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ABOUT COVER

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Retrospective Study

Serum vascular endothelial growth factor and cortisol expression to predict prognosis of patients with hypertensive cerebral hemorrhage

Chao-Yong Zhang, Bin Wang, Xiang-Ting Hua, Kui Fan, Yu-Feng Li

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Cerebral hemorrhage is a common and severe complication of hypertension in middle-aged and elderly men.

AIM

To investigate the correlation between vascular endothelial growth factor (VEGF) and cortisol (Cor) and the prognosis of patients with hypertensive cerebral hemorrhage.

METHODS

A hundred patients with hypertensive intracerebral hemorrhage were enrolled from January 2020 to December 2022 and assigned to the hypertensive intracerebral hemorrhage group. Another 100 healthy people who were examined at our hospital during the same period were selected and assigned to the healthy group. Peripheral venous blood was collected, and serum Cor and VEGF levels were measured through enzyme linked immunosorbent assay.

RESULTSA statistically significant difference in serum Cor and VEGF levels was observed among patients with varying degrees of neurological impairment ($P < 0.05$). Serum Cor and VEGF levels were significantly higher in the severe group than in the mild-to-moderate group. Cor and VEGF levels were significantly higher in patients with poor prognoses than in those with good prognoses. Multiple logistic regression analysis revealed that serum Cor and VEGF levels were independent factors affecting hypertensive intracerebral hemorrhage ($P < 0.05$).

CONCLUSION

Cor and VEGF are associated with the occurrence and development of hypertensive cerebral hemorrhage and are significantly associated with neurological impairment and prognosis of patients.

Key Words: Hypertension; Cerebral hemorrhage; Vascular endothelial growth factor; Cortisol; Prognosis; Treatment

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Core Tip: Investigation of the correlation between vascular endothelial growth factor (VEGF) and cortisol (Cor) levels and the prognosis of patients with hypertensive intracerebral hemorrhage indicated that Cor and VEGF are associated with the occurrence and development of cerebral hemorrhage, as well as neurological impairment and patient prognosis. Thus, Cor and VEGF may act as potential biomarkers for predicting the prognosis of patients with hypertensive intracerebral hemorrhage.

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INTRODUCTION

Cerebral hemorrhage is a common and severe complication of hypertension in middle-aged and elderly men[1-3]. This complication usually occurs in hypertensive patients who are emotionally disturbed or overworked. It is characterized by rapid onset, rapid progression, poor prognosis, and high mortality and is a severe health risk. Brain hemorrhage is associated with risk factors such as age, smoking, and alcohol abuse; however, its exact pathogenesis remains unclear and effective treatment is lacking.

Vascular endothelial growth factor (VEGF) is a cytokine that specifically enhances vascular permeability, promotes neovascularization and participates in neuroprotection and other biological functions[4-9]. The relationship between VEGF and hypertensive cerebral hemorrhage has recently become a hot research topic. In addition, cortisol (Cor) is a sensitive indicator of stress *in vivo*[10-14]. VEGF and Cor play a crucial role in secondary brain injury in patients with cerebral hemorrhage[15-20]; however, the relationship of VEGF and Cor with the prognosis of hypertensive cerebral hemorrhage has rarely been reported. Moreover, the effect of VEGF and Cor on serological parameters in patients with hypertensive cerebral hemorrhage remains unclear. We here investigated the usefulness of serum VEGF and Cor expression in predicting the prognosis of patients with hypertensive cerebral hemorrhage[21-23].

MATERIALS AND METHODS

General information

One hundred patients with the hypertensive cerebral hemorrhage who were admitted to our hospital from January 2020 to December 2022 were selected and assigned to the hypertensive cerebral hemorrhage group. Another 100 healthy people who were examined at our hospital during the same period were selected as the healthy group. Patients with first-onset hypertensive cerebral hemorrhage in whom the diagnosis was confirmed through head magnetic resonance or computed tomography imaging and who were 60 years of age were included in the study. Patients with traumatic cerebrovascular disease; occult cerebrovascular malformation; cerebral hemorrhage; transient ischemic attack; cardiogenic cerebral embolism; recent history of major surgery; head trauma injuries; organic lesions of the liver, heart, and kidney; vasodilation; volume expansion and thrombolytic therapy before blood collection; severe infections; malignant tumors; immune system diseases; hematological diseases; and cardiovascular diseases were excluded. The healthy group included 51 men and 49 women having a mean age of 69.40 ± 3.19 years and a body mass index of 59.99 ± 7.08 kg/m². The cerebral hemorrhage group included 52 men and 33 women having a mean age of 69.47 ± 3.26 years and a body mass index of 60.00 ± 7.04 g/m². The differences between the groups were not statistically significant ($P > 0.05$) and were comparable. Patients in the cerebral hemorrhage group were divided into three subgroups, severe ($n = 33$), moderate ($n = 34$), and mild ($n = 33$), according to their degree of disease[24-28]. Patients in the cerebral hemorrhage group were divided into the vulnerable plaque subgroup ($n = 50$) and the stable plaque subgroup ($n = 50$) based on the nature of the carotid atherosclerotic plaque. The study was approved by the ethics committee of the hospital. All study participants signed the informed consent form.

Treatment methods

The hypertensive cerebral hemorrhage group was provided basic symptomatic treatment upon admission, including thrombolysis, oxygenation, anticoagulation, cerebral nerve nutrition, cerebral edema relief, maintenance of acid-base balance, anti-platelet aggregation, and blood glucose and blood pressure control.

Observation indicators

First, 3–5 mL of fasting elbow venous blood is collected from all participants, left to stand for 60 min at room temperature, and centrifuged at 3000 r/min for 10 min. The supernatant was stored in a refrigerator at -80°C . Serum VEGF and Cor levels were measured using enzyme linked immunosorbent assay (ELISA) by strictly following the instructions of the ELISA kit (Shanghai Qiao Yu Biotechnology Co., Ltd.).

Statistical methods

SPSS 22.0 statistical software was used for data processing and analysis. The measured data were expressed as mean \pm SD deviation, and a t-test was used for comparison between groups.

RESULTS

Comparison of the serum VEGF and Cor levels between the healthy and cerebral hemorrhage groups

The levels of serum VEGF and Cor in the cerebral hemorrhage group were significantly higher than those in the healthy group, and the differences were statistically significant (all $P < 0.05$, Table 1).

Comparison of the serum VEGF and Cor levels in patients with different degrees of injury in the brain hemorrhage group

There were significant differences in the serum VEGF and Cor levels among patients with different degrees of injury (all $P < 0.05$). The levels of serum VEGF and Cor in the severe group were significantly higher than those in the mild and moderate groups, and the levels of serum VEGF and Cor in the moderate group were significantly higher than those in the mild group (all $P < 0.05$, Table 2).

Comparison of the serum VEGF and Cor levels in patients with different prognosis levels in the cerebral hemorrhage group

The levels of serum VEGF and Cor in patients with poor prognosis were significantly higher than those in patients with good prognosis (all $P < 0.05$, Table 3).

Multi-factor logistic regression analysis of patient prognosis

Multivariate logistic regression analysis was performed using the prognosis level of patients with hypertensive cerebral hemorrhage as the dependent variable and serum VEGF and Cor as the independent variables. The results showed that serum VEGF and Cor were independent influencing factors of hypertensive cerebral hemorrhage (all $P < 0.05$, Table 4).

DISCUSSION

Cerebral hemorrhage is among the severe complications of hypertension that mainly occurs in middle-aged and elderly populations[29-32]. It is characterized by the rapid onset and progression of the disease, which can lead to sequelae such as hemiplegia, cognitive impairment, and cerebral hernia, thus bringing a heavy burden to families and society[33-35]. To formulate reasonable treatment plans and improve patients' living standards, rapidly and accurately assessing the prognosis of hypertensive intracerebral hemorrhage is crucial. With the rapid development of molecular biology, the role of various active factors in the development of hypertensive intracerebral hemorrhage has recently attracted considerable attention[36-38]. VEGF is a homologous dimer glycoprotein. It is a specific mitogen that directly acts on vascular endothelial cells. VEGF mainly increases vascular permeability, promotes vascular regeneration, and participates in neuroprotection[39,40]. The study results revealed that the VEGF expression level was statistically and significantly higher in patients with cerebral hemorrhage than in the control group ($P < 0.05$). As the main stressor, hypertensive intracerebral hemorrhage can rapidly activate the hypothalamus pituitary adrenal axis, upregulate adrenal function, and increase the Cor levels. The present results indicated that the serum levels of VEGF and Cor in the observation group were higher than those in the control group, implying that VEGF and Cor may be involved in the occurrence of acute cerebral hemorrhage. Past studies have shown that, when compared with the healthy controls, the serum VEGF and Cor levels in patients with acute cerebral hemorrhage were significantly increased, while the serum VEGF and Cor levels were positively correlated with the American Institutes of Health Stroke Scale scores. The present results also suggested that, with the aggravation of neurological deficits in patients with acute cerebral hemorrhage, the serum VEGF and Cor levels gradually increased. This could be because an increase or decrease of the VEGF and Cor levels can promote the enhancement of inflammatory response.

Table 1 Comparison of the serum vascular endothelial growth factor and cortisol levels between the healthy and cerebral hemorrhage groups

Group	<i>n</i>	VEGF (pg/L)	Cor (nmol/L)
Cerebral hemorrhage group	100	1.43 ± 0.52	796.61 ± 50.23
Healthy group	100	1.01 ± 0.34	499.42 ± 47.11
<i>t</i> value		12.374	27.142
<i>P</i> value		0.000	0.000

VEGF: Vascular endothelial growth factor; Cor: Cortisol.

Table 2 Comparison of the serum vascular endothelial growth factor and cortisol levels in patients with different degrees of injury in the brain hemorrhage group

Degree of damage	<i>n</i>	VEGF (pg/L)	Cor (nmol/L)
Mild	33	1.13 ± 0.78	547.33 ± 40.19
Moderate	34	1.50 ± 0.59 ^a	746.34 ± 46.22 ^a
Severe	33	1.66 ± 0.64 ^{a,b}	998.42 ± 35.36 ^{a,b}
<i>t</i> value		9.278	19.741
<i>P</i> value		0.012	0.000

^a*P* < 0.05 when compared to patients with a mild injury.

^b*P* < 0.05 compared to patients with a moderate injury. VEGF: Vascular endothelial growth factor; Cor: Cortisol.

Table 3 Comparison of the serum vascular endothelial growth factor and cortisol levels in patients with different prognosis levels in the cerebral hemorrhage group

Prognosis level	<i>n</i>	VEGF (pg/L)	Cor (nmol/L)
Good	61	1.21 ± 0.69	661.75 ± 35.42
Difference	39	1.58 ± 0.71	899.31 ± 36.78
<i>t</i> value		15.617	24.874
<i>P</i> value		0.000	0.000

VEGF: Vascular endothelial growth factor; Cor: Cortisol.

Table 4 Multi-factor logistic regression analysis of patient prognosis

Influencing factors	B	SX	Wald χ^2	<i>P</i> value	OR (95%CI)
VEGF	1.526	0.025	22.623	0.000	2.985 (1.261-5.328)
Cor	1.102	0.024	16.375	0.000	2.036 (0.857-2.235)

OR: Odds ratio; CI: Confidence interval; VEGF: Vascular endothelial growth factor; Cor: Cortisol.

However, this study still has certain limitations. Firstly, we only analyzed regional research data, and information were obtained from a single hospital, which may lead to biased results. In the future, data from different countries, regions, and age groups should be analyzed to eliminate contingency and address the aforementioned limitations. In addition, follow-up studies should enrol a larger sample size and increase the scope of oral education to cover subjects such as educational forms and educational models.

CONCLUSION

The study results thus revealed that serum Cor and VEGF levels were significantly higher in the study group than in the control group. These levels increased with the degree of nerve injury, thus indicating that serum Cor and VEGF mediate the occurrence and development of hypertensive cerebral hemorrhage. Moreover, serum Cor and VEGF levels may be related to the prognosis of hypertensive intracerebral hemorrhage.

ARTICLE HIGHLIGHTS

Research background

Cerebral hemorrhage is a common and serious complication of hypertension affecting middle-aged and elderly men. General anesthesia can easily induce complications such as cognitive dysfunction in such patients, which is not conducive to postoperative recovery.

Research motivation

To investigate the correlation between vascular endothelial growth factor (VEGF) and cortisol (Cor) and the prognosis of patients with hypertensive cerebral hemorrhage.

Research objectives

To provide a reference for the prognosis and anesthesia of clinically related operations.

Research methods

Randomized controlled method and double-blinded method.

Research results

Cor and VEGF levels were statistically and significantly higher in patients with poor prognosis than in those with good prognosis ($P < 0.05$). Multifactor logistic regression analysis revealed that serum Cor and VEGF levels were independent factors influencing hypertensive cerebral hemorrhage.

Research conclusions

Cor and VEGF are associated with the occurrence and development of hypertensive cerebral hemorrhage and are significantly associated with neurological impairment and prognosis of patients.

Research perspectives

Future studies could focus on exploring the potential mechanisms underlying the correlation between serum Cor and VEGF levels and hypertensive intracerebral hemorrhage. Additionally, more clinical studies are needed to validate the potential of serum Cor and VEGF as biomarkers for predicting patient prognosis and guiding clinical treatment decisions. Finally, further research could aim to investigate potential therapeutic strategies targeting Cor and VEGF to improve patient outcomes.

FOOTNOTES

Author contributions: Zhang CY and Wang B contributed equally to this work; Zhang CY, Wang B, Hua XT, Fan K, and Li YF, designed the research study; Zhang CY, Wang B, Hua XT, and Fan K performed the research; Zhang CY, Wang B, and Li YF analyzed the data and wrote the manuscript; All authors have read and approve the final manuscript.

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