adverse reactions

Index	Group A (n=45)	Group B (n=45)	Group C (n=45)	P value
Nausea and Vomiting	4 (8.89%)	3 (6.67%)	3 (6.67%)	0.898
Hypotension	1 (2.22%)	2 (4.44%)	3 (6.67%)	0.593
Respiratory Depression	0 (0.00%)	1 (2.22%)	0 (0.00%)	0.365
Agitation	2 (4.44%)	1 (2.22%)	0 (0.00%)	0.360
Total incidence rate	7 (15.56%)	7 (15.56%)	6 (13.33%)	0.943

Values are shown as a Number (percentage) and analyzed using Chi-square test

Influence of anaesthesia depths on early postoperative cognitive function. The cognitive function of the patients was evaluated using the MMSE scale (Tab. 5). There was no difference in MMSE scores among the 3 groups at t0 (*P*>0.05). However, at t1, t2 and t3, the MMSE scores in group B and group C were higher than those of group A (*P*<0.05), but there was no difference between group B and group C.

Table 5. Comparison of cognitive function between different depths of anesthesia

Index	Group A (n=45)	Group B (n=45)	Group C (n=45)
MMSE score			
t0	27.91±1.30	28.20±1.32	28.11±1.27
t1	25.11±2.08	26.02±1.51[a]	25.84±1.77
t2	26.00±1.43	27.20±1.29[a]	26.60±1.53[ab]
t3	26.60±1.81	27.93±1.39[a]	27.44±1.98[a]

MMSE score – Mini-Mental State Examination score; t0 (One day before the operation), t1 (One day after the operation), t2 (Three days after the operation) and t3 (Seven days after the operation). Values are shown as Mean ± SD and analyzed using One-way ANOVA. [a]*P*<0.05 – Significantly different from Group A – [b]*P*<0.05: Significantly different from Groups B

Comparison of cerebral oxygen metabolism levels. Compared with T1, the levels of Da-jv0_2 and CER0_2 in group B and group C decreased at each time point (*P*<0.05) However, no significant changes were observed in Da-jv0_2 and CER0_2 in group A at each time point (*P*>0.05). Compared with group A, the levels of Da-jv0_2 and CER0_2 in group B and group C were significantly lower at T2, T3, T4, and T5 (*P*<0.05) (Tab. 6). This result indicates that maintaining the depth

Table 6. Comparison of cerebral oxygen metabolism among patients

Index	Group A (n=45)	Group B (n=45)	Group C (n=45)
Da-jv0_2 (ml/l)			
T1	61.34±9.49	62.01±9.32	62.23±11.46
T2	58.61±9.58	38.20±12.04[ab]	35.82±10.79[ab]
T3	57.05±8.55	35.99±8.35[ab]	34.25±11.16[ab]
T4	56.11±13.74	36.13±8.58[ab]	33.90±11.44[ab]
T5	55.87±12.95	33.37±9.75[ab]	31.73±7.75[ab]
CER0_2 (%)			
T1	35.9±5.8	35.2±5.1	36±5.8
T2	33.3±4.6	25.6±3.1[ab]	22.6±3.3[abc]
T3	34.3±4.1	24.4±3.1[ab]	23.1±3.0[ab]
T4	32.3±3.8	23.3±4[ab]	23.1±3.5[ab]
T5	35.3±3.5	27.6±3.7[ab]	25.3±2.8[abc]

Da-jv0_2 Difference of arteriovnous oxygen; CER0_2 Cerebral oxygen etrction ratio.
T1 (before anesthesia), T2 (before intubation), T3 (after intubation), T4 (during surgery), T5 (at the end of surgery). Values are shown as Mean ± SD and analyzed using One-way ANOVA; [a]*P*<0.05 – significantly different from T1; [b]*P*<0.05 -significantly different from Groups A; [c]*P*<0.05 – significantly different from Groups B

of anaesthesia at D0 has little effect on the cerebral oxygen metabolism rate. Furthermore, when the depth of anaesthesia is maintained at D2 and E1, the inhibitory effect on cerebral oxygen metabolism is more obvious.

DISCUSSION

Over the past few decades, due to the fact that elderly patients not only suffer from underlying diseases but also have organ dysfunction[14], the proportion of elderly people undergoing surgical treatment has not been high. However, with the advancement of medical technology and the change in the mindset of the elderly, more and more elderly patients are choosing to undergo surgery for recovery. However, due to the decline in physical functions and the reduced tolerance for surgical trauma, the risk of anaesthesia and the incidence of postoperative cognitive dysfunction, are relatively higher in elderly patients [15]. Therefore, how to successfully administer anesthesia to elderly patients has gradually become the focus of attention for anaesthesiologists.

In the current study, under the guidance of Narcotrend, elderly patients were maintained at different levels of anaesthesia during the operation. This study evaluated the changes in patients' cognitive functions by comparing MMSE scores before and after the surgery. The study found that, compared with patients with an anaesthesia depth of D0, the postoperative MMSE scores were significantly higher when the anaesthesia depth was D2 and E1. Therefore, the results initially indicate that maintaining a deeper level of anesthesia (such as D2 and E1) may be more beneficial for elderly patients in reducing the risk of postoperative cognitive dysfunction compared to D0. Some studies also support this conclusion. For instance, research has shown that anesthetics can inhibit the transmission of excitatory neurotransmitters, thereby reducing neuronal damage caused by surgical stress [16]. On the other hand, studies have shown that appropriate anaesthesia can block the systemic inflammatory response triggered by surgical trauma and reduce the damage to the blood-brain barrier caused by pro-inflammatory cytokines [17].

However, it is necessary to point out that although the MMSE score is widely used to assess cognitive dysfunction, its sensitivity for mild cognitive impairment is limited, which may make it difficult to detect some subtle cognitive changes. Studies have shown that the MoCA score is specifically used to detect mild cognitive impairment [18, 19]. Therefore, combining these 2 methods can further enhance the accuracy of the results. In the future, it will still be necessary to accurately assess the postoperative cognitive function of elderly patients by using both the MMSE score and the MoCA score simultaneously. Furthermore, after surgery under general anaesthesia, cognitive dysfunction in elderly patients involves short-term memory, attention, orientation, and executive functions [20]. Therefore, some tests specifically targeting attention and executive function, such as the Trail Making Test and the Digit Symbol Substitution Test [21], should also be considered.

Postoperative cognitive dysfunction is also closely related to a variety of neurobiological markers (β-amyloid protein, neurofilament light chain), especially in diseases such as Alzheimer's disease, in which these neurobiological markers have significant value for early warning and diagnosis [22, 23]. Therefore, revealing the dynamic changes of these neural markers under different levels of anaesthesia also helps to elucidate the relationship between the depth of anaesthesia and postoperative cognitive function.

The current study also monitored changes in heart rate and blood pressure during the operation. It was found that, compared with D0, maintaining the anaesthesia depth at the levels of D2 and E1 resulted in smaller fluctuations in heart rate during the surgical procedure. However, compared with E1, when the depth of anaesthesia is maintained at the D2 level, the dosage of anaesthetic drugs was lower and the extubation time was shorter. Compared with E1, the depth of anaesthesia in D2 was lower. It is speculated that light anaesthesia might significantly shorten the postoperative extubation time by accelerating drug clearance and restoring physiological functions. Therefore, it seems that for elderly patients maintaining the anaesthesia depth at D2 can better protect the neurological function of patients, maintain the stability of haemodynamics, and shorten the extubation time. This study show that a certain proportion of elderly patients experience a decline in cognitive function, which indicates the necessity of adopting cognitive rehabilitation therapies after surgery, such as EEG neurofeedback [24], short-term memory exercises [25], and cognitive control training [26]. For elderly patients undergoing general anesthesia surgeries, in addition to controlling the depth of anaesthesia during the operation, cognitive training is also necessary after the surgery. This may play a crucial role in reducing postoperative cognitive dysfunction.

There are many factors related to postoperative cognitive dysfunction. Apart from the neurotoxicity of anaesthetic drugs, changes in brain oxygen metabolism during the surgery, or stress responses which can also affect cognitive function [27–29]. The literature indicates that cerebral oxygen metabolism can affect the postoperative cognitive function and prognosis of elderly patients [28, 30]. In the current study, it was found that when the depth of anaesthesia was maintained at D2 and E1, $CER0_2$ significantly decreased. $CER0_2$ indicates that the oxygen consumption is lower than the oxygen supply, resulting in a decrease in the metabolic activity of the brain. Reducing the oxygen metabolism rate can minimize the brain tissue damage caused by insufficient oxygen supply during surgery. Therefore, the authors of the current study believe that increasing the depth of anaesthesia within a safe range may partially exert a protective effect on neurons by reducing the oxygen metabolism rate.

It is worth noting that the differences in the history of COVID-19 infection among the groups may have an impact on the interpretation of the results. As previous studies have confirmed that SARS-CoV-2 can directly invade the central nervous system and cause a series of short-term or long-term neurological disorders [31, 32]. Furthermore, this disease can also lead to autonomic nerve dysfunction, impaired cerebral perfusion, and changes in the cardiovascular system [33, 34]. These factors may have an impact on the results of the MMSE, haemodynamic parameters, and brain metabolic indicators. Future research should therefore further assess the history of COVID-19 infection among the population to increase the homogeneity of the sample.

Furthermore, after surgery under general anaesthesia, there is indeed a risk of cognitive dysfunction in elderly patients, which is significantly increased in those with a history of cardiovascular or cerebrovascular diseases [35, 36].

The main reason is that cardiovascular and cerebrovascular diseases reduce the brain's tolerance to ischemia and hypoxia. Therefore, adopting stricter screening criteria (such as excluding patients with a history of cardiovascular and cerebrovascular diseases) is also necessary for accurately studying the relationship between the depth of anaesthesia and cognitive impairment.

Limitations of the study. This study initially determined the appropriate level of anesthesia for elderly patients through clinical experiments. However, this study still has several limitations. Firstly, the subjects were from a single research center and the sample size was small, which might affect the stability of the results. Secondly, relying solely on the MMSE score to assess cognitive function may result in an insufficient detection rate of mild cognitive impairments. Therefore, in order to more accurately evaluate the relationship between anesthesia depth and postoperative cognitive function, it is necessary to conduct a multi-center study and use multiple neuropsychological tools to comprehensively assess cognitive function. Furthermore, in future research, every effort should be made to ensure the homogeneity of the samples. For instance, consider the potential impact of confounding factors (such as the status of COVID-19 infection and the history of cardiovascular and cerebrovascular diseases) on the experimental results.

CONCLUSIONS

The study confirms that compared with the D0 level, maintaining the anaesthesia depth at the D2 and E1 levels under the guidance of Narcotrend is more conducive to maintaining haemodynamic stability, inhibiting cerebral oxygen metabolism, and may reduce the risk of cognitive decline in elderly patients. Furthermore, compared with E1, the anaesthesia depth at the D2 level can reduce the dosage of anaesthetic drugs and shorten the extubation time.

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