The Application of Target-Controlled Sevoflurane Anesthesia after Saturation

Zhiyang Chen[1,2]*

[1]Department of Anaesthesiology, Fudan University Shanghai Cancer Center, China

[2]Department of Oncology, Fudan University, China

Abstract

Objectives: To achieve two targets Fet of Sevoflurane, 1.8% vol and 2.2% vol, which were fulfilled as quickly as possible in the wash in stage and stabilized on the levels all the time during the operations?

Methods: This randomized prospective study included 330 consecutive patients. The breath parameters on the anesthesia machine were set before the ventilation: TV=10 ml/kg, I:E=1:1.5, RR=15 BPM, FGF=MV. FD was set to 2.2% vol (group A) and 2.6% vol (group B) respectively. After the ventilation, the FI would reach to FD at first, and then the Fet would reach to the maximums (Group A, 1.8% vol, Group B, 2.2% vol) and stabilized on the levels. 5 minutes later again, TV was decreased to 6 ml/kg, RR was decreased to 10 BPM, a new FGF which was also equal to the new MV was set in group A and a new FGF which was equal to 50% of the new MV was set in group B, the Fet was recorded every 10 minutes in 0 min to 60 min since then. t test was used to compared the differences between the Fet at all of the time points and the expected Fet (1.8% vol, 2.2% vol) in the two groups.

Results: There were no differences between the expected target Fet and the Fet at all of the time points in the two groups.

Conclusions: By means of the settings, two targets Fet were achieved.

Correspondence:
Zhiyang Chen, Department of Anaesthesiology, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, 270 Dongan Road, Xuhui District, Shanghai 200032, China, Tel: 0086-18918818399; Fax: 0086-021-24206652;
E-mail: chzhygg@sina.cn

Introduction

In clinical practice, Target-Controlled Intravenous Infusion Anesthesia (TCI), especially the target-controlled self-regulating closed-circuit infusion anesthesias have been used for many years. But their main weakness is that the actual blood concentration of the intravenous anesthetics which are employed can't be monitored continuously. And the stable and exact target concentration can't be acquired easily for the reasons of the patient's individual difference in liver and kidney function, obesity index and so on. So the anesthesia depth of TCI anesthesia patients may be not stable during the whole surgery.

With the popularity of the monitors with Fet (Fraction of End-Tidal Anesthetics) monitoring in anesthesia, it is easy to monitor continuously the concentration of inhalational anesthetics in blood during the whole surgery. This is helpful for the developing of target-controlled inhalation anesthesia. Unfortunately, no guidelines for this have been published by now. Nevertheless, the target-controlled self-regulating closed-circuit inhalational anesthesia has been used for a long time [1-2]. The target-controlled self-regulating closed-circuit system increases subsequently the Fraction of Delivered (FD) anesthetics to answer [3-5] when the patients can sense pain or other discomforts which are expressed by the fluctuation of the indexes reflecting the depth of the general anesthesia on the monitor during surgery. Because the absorbing velocity of inhalational anesthetics which are inhaled and diffused with the tidal breath is slow as compared with that of the intravenous anesthetics which their whole dosage can be injected into blood in several seconds, the fraction of the anesthetics in brain may not be lifted in time in respond to the changes of the indexes on the monitor. So the most important problem of this method is that the insufficient depth of general anesthesia may exist during the whole surgery.

In order to avoid the emerging of the insufficient depth of general anesthesia, considering the pharmaceutical features of the inhalational anesthetics which are employed, it is necessary to establish a saturation state with sufficient and constant fraction of the anesthetics in brain which is usually considered as being reflected by Fet. Based on the theory of establishing the saturation

Table 1: General demographic characteristics of patients scheduled to undergo surgery, randomized to one of the two groups.

Groups (cases)	Age, years	Body weight, kg	sex	
			Male	Female
A (150)	55.17 ± 11.39	54.20 ± 5.83	26	124
B (180)	48.95 ± 7.16	53.26 ± 9.79	58	122

Data presented as mean ± SD.

state of Sevoflurane anesthesia [6-7], a method of acquiring target Fet of Sevoflurane as needed had been investigated by means of setting FD and the breath parameters on the anesthesia machine, and the target Fet could be achieved as quickly as possible and stabilized on the levels all the time during the whole surgery.

Patients and Methods

This randomized prospective study included 330 consecutive patients with breast cancer or thyroid gland tumours, who were scheduled to undergo surgery under combined intravenous and inhalation anesthesia at the Department of Anesthesiology, Cancer Hospital, between May 2011 and December 2014 (Table 1). They were divided randomly into 2 groups (groups A, B). All patients were categorized as ASA physical status 1-2. Ethical approval was provided by The Ethics Committee of Cancer Hospital, Fudan University (1501146-4-NSFC) and registered (http://www.chictr.org/cn, ChiCTR-IOR-15006010). Written informed consent was obtained from all study participants. The general material of the A Dräger Fabius Tiro° (Dräger) anesthesia machine with Baxter sevoflurane (Baxter) and a Dräger vaporizer (Vapor 2000; Dräger) were employed for mechanical ventilation. A GE S/5 monitor (Baxter) was used to monitor FI and Fet in the tracheal catheter adapter. After anesthesia was induced with midazolam (0.04 mg/kg to 0.06 mg/kg), propofol (1.5 mg/kg), fentanyl (2 mg/kg to 3 mg/kg) and rocuronium (0.6 mg/kg to 0.8 mg/kg), all patients underwent tracheal intubation and inhaled Sevoflurane (dose adjusted based on study protocol) and combined with fentanyl injected intravenously to maintain the depth of general anesthesia.

In the two groups, it was expected to acquire two target Fet of Sevoflurane, 1.8% vol (1 MAC, groups A) and 2.2% vol (1.3 MAC, groups B) respectively. The breath parameters on the anesthesia machine were set before the ventilation: TV (Tidal Volume)=10 ml/kg, I:E (Inhalational time to Exhalant time)=1:1.5, RR (Respiratory Rate)=15 BPM (Breath Per Minute), FGF (the Fresh Gas Flow)=MV (Minute Volume). FD was set to 2.2% vol (group A) and 2.6% vol (group B) respectively considering Fet =FI-0.4 when Sevoflurane anesthesia is in saturation state [6-7].

After the ventilation, the Fraction of Inhaled (FI) Sevoflurane would reach to FD at first, then the Fet would reach to its maximum (Group A, 1.8% vol, Group B, 2.2% vol) and stabilized on the levels. 5 minutes later again, the concentration of Sevoflurane in brain would reach its maximum; a saturation state associated with this FD would be acquired. TV was decreased to 6 ml/kg, RR was decreased to 10 BPM, a new FGF which was also equal to the new MV was set in group A and a new FGF which was equal to 50% of the new MV

was set in group B. From this time on, the Fet in the two groups was recorded every 10 minutes in 0 min to 60 min.

Statistics

T test was used to compared the differences between the Fet at all of the time points and the expected target Fet (1.8% vol, 2.2% vol), P-value <0.05 was considered statistically significant and P<0.01 highly significant.

Results

In the two groups, FI had reached to FD in 3 minutes to 5 minutes after the ventilation, and Fet had reached to the maximums (1.8% vol or 2.2% vol, the expected target Fet) and stabilized on these levels in 6 minutes to 9 minutes, 5 minutes later again, two saturation states of Sevoflurane were acquired. There were no differences between the Fet at all of the time points and the expected target Fet. By means of the setting, the Fet of the two groups had stabilized on the levels as expected, two stabilized target Fet were achieved (Table 2).

Discussion

In the clinical practice, Sevoflurane anesthesia is usually employed to maintain the depth of general anesthesia in patients who have been tracheal intubated after being induced quickly under intravenous anesthesia. If a high FD and a high FGF are employed in these patients as recommended in awake patients who are induced to be tracheal intubated with Sevoflurane [8-10], the patients' circulation collapse may occur. This is for the reason that too much Sevoflurane is inhaled into the patients' body in short time and high dosage of intravenous anesthetics have just been injected into the patients' body after the tracheal intubation, which lead to a excessive depth of anesthesia. And what is more that many of our anesthesiologists would have to decrease the FD to answer in this circumstances, and then the depth of anesthesia would go shallow in several minutes later and could not meet the need of surgery as a result.

Some of the intravenous anesthetics, such as propofol, which have been injected into the patients' blood before the tracheal intubation, will be eliminated in several minutes after the tracheal intubation, so it is primary important that an enough Fet of Sevoflurane which is usually considered as reflecting an enough depth of general anesthesia must be reached as quickly as possible in the wash in stage to meet the need of surgery. Moreover, the Fet must be constant in the maintaining stage in order to achieve a constant depth of anesthesia. This enough and constant Fet may be the target Fet which is expected to reach. Then the challenge for us is how can we acquire and maintain this target Fet of Sevoflurane.

It is widely recognized that a sufficient depth of general anaesthesia can be acquired by increasing Fet to the needed concentration according to the MAC of the anaesthetics which are employed. The absorbing and diffusing of sevoflurane are related to MV, FGF/MV, inhalational time in a breath cycle which is determined by I:E, RR, the patient's functionality of the respiratory and cardiovascular systems, body temperature, atmospheric pressure, and so on. The depth of sevoflurane inhalational anaesthesia is related to the fractional

Table 2: The Fet at all of the time points in the two groups.

Group	Target Fet (vol %)	0 (min)	10 (min)	20 (min)	30 (min)	40 (min)	50 (min)	60 (min)
A	1.8	1.81 ± 0.21	1.83 ± 0.13	1.83 ± 0.01	1.85 ± 0.07	1.86 ± 0.11	1.86 ± 0.29	1.88 ± 0.21
B	2.2	2.23 ± 0.11	2.15 ± 0.34	2.11 ± 0.17	2.10 ± 0.35	2.11 ± 0.21	2.11 ± 0.18	2.11 ± 0.29

Data presented as mean ± SD. As compared with the target Fet, ˙means P<0.05, ᐃ means P<0.01.

concentration in brain tissue, which is considered as being reflected by the fractional concentration in venous blood and Fet. The whole procedure of sevoflurane anesthesia can be devided into three stages, the washin stage, the maintaining stage and the eliminating stage. In the washin stage, the first step is to promote FI up to the FD which is set in advance, because the fractional concentration of sevoflurane in pulmonary alveoli, arteries, veins, and tissues and Fet are positively related to FI and will increase following the increasing of FI. When FGF=MV, FI will go up to and stabilize on FD because the exhaled TV in which there is lower fractional concentration of sevoflurane does not join the next inhaled TV after the circuit is filled with the sevoflurane gas with the fractional concentration of FD. At the same time, a higher MV and a higher RR are helpful to the more absorbing and diffusing of sevoflurane. After the patients have been inhaling this constant FI of sevoflurane for some time, Fet on the monitor will go up to and stabilized on a relative maximum value. In the maintaining stage, Fet can be constant if FGF=MV, and even a lower FGF is given after saturation [11]. Only by this means can we acquire saturation 1state as quickly as possible. This is the basis of target-controlled sevoflurane inhalational anesthesia after saturation.

In our routine clinical anesthesia, it is often employed that the Fet of sevoflurane is lifted up to 1 MAC and 1.3 MAC. What is expected is that the Fet can reach to the target numerical value as soon as possible and stabilized on this level during the whole surgery, which is associated with a enough and constant anesthesia depth. As you can see from the results of Table 2, a relative constant target Fet could be acquired in the two groups, target-controlled sevoflurane inhalational anesthesia after saturation could be fulfilled.

At the washin stage of sevoflurane anesthesia in this investigation, TV was set as 10 ml/kg, RR as 15 BPM, FGF=MV, this is for the reason that high ventilation could carry out the rapid absorbing and diffusing of sevoflurane, which can establish the saturation state as soon as possible. In the maintaining stage after saturation, TV was decreased to 6 ml/kg, RR to 10 BPM, FGF=MV (group A), and even FGF was also be decreased to 50% MV (group B) in order not to waste too much of sevoflurane, we have not employ very low FGF for fear the toxicity of the compound A which is the degeneration products of sevoflurane [11-16].

And it is very important that the FGF can be decreased only in 5 minutes since the Fet has reached its maximum, because there is a lot of arteriovenous shunts in human body, some of sevoflurane in arteries can get into veins directly through these arteriovenous shunts in the washin stage, this part of sevoflurane forms the false Fet which can not reflect the real depth of general anesthesia [10]. So Fet may reach to the maximum earlier than the Fb. 5 minutes after the Fet has reached its maximum, the absorbing and diffusing of sevoflurane in brain may be in saturation. Clearly, the saturation state cannot be broken if the low MV (FGF=MV) are set, and even FGF=50% MV [10].

Although this application of target-controlled sevoflirane inhalational anesthesia can make a fast, constant and accurate Fet as needed, its main flaw is that sevoflurane can effect perfectly in 10 minutes to 12 minutes after the ventilation when the saturation of the absorbing and diffusing of sevoflurane in brain is acquired. If the surgery need to be begun too early, additional intravenous anesthetics are needed.

Conclusions

By means of the settings, the Fet of the two groups had stabilized on the levels as expected, two stabilized target Fet were achieved.

References

1. Nathan N, Sperandio M, Erdmann W, Westerkamp B, Van Dijk G, Scherpereel P, et al. [PhysioFlex: a target-controlled self-regulating closed-circuit inhalation anesthesia regulator]. Ann Fr Anesth Reanim. 1997;16(5):534-40.

2. Verkaaik AP, Van Dijk G. High flow closed circuit anaesthesia. Anaesth Intensive Care. 1994;22(4):426-34.

3. Meyer JU, Kullik G, Wruck N, Kück K, Manigel J. Advanced technologies and devices for inhalational anesthetic drug dosing. Handb Exp Pharmacol. 2008;(182):451-70.

4. Fritsch N, Nouette-Gaulain K, Bordes M, Semjen F, Meymat Y, Cros AM. Target-controlled inhalation induction with sevoflurane in children: a prospective pilot study. Paediatr Anaesth. 2009;19(2):126-32.

5. Nouette-Gaulain K, Lemoine P, Cros AM, Sztark F. [Induction of anaesthesia with target-controlled inhalation of sevoflurane in adults with the ZEUS anaesthesia machine]. Ann Fr Anesth Reanim. 2005;24(7):802-6.

6. Chen Z-Y. Analysis on the difficulties of clinical anesthesia. Beijing: People's Health Publishing House. 2010;72-7.

7. Zhi-Yang Chen. Establishing the relationship between FGF/MV and FI/FD, and determining the saturation state of sevoflurane anesthesia during the induction phase and factors affecting nonrespiratory tract ejection volume. Journal of International Medical Research. 2013;41(3):785-94.

8. Sloan MH, Conard PF, Karsunky PK, Gross JB. Sevoflurane versus isoflurane: induction and recovery characteristics with single-breath inhaled inductions of anesthesia. Anesth Analg. 1996;82(3):528-32.

9. Levine, Wilton C, Allain Rae M, Alston Theodore A. Clinical Anesthesia Procedures of the Massachusetts General Hospital [M]. 2008;200-01.

10. Lin TC, Lu CC, Li CY, Chang CC, Ho ST. Arterial blood concentration of sevoflurane during single-breath induction and tracheal intubation in gynecologic patients. J Clin Anesth. 2008;20(7):496-500.

11. ZHU Yun, CHEN Zhiyang. The feasibility of low fresh gas flow following saturation of sevoflurane anesthesia. Fudan university journal of medical sciences. 2014;41(3):380-3.

12. Brattwall M, Warrén-Stomberg M, Hesselvik F, Jakobsson J. Brief review: theory and practice of minimal fresh gas flow anesthesia. Can J Anaesth. 2012;59(8):785-97.

13. Di Filippo A, Marini F, Pacenti M, Dugheri S, Focardi L, Novelli GP. Sevoflurane low-flow anesthesia: best strategy to reduce Compound A concentration. Acta Anaesthesiol Scand. 2002;46(8):1017-20.

14. Osafumi Yuge. Renal toxicity of compound A with sevoflurane anesthesia: The benefits of sevoflurane appear to outweigh the risks. J Anesthesia. 1997;11(1):1-2.

15. Faizov II, Levshankov AI, Shchegolev AV, Elizarov AIu. Mass-spectrometric control of compound A during minimal flow anesthesia and its influence on liver and kidneys functions. Anesteziol Reanimatol. 2013;(4):14-8.

16. Wang F, Polavarapu PL, Schurig V, Schmidt R. Chirality. Absolute configuration and conformational analysis of a degradation product of inhalation anesthetic Sevoflurane: A vibrational circular dichroism study. Chirality. 2002;14(8):618-24.