Analysis of Relevant Factors of Delayed Recovery after General Anesthesia and Exploration of the Countermeasures

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Abstract：Objective: To analyze the related factors and the countermeasures of delayed recovery after general anesthesia. **Method:** By taking 5042 patients who underwent the gynecological general anesthesia in our hospital during January 2017 - February 2019 as the research object, the number of patients with delayed recovery after operation was counted, and the clinical data of all patients were analyzed in detail. The related factors of delayed recovery after general anesthesia were then discussed with the countermeasures were given. **Result:** All patients in the study group completed their surgical treatment successfully, with in total 984 cases (19.52%) of delayed recovery occurred. The results of single factor analysis were as follows: The occurrence of delayed recovery may be affected by factors such as patient's age, time of anesthesia, anesthetic dosage, alcohol consumption, smoking, anemia, general anesthesia history, and ASA grading and other factors($P < 0.05$); The results of multiple factors analysis show that: Age, time of anesthesia, anesthetic dosage, alcohol consumption, smoking, anemia and other factors are the main influencing factors of delayed recovery after general anesthesia surgery($P < 0.05$). **Conclusion:** After the clinical application of general anesthesia, patients may have delayed recovery under the influence of many factors. Therefore, it is necessary to formulate strict measures to reduce the risk of delayed recovery for patients.

1. Introduction

In recent years, with the rapid development of China's medical level and the continuous improvement of anesthesia-related monitoring facilities, patients under general anesthesia are usually able to wake up within a short time after stopping using anesthetics, but there are still some patients who may still be in the stage of anesthesia awakening for a long time after stopping using anesthetics. [1] If 90min after being relieved of the anesthesia the patient was still not recovered back to his or her 90min Consciousness, condition can be judged as delayed recovery. The occurrence of delayed recovery will not only affect the effect of surgical treatment to a certain extent, but also increase the perioperative risk of the patient, and hinder the recovery of various functional areas after surgery. Generally, general anesthesia surgery are featured with large trauma, long operation time and large amount of anesthetic drugs. Therefore, the risk of delayed recovery after general anesthesia surgery is higher than other types of surgery. [2-3] At present, there are many studies on the occurrence of delayed recovery after general anesthesia surgery both at home and abroad, but most of them are limited to the centralized analysis of certain anesthetics or specific age groups, lacking of comprehensive discussion at multiple factors level based on the clinical practice. [4] In previous studies, some scholars have identified that the age of the patients, the grading of liver function, anesthesia time and the duration of anesthesia as well as ASA Grading will all have a significant impact on the occurrence of delayed recovery after general anesthesia surgery. [5-6] In this research, a collection of 5042 recent hospitalizations were selected for analysis to confirm the accuracy of above-mentioned reports, and to explore the specific factors affecting the

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recovery delay after anesthesia for patients undergoing general anesthesia, and then formulate specific measures to improve the therapeutic effect and safety of patients undergoing surgery, with the report as follows.

2. Materials and Methods

2.1 clinical data

A total of 5042 cases of hospitalization where the patients underwent gynecologic general anesthesia in our hospital during January 2017- February were selected for study. The age of this group ranges from 25~66 years, averaged (46.53±5.22) years old.

2.2 Selection Criteria

2.2.1 Inclusion criteria

① All patients were informed of the study and signed voluntarily the informed consent. ② Patients are all of age ≥18, conscious, and with no occurred communication barrier.

2.2.2 Exclusion criteria

① Patients showed severe intolerance to the surgical treatment; ② Patients with malignant tumors progressed to advanced stage. ③Patients with severe functional disorders involving heart, kidney or other important organs; patients in pregnancy or lactation; ④ Patients lack of case data or with low compliance.

2.3 Method of case data collection

Statistics of case data include: Age, drinking history, smoking history, anemia degree, lung disease, general anesthesia history, liver function grading, ASA Grading, inhalation anesthesia or not, anesthesia time, anesthetic dosage, etc. In the process of the above statistical collection, the patient's own information should be inquired in detail, and the data items should be improved according to the anesthesia records, resuscitation records and patient's ward case information.

2.4 Anesthetic methods

30min prior to the operation, 0.1g sodium phenobarbital and 0.5mg atropine was injected intramuscularly. The vital signs, ECG, pulse, oxygen saturation and muscle relaxation were observed and monitored after releasing the venous channel. Used narcotic drugs, i.e., 0.05mg/kg midazolam, 1μg/kg remifentanil, 2mg/kg propofol and 1mg/kg vecuronium for combined induction, respirator with continuous mechanical ventilation in a intermittent positive pressure manner, When auditory evoked potential index (AAI) Value reached 40, the tracheal intubation was applied with maintained anesthesia: Midazolam was administered at 0.5~1.5μg/kg for continuous infusion treatment, surgical treatment, with patient receiving additional 1μg/kg fentanyl every 30min, and every 30~40min additional 0.05mg/kg vecuronium bromide, taking reference of AAI Value and mean arterial pulsation for adjusting the dosage of drug, and maintaining the AAI value within the range at 10-20, the mean arterial pressure was maintained preoperatively. The mean arterial pressure should be maintained at 85%~115% of that before operation. Atropine and neostigmine were injected intravenously after operation to antagonize the residual effects of muscle relaxants. Tracheal tube was removed when the extubation conditions were met.

2.5 Grading standard

① Liver function grading: by the use of child-pugh improved grading method to classify the patients' liver function, with the specific grading criteria listed below in the Table 1:

Table 1: Classification of Liver Function

Clinical biochemical indicators	1 point	2 points	3points
hepatic encephalopathy	Nil	1~2 degree	3~4 degree
ascites	Nil	Light	Moderate and severe
TBil (μmol/L)	＜ 34	34~51	＞ 51
Alb (g/L)	＞ 35	34~51	＜ 28
Prothrombin prolongation (s)	＜ 4	4~6	＞ 6

② ASA Classification: Mainly based on the patient's own condition and the tolerance to surgical treatment to carry out the comprehensive evaluation with 6 evaluation items in total, of which are: Class I: healthy body, with good nutritional status, and no abnormalities of the organ functions. Class II: In addition to the patient's own primary conditions, there are mild complications, but with the body organs function in normal status. Level III: In addition to the patient's own primary disease, there are more serious complications, with daily activities slightly limited, but basically free of being affected; Class IV: While patient has their own primary diseases, there are more serious complications, with daily life limited to a large extent, and higher degree of the severity of the disease endangering patient' own life safety. Class V: Having the surgical treatment mode implemented or not does not alleviate the patient's condition. Class VI: Brain death has been confirmed by imaging or other diagnostic measures, and organs to be used in other transplant operations.

③ Anemia grade: The comprehensive evaluation was conducted mainly based on the level of hemoglobin, red blood cell count and specific volume of erythrocyte in patient's peripheral blood. At present, the commonly used evaluation methods in clinic are as follows: If lower than 110g/L Anemia can be clearly diagnosed, and see Table 2 for the severity grading of anemia.

Table 2 Anemia Grading Standard

Anemic grading	Range
Light	90~110g/L
moderate	60~90g/L
severe	30~60g/L
Extremely severe	＜ 30g/L

2.6 Statistical methods

Data from this study are input into SPSS20.0 software. Measurement data is presented as (±s). Individual sample T test was used to compare the mean difference between the two groups. History of drinking, smoking, etc. Chi-square analysis was used to compare the counting data between groups. The correlation analysis was carried out by single factor analysis of variance and multifactor logistic regression analysis.

3. Result

3.1 Analysis of the occurrence of delayed recovery

This study was conducted with the involvement of 5042 patients who had successfully completed the operation after general anesthesia, of which, 984 cases of delayed recovery occurred in the patients, and the incidence of delayed recovery was: 19.52%.

3.2 Analysis of basic clinical data

The types of data obtained in this study were classified, of which data such as patient age, anesthesia time, dosage of anesthetic drugs and other measurement data were separately included in

the Table 3 for analysis with independent sample t was used for verification. History of drinking, smoking, anemia, lung disease, history of general anesthesia, liver function grading, ASA grading, inhalation anesthesia or not were included in the Table 4 and tested with Chi-square test in groups. The results show that: Age, duration of anesthesia, anesthetic dosage, alcohol consumption, smoking, anemia, history of general anesthesia, ASA Grading may lead to prolongation of anesthesia recovery time after general anesthesia surgery (P <0.05 Detailed statistics and comparison are shown in Table. 3 and Table 4 :

Table 3 Statistics of Single Factor Analysis Results of Measurement Data ($\bar{x}$±s)

influencing factor	delayed recovery group (n=984)	Non-delayed recovery group (n=4058)	t	P
Age	51.34±6.83	34.81±5.33	14.164	0.000
Anesthesia time	5.42±0.61	4.73±0.58	5.697	0.000
Dose of anesthetics used	2034.3±311.6	1537.6±278.4	8.430	0.000

Table 4 Statistics of Single Factor Analysis Results of Counting Data ($\bar{x}$±s)

influencing factor	classification	delayed recovery group (n=984)	Non-delayed recovery group (n=4058)	x^2	P
Drink wine	Yes	8 (0.16)	5 (62.50)	3.070	0.002
smoke	No	5034 (99.84)	979 (19.45)	4.232	0.000
anemia	Yes	14 (0.28)	9 (64.29)	23.368	0.000
General anesthesia	No	5028 (99.72)	975 (19.39)	33.567	0.000
history	yes	2631 (52.18)	842 (32.00)	36.616	0.000
History of	no	2411 (47.82)	142 (5.89)	52.004	0.000
Pulmonary Diseases	Yes	1523 (30.21)	731 (48.00)	0.046	0.963
ASA Classification	No	3519 (69.79)	253 (16.61)		
Liver function	Yes	503 (9.98)	407 (80.91)		
grading	No	4539 (90.02)	577 (12.71)		
	Ⅰ	231 (4.58)	0 (0.00)		
	Ⅱ	2743 (54.40)	92 (3.35)		
	Ⅲ	1364 (27.05)	481 (35.26)		
	Ⅳ	704 (13.96)	392 (55.68)		
	A	4639 (92.01)	905 (19.51)		
	B	403 (7.99)	79 (19.60)		

3.3 Multi-factors analysis

P<0.05 in the single factor analysis were taken into the multi-factors regression analysis. The results show that: The main influencing factors of delayed anesthesia after general anesthesia operation include: Age, duration of anesthesia, anesthetic dosage, alcohol consumption, smoking, anemia (P <0.05) Detailed statistics are shown in Table 5 :

Table 5 Multi-factors Regression Analysis Results

Factor	B	SE	WaldX^2	OR	P value	OR(95% CI)
Age	2.125	0.824	9.150	2.211	0.001	1.8(24-6.153)
Anesthesia time	2.333	0.945	6.378	1.743	0.003	1.5(25-4.826)
Dose of anesthetic	1.652	0.918	6.376	1.824	0.004	1.2(22-3.572)
Drinking (Yes)	1.728	0.738	7.342	1.928	0.002	1.4(38-4.154)
Smoking (Yes)	1.624	0.911	7.410	1.693	0.003	2.0(19-7.048)
Anemia (Yes)	2.105	0.928	9.423	2.229	0.002	1.5(23-5.031)

4. Discussion

General anesthesia surgery is a common surgical treatment in clinic. The treatment mode has a high degree of cure for patients' diseases, but it still has the characteristics of many complications and poor prognosis. [7] In addition, after general anesthesia surgery, patients may have delayed recovery, eventually affecting the therapeutic effect of surgery, and even pose a threat to patients' life safety. Recent studies have pointed out that the occurrence of delayed recovery is closely related to patient's age, anesthesia time and drug dosage. However, some scholars still believe that the occurrence of delayed recovery may be affected by other clinical items. [8-9] Therefore, a clear analysis of the main factors affecting the occurrence of delayed recovery and a reasonable formulation of corresponding preventive measures are of positive significance for the improvement of treatment outcomes and prognosis of patients.

Different narcotic drugs have different anesthetic effect and recovery time. Midazolam is a benzodiazepine receptor agonist, which is characterized by good water solubility, good stability and long maintenance time. However, it has high incidence of adverse reactions and high incidence of delayed recovery. Midazolam is mostly used in sedation treatment of patients in intensive care unit and maintenance of general anesthesia. [10] Remifentanil is an opioid analgesic with quick effect, strong analgesic effect and short half-life. , It is easy to be cleared and has little effect on respiratory function, but fentanyl can induce arrhythmia, elevated blood pressure and so on. [11] Propofol is also an anesthetic with fast effect, rapid recovery and low incidence of adverse reactions. It is often used in combination with fentanyl in clinical practice, which can enhance the anesthetic effect and reduce the incidence of adverse reactions. In this group of data, midazolam, remifentanil, propofol and vecuronium were used in combination to achieve rapid onset of anesthesia, maintain appropriate anesthesia time and effectively inhibit the patient's nervous prickling sensation, reduce the incidence of adverse anesthetic reactions such as delayed recovery, with relatively high safety.

In order to clarify the main influencing factors of recovery delay after general anesthesia operation and provide data support for the formulation of corresponding countermeasures, the authors selected the recent hospitalization in our hospital. 5042 The patients were studied and analyzed. The results showed that: General anesthesia operation will cause more patients to delay awakening, and the occurrence of delayed recovery may be affected by the patient's age, drinking history, smoking history, anemia and anesthesia time, anesthetic dosage and other items. The above conclusions and scholars such as Shao Bing and Fu Wuchang [12-13] In order to further clarify why the above items lead to prolonged recovery time, the author refers to recent research conclusions of many scholars for comprehensive analysis. He Lin, et al. [14] In previous studies, it has been pointed out that the incidence of prolonged awakening symptoms in elderly patients undergoing general anesthesia surgery will be significantly higher than that in young and middle-aged patients. Considering the reasons for this result, we can conclude that: With the increasing age of patients, the process of central nervous system will be in a declining process, so the sensitivity will increase

after the use of conventional anesthetics, which will lead to a stronger effect of anesthesia on patient's nerve block, and ultimately increase the time needed for patients to recover. In addition, compared with young people, most of the elderly patients have different degrees of organ function decline. The decrease of glomerular filtration rate caused by renal function changes will directly affect the excretion of narcotic drugs, and ultimately maintain the long-term efficacy of drugs in the body. [15] Similarly, the increase of anesthetic dosage and anesthesia time will also lead to the above-mentioned outcomes. The patient's condition should be evaluated carefully before operation. Individual differences in sensitivity of different patients to anesthetics should be fully considered. The dosage of anesthetics should be calculated by referring to the time required for operation and combining the concentration of selected anesthetics and attenuation time in vivo. Therefore, clinical general anesthesia should take full account of its own situation, such as weak or thin people should be moderately less than the tall and strong people, and at the same time to ensure the anesthetic effect can reduce the amount of anesthetic drugs, and reasonable control of anesthesia time, reduce the occurrence of delayed recovery after general anesthesia surgery. Smoking and a history of lung disease often lead to pulmonary dysfunction in patients, leading to in vivo CO_2 accumulation, and causing hypercapnia, and CO_2 is easy to diffuse through the blood-brain barrier in the body fluid of brain cells, and acidosis can be caused in severe cases, thus inhibiting the nervous system. At the same time, smoking may also cause increased HbCO in the patient's blood, leading to a left shift in the dissociation curve of hemoglobin oxide, which eventually leads to a prolonged hypoxia in tissues and induces hypoxemia, which is usually the common cause of delayed recovery. [16] For patients who have long-term drinking behavior, alcohol will change into acetaldehyde through a series of reactions after entering hepatocytes. With the increase of acetaldehyde level, it will cause more serious toxic reactions to hepatocytes, eventually leading to cirrhosis and hepatocellular carcinoma. The damage of liver function will directly lead to the non-degradation of anesthetic drugs in vivo, while most anesthetic drugs can not be degraded in vivo. Drugs need to be decomposed in the liver. At the same time, liver dysfunction is often accompanied by multi-system diseases, such as hypoproteinemia, hepatic encephalopathy, and so on. Diseases of each system interact, which leads to prolongation of the efficacy of anesthetics and enhancement of their antagonism. [17] For patients with anemia symptoms, the decrease of Hb concentration in the body leads to the decrease of the binding rate of anesthetics to plasma protein to a certain extent and the increase of serum free drugs. Therefore, the concentration of anesthetics in blood of such patients will increase to a greater extent, so the duration of drug effect will be longer and eventually lead to the prolongation of recovery time after operation. We believe that in the clinical anesthesia treatment for patients with smoking, drinking history and anemia symptoms, it is necessary to clarify the patient's own situation, and reasonably determine whether they can undergo general anesthesia surgery. In the actual operation process, the vital signs of patients need to be closely monitored to prevent accidents.

To sum up, the risk of delayed recovery after general anesthesia surgery is mainly affected by the increase of patient's age, anesthesia time and intraoperative anesthetic dosage. In addition, the probability of delayed recovery in patients with smoking, drinking history and anemia symptoms will increase to a certain extent. Clinically, reasonable control measures should be formulated for patients with above-mentioned conditions to ensure the anesthetic effect. At the same time, it can improve the safety of surgical treatment, and then improve the outcome and prognosis of surgical treatment.

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