Feasibility analysis TCI etomidate perioperative adrenal function in elderly patient's anesthesia in elderly.

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Abstract

Objective: Feasibility analysis TCI etomidate elderly patients perioperative adrenal function in elderly anesthesia.

Methods: 60 patients undergoing general anesthesia patients were randomly divided into two groups figure that etomidate group and propofol group. All patients were using target-controlled infusion of intravenous anesthesia drugs, for two groups of patients after induction of anesthesia whichever venous blood samples. Until the patient is conscious, breathing normally pulls out after the endotracheal tube. Routine testing and record the ECG, heart rate, noninvasive blood pressure and transcutaneous oxygen saturation changes in two groups of patients; respectively before anesthesia (T0), after anesthesia (T1), before surgery, after surgery 24 h (T2-T4) five time points blood 3 ml, measured in patients with venous blood plasma cortisol, and the use of immunosuppressive biochemical reagents and electrochemical methods of measurement; the two groups were recorded during anesthesia and intensive care unit of adverse reactions.

Results: Compared with T0, two groups of serum cortisol levels in the process of induction of anesthesia and anesthesia are there different degrees lower, but are within the normal range, in which the lowest blood cortisol levels in patients with T3 moment, the difference statistically significant (P<0.05), while the content of other moments, although low, but there was no significant difference (P difference>0.05). Propofol group of patients with systolic blood pressure, diastolic blood pressure and heart rate were to be dropped after anesthesia, and the difference was statistically significant (P<0.05); etomidate group of patients with systolic blood pressure showed a tendency to gradually reduce its diastolic blood pressure at each time point was no statistical difference (P>0.05); and SPO₂ value anesthesia before the period was significantly increased compared with anesthesia, the difference was statistically significant (P<0.05). Two groups of patients with only a few patients during surgery side effects occur nausea, vomiting, etc., but its incidence were compared and found no statistically significant difference (P>0.05), but the two groups are present in 1 patient symptoms of sleepiness, both compared to extubation was no significant difference (P>0.05); there were no cases of the patients had intraoperative awareness.

Conclusions: TCI etomidate and propofol emulsion can better inhibit perioperative stress response, and the control in the normal range, and within 24 h after recovery to normal levels.

Keywords: Target-controlled infusion, Etomidate, Propofol, Cortisol, Hemodynamic.

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Introduction

With unceasing progress of human society, the human's lifespan prolongs continuously, resulting in growing ratio of elderly patients [1,2]. Partly estimated [3-5], people over 60 y in China have accounted to 8.65% of population. As a special group, because their organs degenerate in different extent with increasing age, the elderly patients may suffer some diseases which adds the perioperative risk, so the anesthesia for them is essential during this period [6]. Etomidate, an artificial derivative of imidazole, has a short-acting somnolent effect. Given it cannot relieve patients' pain during operation, etomidate should be used in combination with analgesic [7-9]. This study is to explore the effect of etomidate emulsion and propofol on perioperative adrenal cortical function of the elderly and to analyse its feasibility on the elderly anesthesia through clinical observations on the change of patients' cortisol and hemodynamics during perioperative period.

Materials and Methods

General materials

A total of 60 elderly patients who underwent selective general anesthesia with tracheal intubation admitted from May 2015 to May 2016 in our hospital were enrolled, 38 male, 22 female, aged from 65 to 82, $(72.84 \pm 5.74 \text{ y})$ in average. If the patients were classified as the grades I and II according to the classification on patients' physique and operative risk before surgery of American Society of Anesthesiologists (ASA), if their weight wasn't lower or higher 20% than standard body weight, and if their perioperative mortality was less than 0.40%, they would be eligible for this study. While if patients suffered evident heart and lung dysfunction, if they had severe kidney and liver dysfunction and metabolic diseases, if their fasting blood glucose was 6.0 mmol/L before operation or they had electrolyte disturbances or severe shock, and if they were allergic to emulsion or received hormone therapy, they would be ineligible. There were 12 cases with esophageal cancer, 10 lung cancer, 8 liver cancer, 14 cervical cancer, and 16 thyroid cancer in the study. 60 selective surgical patients with general anesthesia were assigned into two groups by random-digit dialling, namely etomidate group (E group) and propofol group (P group), with all of them or their families gave written informed consent made by the society for the study of medical ethics of our hospital before treatment.

Medicines

Etomidate fat emulsion injections (Fu Erli) were provided by Jiangsu Nhwa Phama. Corporation, China, approval number: guo yao zhun zi H20020511, Specifications: 10 ml: 20 mg. Propofol injections were supplied by Xi'an Libang Pharmaceutical Co., Ltd., China, approval number: guo yao zhun zi H19990281, Specifications: 10 ml: 200 mg. Phenobarbital sodium injections were offered by Jiangsu Nhwa Phama. Corporation, approval number: guo yao zhun zi H20020511, specifications: 10 ml: 20 mg. Scopolamine injections were supplied by Jiangsu Nhwa Phama. Corporation, approval number: guo yao zhun zi H20020511, specifications: 10 ml: 20 mg. Midazolam injections were provided by Jiangsu Nhwa Phama. Corporation, approval number: guo yao zhun zi H20020511, specifications: 10 ml: 20 mg. While immunobiochemical reagents were offered by Roche, America.

TCT-III bichannel target-controlled infusion pumps were provided by Wuhang Changfeng Medical Instrument Co., Ltd., China, the anesthetic machine was supplied by Beijing Readegal Technology Co., Ltd., China, type: 011, the multifunctional and combined monitors were provided by Heilongjiang Huaxiang Technology Development Co. Ltd., China, and the medium laryngoscope was supplied by Taixing Mester Medical Equipment Co., China.

Methods

60 selective surgical patients with general anesthesia were split up into two groups by random-digit dialing, namely etomidate group and propofol group, and received intramuscular injection of phenobarbital and scopolamine before operation. Mechanical ventilation was performed after trachea incubation, with setting tidal volume to 6-8 ml/kg, respiratory rate at 12-16 bpm, inspiratory/expiratory ratio at 1:2, maintaining end-tidal CO₂ between 35 and 45 mmHg. Both groups were given anesthesia drugs intravenously by target-controlled infusion pumps. In etomidate group, the pharmacokinetic parameter of target-controlled infused etomidate adopted model Arden, and that of remifentanil applied model Minto, and that of vecuronium used model Marche, while in propofol group, the pharmacokinetic parameters of all drugs apart from propofol which adopted model Marsh used same parameters with etomidate group. All patients in both groups were infused remifentanil by means of target-controlled and given cisatracurium besylate by IV push intermittently to maintain their muscular relaxation and steady circulation during surgery [10-12]. All patients were collected venous blood samples after anesthesia induction and extubated when they woke up and got normal breathing.

Detection indexes

The change of ECG, heart rate, non-invasive blood pressure, and SpO_2 of patients in two groups were regularly detected and recorded. In order to test patients' plasma cortisol, each of them were collected 3 ml venous blood at five different times, including before anesthesia (T0), after anesthesia (T1), before operation (T2), during operation (T3), and 24 h after operation (T4), which were detected using immune-biochemical reagents and electrochemistry, of which manipulations were strictly under introductions. Adverse reactions of both groups, like fibrillation atrial, restlessness, cough, hypertension, and palpitation, appeared during anesthesia and in ICU, were recorded.

Statistical analysis

The data was analysed by software SPSS 17.0. Quantitative data was expressed as mean \pm SEM, and patients' data in two groups was analysed by either t-test or within-group repeated-measures ANOVA. The statistical difference was defined as P<0.05.

Results

Effect on the change of perioperative blood glucose, cortisol levels, and hemodynamic in two groups

Statistical outcomes were classified and analysed as follow. Compared with T0, the cortisol level of both groups during anesthesia induction and anesthesia procedure decreased in various degrees but was still normal, and that at T3 was lowest, with a statistical difference (P<0.05), and that at other times were lower, but without statistical difference (P>0.05). The systolic pressure, diastolic pressure, and heart rate of patients in propofol group all declined somewhat after anesthesia, having significant difference (P<0.05), and in etomidate group, the systolic pressure dropped gradually, and compared the

diastolic pressures at five times, the differences had no significance (P>0.05). And SPO_2 in two groups during

anesthesia raised much more than that before anesthesia, having statistical difference (P < 0.05, Table 1).

Table 1. Two groups of patients affected perioperative blood glucose, cortisol levels and hemodynamic changes.

Index	Group	t0	t1	t2	t3	t4
Cortisol (mol•L ⁻¹)	E	485.87 ± 198.24	455.78 ± 188.42	375.87 ± 158.24	235.57 ± 174.64 [*]	455.87 ± 198.24
	Р	532.97 ± 203.13	481.57 ± 165.64	450.35 ± 158.65	350.53 ± 68.29 [*]	545.96 ± 168.32
SBP (mmHg)	E	135.64 ± 17.54	125.44 ± 27.45▲	127.28 ± 22.63 [*] ▲	132.64 ± 24.45	115.34 ± 27.74 [*]
	Р	134.86 ± 16.97	104.68 ± 22.79 [*]	106.33 ± 12.26 [*]	129.34 ± 17.54	125.46 ± 24.13 [*]
DBP (mmHg)	E	81.76 ± 8.87	71.67 ± 18.85	77.62 ± 14.58	78.45 ± 5.74	$69.28 \pm 7.84^*$
	Р	82.83 ± 7.98	$67.38 \pm 7.48^*$	70.64 ± 13.45 [*]	$74.41 \pm 8.62^{*}$	77.62 ± 6.21
HR (bpm)	E	83.86 ± 6.35	88.45 ± 16.15▲	78.26 ± 12.11	80.54 ± 6.27	89.25 ± 13.07▲
	Р	80.45 ± 6.47	74.14 ± 9.26	74.22 ± 10.16 [*]	$72.24 \pm 4.26^{*}$	78.37 ± 10.15
SPO ₂ (%)	E	97.04 ± 1.87	99.13 ± 0.37*	99.73 ± 0.28 [*]	$99.43 \pm 0.65^{*}$	97.64 ± 1.36
	Р	97.22 ± 1.69	99.10 ± 0.28 [*]	99.13 ± 0.57 [*]	99.19 ± 0.45 [*]	97.85 ± 1.12

Analysis on patients' adverse reactions

Only a fraction of patients in two groups suffered side effects including nausea and vomiting during surgery, and compared their incidence, the difference had no significance (P>0.05), however, both groups had one patient with sleepiness after extubation, there was no statistic difference (P>0.05). Furthermore, no patients had intraoperative awareness after surgery (Table 2).

 Table 2. Postoperative adverse reactions (n, %).

Group	Nausea, vomiting	Restlessness after extubation	Sleepiness after extubation	Intraoperativ e awareness
Group E	4 (6.67%)	5 (8.33%)	1 (1.67%)	0 (0.00%)
Group P	4 (6.67%)	1 (1.67%)	1 (1.67%)	0 (0.00%)

Discussion

In recent years' clinical operations, general intravenous anesthesia has been widely applied for its advantages, such as giving drugs through vein instead of airway, reducing the contamination in operation room, and lowering patients' and doctors' discomfort. With the advance of science, technology, and anesthesia instrument, Target-Controlled Infusion (TCI) has brought into general anesthesia, providing probability on accurately controlling the depth of anesthesia, and it is increasingly used in clinical anesthesia for the elderly patients [13,14]. After analysed on operative risks of the elderly patients, it is known that age, whole physiology, emergency or selective surgery, and the type of operation are four major factors.

Most past general anesthesia might adopt etomidate emulsion and protofo to anaesthetize patients, nevertheless, for the elderly patients with special physique and worse tolerance, etomidate emulsion with better cardiovascular stability, during the surgery, has little effect in anesthesia because of its definite inhibition on patients' adrenocortical function. Some researches indicates [15-19] that, etomidate, only through general intravenous anesthesia, can consistently control patients to maintaining anesthesia secretor state for 24 h during perioperative period, which proves that this control only has chronergy.

In this study, compared with T0, the cortisol level of both groups during anesthesia induction and anesthesia procedure fall in various degrees but are still normal, and that at T3 is lowest, with a statistical difference (P<0.05), and that at other times are lower, but without statistical difference (P>0.05). The systolic pressure, diastolic pressure, and heart rate of patients in propofol group all drop somewhat after anesthesia, having significant difference (P<0.05), and in etomidate group, the systolic pressure reduces gradually, and compared the diastolic pressures at five times, the differences have no significance (P>0.05). And SPO₂ in two groups during anesthesia raises much more than that before anesthesia, having statistical difference (P<0.05). In a word, the inhibition on patients' adrenocortical function of these two anesthesia medicines used in TCI anesthesia during perioperative period is acceptable.

References

- Ray DC, Hay AW, McKown DW. Induction drug and outcome of patients admitted to the intensive care unit after emergency laparotomy. Eur J Anaesthesiol 2010; 27: 481-485.
- 2. Hildreth AN, Mejia VA, Maxwell RA. Adrenal suppression following a single dose of etomidate for rapid sequence

induction: a prospective randomized study. Trauma 2009; 65: 573-579.

- 3. Gagnon DJ, Seder DB. Etomidate in sepsis: understanding the dilemma. J Thorac Dis 2015; 7: 1699.
- Toklu S, Lyilikci L, Gonen C, Ciflei L.ComParison of etomidate-remifentani and Propofol-remifentani sedation in patients scheduled for colonoscopy. Eur J Anaesth 2009; 3: 12.
- Cardoso MA. Preoperative management with etomidate of hypercortisolim of metastatic ectopic cushings syndrome: Case Report. Endocrine Society's 97th Annual Meeting and Expo, March 5-8, San Diego 2015.
- Pagel PS, Hettrick DA, Kersten JR. Propofol, but not thiopentoneb or etomidate, enhances isoflurane - induced coronary vasodilatation in dogs. Can J Anaesth 1998; 45: 809-817.
- Strays MM, De STD. Comparison of plasma compartment versus two methods for effect compartment-controlled targeted-controlled infusion for propefol. An Esthesiol 2000, 92; 399-406.
- 8. Wagner RL, White PF. Etomidate inhibits adrenocortical function in surgical patients Anesthesiology 2014; 61: 647-651.
- 9. Ge Y, Grossman RJ, Babb JS. Age-related total gray matter and whitematter changes in mormal adult brain. Parti: Volumrtric MR imaging analysis. AJNR Am J Neuroradiol 2012; 23: 1327-1333.
- Xu C, Seubert C N, Gravenstein N. Propofol, but not etomidate, increases corticosterone levels and induces longterm alteration in hippocampal synaptic activity in neonatal rats. Neurosci Lett 2016; 618: 1-5.
- Cold GE, Eskesen V, Eriksen H. CBF and CMRO2 during continuous etomidate infusion supplemented with N2O and fentanyl in patients with supratentorial cerebral tumour. A dose-response study. Acta Anaesthesiologica Scandinavica 1985; 29: 490-494.

- Dong QL, Sheng ZM, Zhang J. Self-focusing and merging of two copropagating laser beams in underdense plasma. Phys Rev Stat Nonlin Soft Matt Phys 2002; 66: 027402.
- 13. Schenarts CL, Burton JH, Riker RR. Adrenocortical dysfunction following etomidate induction in emergency department patients. Acad Emerg Med Off J Soc Acad Emerg Med 2001; 8: 1-7.
- 14. Gagnon DJ, Seder DB. Etomidate in sepsis: understanding the dilemma. J Thorac Dis 2015; 7: 1699.
- 15. Newson C, Joshi GP, Victory R. Comparison of propofol administration techniques for sedation during monitored anesthesia care. Anesth Analg 1995; 81: 486-491.
- Rigby-Jones AE, Sneyd JR. Propofol and children-what we know and what we do not know. Paediatr Anaesth 2015; 21: 247-254.
- Radtke FM, Franck M, Hagemann L. Risk factors for inadequate emergence after anesthesia: emergence delirium and hypoactive emergence. Minerva Anestesiologica 2010; 76: 394-403.
- Zou Y, Moreel L, Lin H. Solution processing and resist-free nanoimprint fabrication of thin film chalcogenide glass devices: inorganic-organic hybrid photonic integration. Adv Opt Mater 2015; 2: 759-764.
- 19. Doenicke AW, Roizen MF, Hoernecke R. Solvent for etomidate may cause pain and adverse effects. Br J Anaesth 1999; 83: 464-466.

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