Propofol Target-controlled Infusion in Anesthesia Induction during Painless Gastroscopy

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ABSTRACT

Objective: To investigate the feasibility of using the eyelash reflex as an indicator to calculate the individualised optimal target concentration in anesthesia induction during painless gastroscopy.
Study Design: Experimental study.
Place and Duration of Study: China-Japan Union Hospital of Jilin University, China, from January to December in 2016.
Methodology: A total of 180 patients, who were scheduled to receive painless fibergastroscopic examination or treatment in the last three months, were enrolled in this study. All patients were randomly divided into three groups, according to the doctor visiting order (n=60, each). During the induction of anesthesia using propofol target-controlled infusion, the effect-site concentration upon the disappearance of the eyelash reflex (C0) was recorded first. Then, one μg/kg of fentanyl was injected. At the same time, the target effect-site concentration induced by propofol was determined: the effect-site concentration in group A was 1.5 times of C0, the effect-site concentration in group B was two times of C0, and the effect-site concentration in group C was 2.5 times of C0.
Results: During anesthesia induction, the incidence of motor responses was higher in group A than in groups B and C (p<0.05), and the incidence of hypoxemia was significantly higher in group C than in groups A and B (p<0.01).
Conclusion: In the anesthesia option of fentanyl combined with propofol target-controlled infusion, the effect-site concentration of propofol can be set to two times of that at the time the eyelash reflex disappears. This study provides a new pre-assessment method for the induction dose of propofol in painless gastroscopy.

Key Words: Propofol, Target-controlled infusion, Anesthesia induction, Eyelash reflex, Gastroscope.

INTRODUCTION

With the improvement in life expectancy and the progress of the healthcare industry in China, gastroscopy has become a routine method for upper digestive tract examination and treatment.[1] However, gastroscopy is usually performed only under superficial anesthesia. Endoscope directly stimulates the pharynx, the adverse stimuli and cardiovascular responses during the examination gives the subjects an unusual painful feeling and fear, and even induces more serious complications such as delayed operation, perforation of the esophagus, myocardial infarction and stroke.[1-3]

Patients have no painful memory and good tolerance during painless gastroscopy, and the doctors can also leisurely, carefully and thoroughly complete the operation. Painless gastroscopy has been gradually accepted by both doctors and patients, and also enables long-time, high risk gastroscopic treatment. Propofol has the characteristics of rapid onset of effect, short action time

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and rapid clearance, and is the first choice of drug for endoscopy.[3-6] However, it has strong inhibitive effects on circulation and respiration, and may decrease blood pressure and induce apnea when severe.[3,7,8] The target-controlled infusion (TCI) of propofol is an intelligent infusion system that can well-maintain the stability of the effect-site concentration of the drug, making the anesthesia process more stable.[7] However, determining the individualized target concentration is an urgent clinical problem that needs to be solved.[7,9,10] In a previous clinical study, a close correlation between the disappearance of the eyelash reflex and the effect-site concentration was found upon insertion of the gastroscope into the pharynx.[11]

Therefore, this study mainly aimed to observe the correlation between the disappearance of the eyelash reflex and the gastroscopic operation during anesthesia induction in painless gastroscopy, and explore the rapid individualised assessment of the dose of propofol, as well as the clinical feasibility of its corresponding anesthetic scheme.

METHODOLOGY

This experimental study was approved by China-Japan Union Hospital of Jilin University Institutional Review Board and written informed consent was obtained from all participating subjects.

A total of 180 patients with American Society of Anesthesiologists (ASA) I-II, who were scheduled to receive painless fibergastroscopic diagnosis or treatment in

the Endoscopy Examination Center of the hospital from January to December in 2016, were included in the present study. These patients had no history of respiratory, circulatory, nervous system, liver, or metabolic diseases. Patients who were overweight (BMI >25 Kg/m2), or with syntexis (BMI <18 Kg/m2), snoring, smoking, and histories of thoracic and abdominal surgery in the past three months, were excluded. All patients were randomly divided into three groups according to the doctor visiting order (n=60, each). Anesthesia was induced using propofol target-controlled infusion. The effect-site concentration upon the insertion of the gastroscope was respectively set as 1.5 times (group A), two times (group B) and 2.5 times (group C) of the effect-site concentration upon the disappearance of the patient's eyelash reflex.

Routine preoperative preparation was carried out. In the waiting room, the vein of the patient was opened and approximately 3 ml/Kg of fluid was infused. Prior to anesthesia, 3mL 2% lidocaine was sublingually administered for 10 minutes, which was swallowed five minutes later. The patient was laid on the examining table on the left side, and was given pure oxygen using a mask for three minutes. Electrocardiogram (ECG), blood pressure, and pulse oxygen saturation (SpO_2) were monitored. A target-controlled intravenous infusion pump was used. According to the age, height and weight of the patient, the target-controlled concentration was set at 4.0 μg/ml in advance for anesthesia induction. Then, propofol was infused. The effect-site concentration at the time of the patient's eyelash reflex (C0) was recorded, and 1 μg/Kg of fentanyl was intravenously infused upon the disappearance of the eyelash reflex. Next, the target effect-site concentration was adjusted to 1.5 times (group A), two times (B) and 2.5 times (group C) of C0, in order to handle the gastroscope through the pharynx of the patient. The intraoperative concentration was maintained at 1.5 times of C0, and fentanyl was stopped when the gastroscope was withdrawn.

When mean arterial pressure (MAP) was <80 mmHg during the operation, 5-10 mg of ephedrine was intravenously injected. When heart rate was <45 bpm, 0.5 mg of atropine was intravenously injected. When the SpO_2 was <90%, auxiliary respiration was performed by pressing the chest. When severe hypoxemia (SpO_2 <85%) occurred, the gastroscope was immediately withdrawn, and positive pressure-assisted ventilation was given through the mask. When motor responses occurred, the operation was stopped, and the propofol effect-site concentration was increased by 0.5 μg/mL. After waking up, the patient was sent to the observation room and waited for 30 minutes. If no discomfort manifested, the patient was discharged from the hospital, and the family members of the patient were informed that the patient should be accompanied for two hours.

The frequency and amplitude of respiration, heart rate, SpO_2 and MAP were observed and recorded. Furthermore, the frequency of hypotension and bradycardia, the use frequency of ephedrine and atropine, motor responses (frowning, shaking, inversing, choking, limb movement, etc.), the frequency of hypoxemia, and awakening time (set as the time from stopping the propofol pump to eye opening time) were recorded.

Measurement data were expressed as mean ± standard deviation (χ ± SD), and count data were expressed as a frenquency along with percentages. All experimental data were processed using statistical software SPSS 13.0, and compared using t-test and ANOVA for the measurement data or χ^2-test for the frenquency data. P<0.05 was considered statistically significant.

RESULTS

The age of these patients ranged from 20 to 60 years. Differences in gender, age, body mass index (BMI) and operation time between the three groups were not statistically significant (0.648, 0.262, 0.009 and 0.643, respectively, Table I), and the difference in BMI may be due to the large sample number in this clinic trial.

Before anesthesia, the differences in MAP, heart rate and SpO2 among the three groups were not statistically different (0.374, <0.001 and 0.980, respectively, Table II). During the induction and maintenance of anesthesia, the lowest MAP, heart rate and S_pO_2 in group A were

Table I: Demographic data in three groups (±s).

	Group			p-value	P B-C
	A	B	C		
Sex (female / male)	33/27	26/34	31/29	0.648	
Age (Y)	45.8 ±3.2	46.8 ±3.2	46.1 ±3.9	0.262	
BMI (kg/m2)	22.1 ±1.9	22.4 ±1.8	21.4 ±1.8**	0.009	0.002
Surgery time (min)	20.9 ±3.6	21.2 ±3.2	21.4 ±2.3	0.643	

*p<0.05, **p<0.01 compared with Group B.   BMI: Body mass index.

Table II: Preoperative and perioperative minimum hemodynamic parameters in three groups (±s).

Group	MBp (mmHg)		HR (bpm)		SpO2 (%)	
	Preoperative	Minimum	Preoperative	Minimum	Preoperative	Minimum
A	113.0 ±13.3	112.4 ±13.7**	76.3 ±3.3*	80.6 ±6.9**	97.2 ±1.3	96.8 ±2.1
B	112.3 ±11.2	105.5 ±8.1	78.4 ±5.4	75.7 ±4.3	97.2 ±1.5	96.5 ±1.7
C	115.4 ±12.4	90.6 ±6.4**	79.1 ±2.6**	68.2 ±5.1**	97.2 ±1.8	93.1 ±1.1**
p-value	0.374	0.000	<0.001	<0.001	0.980	<0.001
P A-B		0.001		0.006	<0.001	0.472
P B-C	<0.001		<0.001		<0.001	<0.001

*p<0.05, **p<0.01 compared with Group B.

Table III: Complications during anesthesia (n (%), $\chi \pm s$).

Group	Body movement	Hypoxemia	Awakening time (min)
A	18 (30)*	1 (1.7)	3.32 ±1.32
B	5 (8.3)	1 (1.7)	3.28 ±1.44
C	3 (5)	11 (18.3)*	3.40 ±1.46
p-value	<0.001	<0.001	0.897
P A-B	0.007	0.999	
P B-C	0.480	0.004	

*p<0.05, **p<0.01 compared with Group B.

significantly different, when compared with those in the other two groups (<0.05, Table II).

During the gastroscopic operation, motor responses were significantly higher in group A (18/60, 30%) than in group B (3/60, 5%, 0.007). Furthermore, the incidence of hypoxemia was significantly higher in group C (11/60, 18.3%) than in group B (1/60, 1.7%, 0.004). No severe hypotension and bradycardia occurred in all three groups. After insertion of the gastroscope, differences in the incidence of motor responses and hypoxemia, and awakening time among the three groups were not statistically significant (Table III).

DISCUSSION

This study revealed that when the initial target-controlled concentration of propofol was set at twice the corresponding effect-site concentration upon the disappearance of the eyelash reflex so that meet the clinical needs of the vast majority of patients. Furthermore, this anesthetic option reduces the complications of anesthesia, the failure rate for inserting the gastroscope due to severe motor responses, and the interruption rate of gastroscopy due to respiratory depression and hypoxemia, improves the safety of individualised medication, and ensures the safety and comfort of painless gastroscopy.

Propofol has superior pharmacological properties,[3] such predictable recovery and few postoperative side-effects, so it has been widely used in the outpatient department and short-time surgery.[4,6,12] However, propofol has a strong circulatory and respiratory inhibition in the traditional manners of administration,[4,5,13] including single intravenous infusion and continuous intravenous infusion. This would increase the incidence of adverse events in high risk patients, such as elderly and obese patients.[10,14-16] Therefore, the effect-site target-controlled propofol infusion gradually became the first choice for anesthesia.[3,17] During general anesthesia with intra-venous target-controlled infusion of propofol, patients have great individualised differences, and anesthesio-logists need to predict the target concen-tration of patients, according to monitoring indexes and clinical indications.[14,17] Although, closed-loop anesthesia (CLAN) systems have been used in which the infusion of propofol is regulated by the BIS. However, the bispectral index (BIS) and other clinical monitoring indexes have limitations in monitoring anesthesia depth and estimating

the appropriate dose of drugs.[5,18,19] Also, the expensive equipment and cumbersome operation limits its application in painless microscopic examination. Furthermore, the effect-site concentration of propofol anesthesia was the average estimated value in a population,[20] not the real individualised medication, and cannot change the depth of anesthesia corresponding to the stimulus intensity.[21] Hence, this anesthetic option urgently needs to be improved for clinical applications.[10]

Previous studies have confirmed that the anesthesia depth required for painless aneasthesia is closely correlated to the time when a patient's eyelash reflex disappears.[11] The present study revealed that there is a close correlation between the effect-site concentration of propofol upon the disappearance of the patient's consciousness (the time when the patient's eyelash reflex disappeared) and the anesthesia depth needed at the beginning of gastroscopy.[11,22] That is, with the effect-site concentration upon the disappearance of the eyelash reflex as the baseline, the target concentration during the maintenance period was set at 1.5 times, and the pump was stopped at the ending of the gastroscopy.

In the present study, patients' motor responses, including limb movements, head shaking, inversing, choking cough and frowning, were significantly higher in Group A. These results revealed that the depth of anesthesia in Group A was slightly inadequate because adverse stress response could not be effectively inhibited. However, MAP, heart rate and SpO_2 were significantly lower in Group C than that in Group A and Group B and before anesthesia. The higher incidence of hypoxemia revealed that the anesthetic was overdose, and respiratory depression and fatal overdose must be viligant. The maintenance effect-site concentration in all patients was set to 1.5 times of the effect-site concentration upon the disappearance of the patient's eyelash reflex, and the effect was satisfactory.

In the present study, due to the limitations of conditions in the examination room of the Endoscopic Examination Center, the depth of anesthesia was not monitored by the BIS monitoring system. Further, comparative studies will be carried out as the next step.

CONCLUSION

In the compound medication of propofol and fentanyl with target-controlled infusion technology, when the effect-site concentration of propofol was set at two times of that upon the disappearance of patient's eyelash reflex at the time of insertion of the gastroscope, this was able to effectively control adverse reflexes, and prevent the extension of awakening time, leading to a satisfactory anesthesia effect. This study provides a new pre-assessment method for the induction dose of propofol in painless gastroscopy, which can be used as reference by clinical medical staff, including those in primary hospitals.

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