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Effect of 2 different anesthesia methods on stress response in neurosurgical patients with hypertension or normal

A prospective clinical trial

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Abstract

Hypertensive patients in neurosurgery are becoming more common, which increased the risk of surgical stress response. Meanwhile, the relationship between hypertension and anesthesia methods is unclear on the stress response. The purpose of this study is to compare the effect of different anesthesia methods on high-sensitivity C-reactive protein (Hs-CRP), blood glucose, and leucocyte levels in neurosurgical patients with hypertension or normal.

Eighty neurosurgical patients were randomly divided into 4 groups (n = 20): balanced anesthesia group (A), balanced anesthesia with hypertension group (B), total intravenous anesthesia group (C), total intravenous anesthesia with hypertension group (D). The levels of Hs-CRP, blood glucose, leucocyte count, and neutrophil percentage and were detected at before anesthesia (T0), during anesthesia (T1), 2 hours post anesthesia (T2), 24 hours post anesthesia (T3).

Patients with hypertension had higher Hs-CRP expression, blood glucose, and neutrophil percentage at time T0 than those of normal, but not leucocyte count. At time T3, patients with hypertension in D group had lower Hs-CRP expression than those in B group ($P < 0.01$). Patients with normal in C group had lower Hs-CRP expression ($P < 0.01$), blood glucose ($P < 0.05$), and leukocyte count ($P < 0.05$) than those in A group. Both hypertension history and anesthesia method had significant effects on the Hs-CRP expression, blood glucose, and leukocyte count.

Total intravenous anesthesia decreases Hs-CRP expressions more efficiently than balanced anesthesia in neurosurgical patients with hypertension or normal. Moreover, total intravenous anesthesia can availably reduce the perioperative stress response by attenuating the increase of blood glucose and leukocyte count in normal tensive patients.

Abbreviations: COR = cortisol, CPB = cardiopulmonary bypass, Hs-CRP = high-sensitivity C-reactive protein, IL-6 = interleukin-6, NE = norepinephrine.

Keywords: balanced anesthesia, Hs-CRP, hypertension, neurosurgery, total intravenous anesthesia

1. Introduction

With economic growth and the improvement of living, the prevalence of hypertension increases gradually in China.[1] More and more surgical patients have history of hypertension. Hypertension patients are often prone to concurrent brain, heart, kidneys, and other organ damages. Neurosurgery trauma, anesthesia, hypoxia, and pain can make the body produce the stress response,[2] so that the body produces severe metabolic and homeostasis disorders and immune suppression, leading to massive release of hormones and blood sugar into the blood, causing serious physiological dysfunction, inflammation, and proliferation.[3] However, hypertension is a special disease, especially in patients with long-term high blood pressure in which the body functions are degraded corresponding pathological changes, in particular dyfunctions of the cardiovascular system.[4,5] Therefore, hypertension patients are more likely to have strong stress response caused by injury of surgery operation compared with non-hypertension patients.

The anesthesia methods may have considerable influence on the surgical stress response and the postoperative immune response. Surgery-induced inflammatory response and alteration in cell-mediated immunity seem to be more pronounced after balanced anesthesia by enhancing stress response.[6] Correspondingly, with respect to limitation of surgery-associated stress, total intravenous anesthesia seems to have a favorable effect. The benefit of total intravenous anesthesia might contribute to the prevention of excessive postoperative inflammation.[7] These data suggest that reasonable anestheic managements may reduce surgical stress on body damage after operations.

Whether the stress response in hypertension patients will affect the effect of anesthesia is rarely reported in literature. For

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compared the different effects between balanced anesthesia and total intravenous anesthesia, high-sensitivity C-reactive protein (Hs-CRP), a marker of acute inflammatory response involved in local or systemic inflammatory reaction was detectived in the present study. Under the normal condition, the amount of Hs-CRP in the blood serum of healthy people is small. Hs-CRP concentration increasing dramatically might be a sensitive indicator of inflammation and tissue damage.[8,9] Our study investigates balanced anesthesia and total intravenous anesthesia effects on Hs-CRP, blood glucose and leucocyte levels in neurosurgical patients with or without hypertension.

2. Materials and methods

2.1. Subjects

Eighty elective neurosurgical patients aged 40 to 65 who underwent elective intracranial aneurysm surgery, sellar surgery, meningioma surgery, or cerebral decompression were chosen for this study. The patients with hypertension had been diagnosed with stage I hypertension for at least 1 year and the blood pressure was under control with medication. Hypertension patients had not taken any other medication that influenced the flow dynamics recently besides the hypertension drugs. The blood pressure of hypertension patients must be controlled at 140/90 mm Hg before the surgery and 180/110 mm Hg during the surgery. All patients who underwent elective neurosurgery, used general anesthesia for endotracheal intubation. Eighty patients were randomly divided into 2 anesthesia methods according to the history of hypertension. Four groups were formed: balanced anesthesia group (A), balanced anesthesia with hypertension group (B), total intravenous anesthesia group (C) and total intravenous anesthesia with hypertension group (D). Patients with endocrine system disease, respiratory system disease, serious cardiovascular disease, liver and kidney dysfunction, obesity, and cachexia were excluded. Patients couldn't have history of drug or alcohol addiction and psychiatric disorders either. All patients informed consent to the study as approved by the Ethics Committee of the First People's Hospital of Lianyungang. The process was conducted in accordance with the Declaration of Helsinki and good clinical practice.

2.2. Anesthesia

After the patient's arrival in the operating room, the venous infusion pathway was established, 30 minutes before anesthesia phenobarbital sodium injection 0.02 mg/kg, atropine 0.007 to 0.01 mg/kg, followed by induction of general anesthesia with intravenous midazolam 0.05 to 0.1 mg/kg, fentanyl, 4 μg/kg, and 2 to 3 mg/kg of propofol, atracurium 0.5 to 0.6 mg/kg, underwent rapid induction and tracheal intubation mechanical ventilation. The maintenance therapy of anesthesia was divided into total intravenous anesthesia and balanced anesthesia in 2 ways: total intravenous anesthesia with fentanyl 0.05 to 0.10 μg/kg/min and 3 to 4 mg/kg/h trace of propofol infusion anesthesia was maintained; balanced anesthesia with isoflurane inhalation, and intermittent intravenous fentanyl 1 to 2 μg/kg. Each group maintained muscle relaxation with atracurium 0.2 to 0.3 mg/kg continuous infusion.

2.3. Postoperative treatment

All patients were continuously monitored heart rate, blood pressure, respiration rate, and blood oxygen saturation. The blood pressure was maintained at between 140 and 120/90 and 70 mm Hg. Intravenous antihypertensive drugs which were the combination of physiological saline 40 mL and continuous intravenous nitroglycerin 50 mg micro-pump syringe were given if the malignant blood pressure emerged. The micro-pump syringe speed needed to be adjusted by the blood pressure changes to keep blood pressure stable. Other specialist care and special treatment were conducted as usual.

2.4. Detection method and the observation index

Patients in each group were extracted vein blood 5 mL at 4 times: before surgery (T0), during surgery (T1), 2 hours after surgery (T2), and 24 hours after surgery (T3). Serum levels of high sensitive C-reactive protein was detected by enzyme-linking immune-absorbent assay (Hs-CRP Assay Kit, Nanjing Jiancheng Bioengineering Institute, China). The levels of blood glucose and leukocyte count were measured respectively by blood glucose meter and automatic blood cell counting equipment.

2.5. Statistical analysis

Mean and stand deviation at each measure time within group were reported. Two sided paired *t* test was conducted to compare the mean between time T0 with other times within the same group. One-way analysis of variance (ANOVA) was used to test whether there was any significant difference between the hypertension and non-hypertension groups before the surgery. Two-way ANOVA was performed to examine the influence of anesthesia method and hypertension history on the interested outcomes. SPSS13.0 (SPSS Inc., Chicago, IL) was used to perform the statistical analyses.

3. Results

3.1. Demographic data

Patients including 40 with hypertension and 40 with normal had general anesthesia. There was no difference between the patients in terms of demographic data, blood loss, and duration of surgery in each group (Table 1).

3.2. Hs-CRP expression

Hs-CRP expression in the A, B, C, and D groups decreased at T0, T1, T2 time point, but increased at T3. Patients with

Table 1

Demographic data of patients ($\bar{x} \pm S$, n = 20).

Group	Age, y	Sex (M/F)	Weight, g	Blood loss, mL	Duration of surgery, h
A	55 ± 6.3	8/12	64 ± 9.6	343 ± 102.4	3.3 ± 0.8
B	54 ± 4.9	11/9	62 ± 8.7	366 ± 135.6	3.2 ± 0.7
C	52 ± 8.1	10/10	63 ± 10.2	358 ± 118.3	3.5 ± 0.4
D	57 ± 5.5	11/9	65 ± 9.3	349 ± 129.7	3.3 ± 0.6

Table 2

High-sensitivity C-reactive protein expression changes in each group ($\bar{x} \pm S$, n = 20).

	Group	T0	T1	T2	T3
Hs-CRP, μg/mL	A	1.22 ± 0.21	1.22 ± 0.31	1.21 ± 0.34	3.75 ± 0.58
	B	2.63 ± 0.32[‡]	2.57 ± 0.28[‡]	2.28 ± 0.15[*,‡]	5.27 ± 0.86[*,‡]
	C	1.29 ± 0.18	1.28 ± 0.22	1.26 ± 0.12	3.32 ± 0.43[*,‡]
	D	2.72 ± 0.22[§]	2.62 ± 0.25[§]	2.34 ± 0.24[*,§]	4.21 ± 0.64[*,†,§]

Hs-CRP = high-sensitivity C-reactive protein.
[*] $P < 0.01$ versus T0 in same group.
[†] $P < 0.01$ versus B group.
[‡] $P < 0.01$ versus A group.
[§] $P < 0.01$ versus C group.

hypertension had higher Hs-CRP expression at time T0 than those of normal. Two-way ANOVA test result showed there was significant difference between hypertension and normal groups at time T0 ($F = 557.32$, $P < 0.01$). At time T3, patients with hypertension in D group had lower Hs-CRP expression than those in B group ($P < 0.01$). In normal patients, Hs-CRP expression in C group was lower than those in A group ($P < 0.01$). Two-way ANOVA test result showed that Hs-CRP expressions were different between 2 anesthesia methods ($F = 26.58$, $P < 0.01$) as well, balanced anesthesia causing higher HS-CRP expression than total intravenous anesthesia method at time T3. Both hypertension history and anesthesia method ($F = 4.75$, $P < 0.05$) had significant effects on the Hs-CRP expression (Table 2).

3.3. Blood glucose, leukocyte count, and neutrophil percentage

Blood glucose, leukocyte count, and neutrophil percentage increased at time T0, T1, T2, and T3 in all 4 groups. At time T0, 2-way ANOVA test result showed blood glucose ($F = 21.66$, $P < 0.01$) and neutrophil percentage ($F = 51.86$, $P < 0.01$) are significantly associated with patient hypertension history. Patients with hypertension had higher blood glucose and neutrophil percentage than those of normal. At time T3, 2-way ANOVA test result showed blood glucose ($F = 4.54$, $P < 0.05$) and leukocyte count ($F = 5.01$, $P < 0.05$) were significantly different between 2 anesthesia methods. Anesthesia methods had no effect on neutrophil percentage. Patients with normal in C group had lower blood glucose and leukocyte count than those in A group ($P < 0.05$). The effect of anesthesia methods on the blood glucose ($F = 4.04$, $P < 0.05$) and leukocyte count ($F = 12.54$, $P < 0.01$) were depending on the presence of hypertension history (Table 3).

4. Discussion

A number of studies have showed that the level of Hs-CRP may reflect the level of vascular disease in patients with hypertension. The severity of vascular lesion and the Hs-CRP level are positively correlated.[10] Our results showed that patients with history of hypertension showed the Hs-CRP expression level and neutrophil percentage were significantly higher than in patients without hypertension during the preoperative tests, suggesting that some patients with the history of hypertension had severe systemic inflammatory response and certain blood vascular lesions. Meanwhile, the results of this experiment showed preoperative blood glucose levels in patients with history of hypertension significantly increased but the value was still within the normal range. Studies have shown that high blood glucose and hypertension are related diseases and they have common risk factors. An abnormal glucose metabolism was diagnosed in 57.1% of the new-onset hypertensive patients without previously diagnosed diabetes in Chinese Han population.[11] The

Table 3

Blood glucose, leukocyte count and neutrophil percentage changes in each group ($\bar{x} \pm S$, n = 20).

	Group	T0	T1	T2	T3
Blood glucose, mmol/L	A	4.85 ± 0.72	5.01 ± 0.94	5.23 ± 1.24	6.36 ± 1.14[†]
	B	6.02 ± 1.31[§]	6.14 ± 1.25[§]	6.31 ± 1.75[§]	6.92 ± 1.27[*]
	C	4.93 ± 1.13	5.08 ± 1.13	5.25 ± 1.31	5.32 ± 0.83[*,‡]
	D	5.91 ± 0.87[‖]	6.07 ± 0.96[‖]	6.17 ± 1.46[‖]	6.89 ± 1.16[*,‖]
Leukocyte count × 10^9/L	A	6.54 ± 1.76	7.14 ± 2.03	8.83 ± 1.93[†]	13.55 ± 2.63[†]
	B	6.38 ± 1.32	6.96 ± 1.57	8.25 ± 2.27[†]	13.27 ± 1.95[†]
	C	6.43 ± 1.16	6.83 ± 1.24	7.92 ± 1.58[†]	11.44 ± 2.24[†,‡]
	D	6.72 ± 0.94	7.08 ± 1.15	8.54 ± 1.24[†,‖]	13.92 ± 2.13[†,‡,‖]
Neutrophil percentage %	A	53.2 ± 7.4	59.4 ± 8.2	71.6 ± 7.6[†]	89.3 ± 16.5[†]
	B	68.4 ± 13.2[§]	71.3 ± 12.5[§]	78.4 ± 11.7[*,‡]	88.2 ± 25.1[†]
	C	50.7 ± 6.5	58.7 ± 7.3	69.6 ± 9.4[†]	87.6 ± 19.4[†]
	D	64.8 ± 9.1[‖]	69.4 ± 11.4[‖]	72.3 ± 12.8[*]	88.5 ± 15.3[†]

[*] $P < 0.05$.
[†] $P < 0.01$ versus T0 in same group.
[‡] $P < 0.05$.
[§] $P < 0.01$ versus A group.
[‖] $P < 0.01$ versus C group.

hyperglycemia as well as higher fasting plasma glucose within the normal range is associated with a higher prevalence of hypertension independent of other cardiovascular risk factors in elderly Chinese.[12] The intracranial lesions and vascular disease coupled with the impact of psychological factor are easy to cause the preoperative high blood glucose within the neurosurgical patients.[13]

Although studies show Hs-CRP may reflect the inflammatory response at certain level, whether it can be used as the independent disease prognosis indicator can't be determined.[14] A number of indicators should be used to conduct a comprehensive assessment of the degree of stress.[15] Within indicators that reflect the stress in surgery, we chose the blood glucose and leukocyte count and neutrophil percentage which will normally increase after neurosurgery as the index. The result showed that in all groups Hs-CRP at 24 hours after surgery significantly increased. Meanwhile, blood glucose, leukocyte count, and neutrophil percentage gradually increased within 24 hours after surgery. All of those suggested apparent stress response occurred at 24 hours after surgery.

The experiment showed that Hs-CRP level at 24 hours after surgery from neurosurgical patients was lower in total intravenous anesthesia method compared with balanced anesthesia. It was found that there was no significant effect of anesthesia methods on the blood glucose and leukocyte count within the patients with hypertension. But for the patients without hypertension, total intravenous anesthesia alleviated the increase of blood glucose and leukocyte count compared with balanced anesthesia. Isoflurane and propofol, both combined with remifentanil, have provided clinically comparable cortisol and insulin responses to surgery in craniotomy operations, whereas propofol attenuated the increase in plasma blood glucose.[16] So total intravenous anesthesia with propofol maintenance is a better way compared with balanced anesthesia in terms of inhibiting the surgical stress response. Two-way ANOVA test showed effects of anesthesia method on Hs-CRP, blood glucose, and leukocyte count were associated with the history of hypertension which means the level of alleviating surgical stress response by anesthesia was affected by the history of hypertension in patients.

Studies have showed that total intravenous anesthesia can better inhibit the increase of cellular interleukin-6 (IL-6), norepinephrine (NE), cortisol (COR) during the preoperative period and stress response.[17,18] Using propofol for maintenance of anesthesia in cardiopulmonary bypass is associated with a less adverse inflammatory profile than is isofluorane which supports the hypothesis that propofol has anti-inflammatory activity.[19] An anesthetic regimen combining propofol and remifentanil attenuates the stress response more efficiently than a isoflurane-remifentanil combination in patients scheduled for diagnostic gynecologic laparoscopy.[20] The present results also showed that total intravenous anesthesia compared with balanced anesthesia can significantly reduce postoperative Hs-CRP levels.

Some data suggest that increased blood pressure may be a stimulus for inflammation and that this is a possible mechanism underlying the role of hypertension as a risk factor for cardiovascular disease.[21] Due to vascular disease and inflammation in patients with hypertension, the ability to control postoperative stress response had a certain degree of decline, thereby affecting the inhibitory effect of different anesthetic methods. Thus, we must consider the impact on surgical stress of hypertensive disease before we made the choice of neurosurgical appropriate anesthesia method.

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