Effectiveness of ginkgolides on neurological function and nutritional status of patients with cerebral hemorrhage

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Abstract: Cerebral hemorrhage (CH) is characterized by acute onset, rapid progression, and poor prognosis, posing a great potential threat to the health of patients. Ginkgolides, an excellent natural perpend, have the functions of vasodilation, anti-inflammation, anti-oxidation and memory and cognitive enhancement and the rich trace elements help improve the nutritional status of the human body, which is an important guarantee for the prognosis and health of CH patients. In this study, we observed the therapeutic efficacy of Ginkgolides combined with all-in-one nursing care for CH, thus providing a new reference for the future treatment of CH. We divided 100 patients with CH into a study group receiving Ginkgolides combined with all-in-one nursing care and a control group receiving all-in-one nursing care and compared their neurological and cognitive function, inflammatory response and nutritional status. The results found that ginkgolides combined with all-in-one nursing care better enhanced the neurological and cognitive functions of CH patients and inhibited inflammatory responses. Besides, ginkgolides significantly promoted the increase of nutritional protein levels in CH patients, better ensuring their health. Therefore, we recommend to popularize the use of ginkgolides combined with all-in-one nursing care in the treatment of CH in the future.

Keywords: Cerebral hemorrhage, ginkgolides, neurological function, nutritional status, self-care skills.

INTRODUCTION

Cerebral hemorrhage (CH) is a kind of intracerebral hemorrhage caused by spontaneous rupture of cerebral blood vessels, which has the characteristics of acute onset, rapid progression and adverse prognosis (Magid-Bernstein *et al.*, 2022). In China, the incidence of CH is about 60-80 per 100,000 people, accounting for 20-30% of acute cerebrovascular diseases (Tu *et al.*, 2023). CH patients usually have enlarged hematomas, aggravated brain edema, and increased intracranial pressure, with surgical removal of hematomas being the most effective treatment (Al-Kawaz *et al.*, 2020). However, invasive surgical procedures inevitably cause nerve damage and sequelae, affecting patient prognosis, rehabilitation and health (Wan *et al.*, 2023). Therefore, individualized care for CH patients is also particularly important. All-in-one nursing care is an emerging nursing intervention that allows effective communication and fast and efficient cooperation between doctors and nurses, thus striving for more timely treatment for patients; meanwhile, based on the specific condition of the patient, targeted and scientific interventions are carried out to prevent adverse events and achieve the goal of improving nursing outcomes (S. Chen *et al.*, 2022). At present, all-in-one nursing care has been confirmed to be excellent in the rehabilitation treatment of Alzheimer's disease and ischemic stroke (Zhang *et al.*, 2021; Feng *et al.*, 2019), but its impact on CH remains unclear.

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In addition, with the gradual attention paid to traditional Chinese medicine (TCM) rehabilitation therapy in clinical practice, we found that the addition of TCM in the treatment of CH can also promote patient rehabilitation (Gachowska *et al.*, 2021). Ginkgolides are an active component existing in ginkgo leaves, which belong to a biologically active component with a complex chemical structure and a variety of pharmacological effects and medical value (Niu *et al.*, 2022). The major components of ginkgolides have the functions of vasodilation, anti-inflammation, anti-oxidation and memory and cognitive enhancement and the rich trace elements are conducive to improving the nutritional status of the human body and comprehensively promoting the rehabilitation of patients with cardio-cerebrovascular diseases (Liu *et al.*, 2019). For CH, ginkgolides may also exert the aforementioned positive potential effects.

Given this, a detailed observation is conducted on the positive effects of ginkgolides combined with all-in-one nursing care on the prognosis, neurological function and nutritional status of CH patients, in order to provide more reliable guarantees for future treatment of CH patients.

MATERIALS AND METHODS

General data
One hundred CH patients admitted to Xingtai People's Hospital from August 2021 to November 2023 were selected as the research subjects after standard screening according to the inclusion (complete clinical data; diagnosis of CH by MRI, CT and other imaging

examinations (Gil-Garcia *et al.*, 2022); treatment in our hospital; written informed consent provided by the patient) and exclusion criteria (obvious liver and kidney dysfunction; other major diseases, including tumors; communication barriers due to mental disorders; poor treatment compliance; withdrawal for other reasons). Using a table of random numbers, they were divided into a research group (n=50) and a control group (n=50). Both groups were given all-in-one nursing care and the research group was further treated with ginkgolides on this basis (ethical approval number: No.2021LL02).

Intervention methods

All-in-one nursing care: A nursing team composed of attending physicians, responsible nurses and rehabilitation teachers was set up to carry out relevant treatment and nursing work according to nursing procedures. The team members cooperated closely and communicated in time to establish a close relationship with patients. A health education plan was developed based on the actual situation of patients and specialized nurses provided detailed information on the health education content to patients and their families through written, demonstration, video and other forms. Patients and their families could ask questions based on their circumstances to better understand the disease and precautions. In addition, the nursing staff proactively learned patients' psychological status, gave targeted interventions, actively communicated with patients and encouraged them to improve treatment compliance. Furthermore, targeted rehabilitation exercises were provided to patients and family members were told to supervise patients to complete rehabilitation exercises regularly and quantitatively. Patients were also given dietary guidance, informing them to give priority to digestible and light foods, to eat more fish, beans and fresh fruits and vegetable and to pay attention to blood sugar and blood lipid levels. Moreover, out-of-hospital supervision was implemented, regularly monitoring the completion of patients' health behavior management plan through phone or We-Chat and assisting patients with difficulties in developing solutions, so that they could ultimately cultivate healthy behavior habits. Ginkgolides treatment: Ginkgolides injection (Chengdu Baiyu Medical Supplies Co. Ltd., 2mL/piece, containing 10mg terpene lactones, Z20110035) was administered intravenously. Five pieces were used each time, which was added with 250 ml of 5% glucose injection or 0.9% sodium chloride injection for intravenous administration, once a day, for 2 weeks.

Sample collection and testing

Venous blood (3 mL) was collected from patients before and after treatment, respectively and serum was separated by centrifugation. Serum levels of total protein (TP), prealbumin (PA) and hemoglobin (Hb) were measured with an automatic biochemical analyzer, while tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β) and C-

reactive protein (CRP) were quantified using an enzyme-linked immunosorbent assay.

Questionnaire surveys

The following investigations were conducted before and after intervention: Patients' cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) (Jia *et al.*, 2021); on a 30-point scale, lower scores suggest more serious cognitive impairment. The National Institute of Health Stroke Scale (NIHSS; total score: 42 points) (Lim *et al.*, 2023) was employed for neurological function evaluation; the score is inversely associated with neurological function recovery. The motor function assessment was made with the Fugl-Meyer Assessment (FMA) (Rech *et al.*, 2020) and the lower the score, the worse the motor function. Patients' self-care ability was evaluated with the Exercise of Self-care Agency Scale (ESCA) (Zhao *et al.*, 2023); The scale includes four dimensions, namely, self-concept, self-responsibility, self-care skills and health knowledge level, with a total score of 0-172; a higher score indicates a stronger self-care ability.

Endpoints

The MoCA, NIHSS, FMA and ESCA scores before and after nursing, as well as the detection results of nutritional proteins and inflammatory factors, were analyzed.

STATISTICAL ANALYSIS

SPSS 23.0 statistical software analyzed the data results, and Graphpad 8.3 software visualized them. Qualitative data were represented by [n(%)] and quantitative data by ($\chi\pm s$). The χ^2 test, independent sample t-test and paired t-test were used to compare the results, with statistical significance indicated by P<0.05.

RESULTS

There was no difference in clinical data

The clinical data were compared and the results showed no significant inter-group difference (P>0.05, table 1).

The research group showed better cognitive and neurological functions than the control group

After nursing, the scores of MoCA and FMA in both groups increased, with those in the research group being (20.50±1.56) and (74.50±6.66), respectively, both of which were higher compared with the control group (P<0.05); while reduction in the NIHSS scores was observed in both patient cohorts after care, with an even lower score in the control group (P<0.05, table 2).

The research group showed less severe inflammatory reactions than the control group

After nursing, the levels of TNF-α, IL-1β and CRP in the research group decreased to (5.92 ± 1.30) ng/mL,

Table 1: Comparison of clinical data.

Groups	n	Age	Sex Male/Female	Body mass index (BMI) (kg/m²)	Cigarette smoking Yes/No	Family history of disease Yes/No	High blood pressure Yes/No
Control	50	58.94±5.18	34 (68.00)/16 (32.00)	24.00±1.44	20 (40.00)/30 (60.00)	10 (20.00)/40 (80.00)	30 (60.00)/20 (40.00)
Research	63	60.24±6.11	39 (78.00)/11 (22.00)	24.40±1.68	26 (52.00)/24 (48.00)	8 (16.00)/42 (84.00)	34 (68.00)/16 (32.00)
χ^2/t		1.148	1.268	1.278	1.449	0.271	0.694
P		0.254	0.260	0.204	0.229	0.603	0.405

Table 2: Comparison of cognitive and neurological functions.

Groups	n	MoCA Before	MoCA After	FAM Before	FAM After	NIHSS Before	NIHSS After
Control	50	10.58±1.42	14.66±1.67*	44.7±5.86	70.82±5.10*	17.00±3.02	11.60±1.50*
Research	50	10.63±1.26	20.50±1.56*	44.82±8.44	74.50±6.66*	17.06±2.98	10.38±1.35*
t		0.657	18.080	0.083	3.102	0.100	4.272
P		0.513	<0.001	0.934	0.003	0.921	<0.001

Note: * indicates P<0.05 compared to before nursing. Montreal Cognitive Assessment, MoCA; Health Stroke Scale, NIHSS; Fugl-Meyer Assessment, FMA.

Table 3: Comparison of inflammatory factors.

Groups	n	TNF-α (ng/mL) Before	TNF-α (ng/mL) After	IL-1β (pg/mL) Before	IL-1β (pg/mL) After	CRP (mg/L) Before	CRP (mg/L) After
Control	50	8.31±1.62	6.64±1.60*	124.30±15.09	94.68±11.60*	6.63±0.89	5.80±0.80*
Research	50	8.16±1.71	5.92±1.30*	123.82±15.01	85.50±10.25*	6.68±0.94	5.16±0.65*
t		0.450	2.470	0.160	4.194	0.279	4.448
P		0.654	0.015	0.873	<0.001	0.781	<0.001

Note: * indicates P<0.05 compared to before nursing. Tumor necrosis factor-α, TNF-α; interleukin-1β, IL-1β; C-reactive protein, CRP.

Table 4: Comparison of nutrient proteins.

Groups	n	TP (g/L) Before	TP (g/L) After	PA (mg/L) Before	PA (mg/L) After	Hb (g/L) Before	Hb (g/L) After
Control	50	55.39±5.43	64.18±3.97*	181.24±21.43	207.40±23.27*	91.26±10.95	107.58±13.74*
Research	50	54.70±5.29	69.87±5.92*	179.96±29.20	234.91±20.75*	91.09±10.45	123.32±14.72*
t		0.644	5.642	0.249	6.242	0.079	5.528
P		0.521	<0.001	0.804	<0.001	0.937	<0.001

Note: * indicates P<0.05 compared to before nursing. Total protein, TP; prealbumin, PA; hemoglobin, Hb.

Table 5: Comparison of self-care ability.

Groups	n	Self-concept Before	Self-concept After nursing	Self-responsibility Before	Self-responsibility After nursing	Self-care skills Before	Self-care skills After nursing	Health knowledge Before	Health knowledge After nursing
Control	50	16.04± 4.48	24.20± 4.30*	11.04± 3.43	17.08± 4.46*	30.34± 3.96	39.24± 6.45*	40.48± 5.02	58.42± 9.22*
Research	50	16.16± 4.32	24.54± 3.56*	11.08± 3.41	17.24± 3.71*	30.42± 4.54	39.78± 3.70*	40.86± 5.30	58.98± 7.08*
t		0.136	0.431	0.059	0.195	0.094	0.513	0.368	0.341
P		0.892	0.668	0.954	0.846	0.925	0.609	0.714	0.734

Note: * indicates P<0.05 compared to before nursing.

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(85.50±10.25)pg/mL and (5.16±0.65)mg/L, while those in the control group decreased to (6.64±1.60)ng/mL, (94.68±11.60)pg/mL and (5.80±0.80)mg/L, respectively. The inter-group comparison revealed lower TNF-α, IL-1β, and CRP levels in the research group compared with the control group (P<0.05, table 3).

The nutritional status was better in the research group than in the control group

After nursing, the nutritional proteins in both groups increased (P<0.05), with TP, PA and Hb in the research group being (69.87±5.92)g/L, (234.91±20.75)mg/L and (123.32±14.72)g/L, respectively, all of which were higher versus the control group (P<0.05, table 4).

There was no inter-group difference in self-care ability

Finally, both groups exhibited increased ESCA scores after nursing; however, no marked inter-group differences were identified in the scores of self-concept, self-responsibility, self-care skills and health knowledge (P>0.05, table 5).

DISCUSSION

This study demonstrates that ginkgolides combined with all-in-one nursing care helps improve the cognitive and neurological functions of CH patients and improve their nutritional status, which has important clinical application value in future treatment of CH.

In this study, we compared the neurological and cognitive functions between two groups of patients. Higher MoCA and FMA and lower NIHSS scores were determined in the research group compared with the control group, indicating that ginkgolides combined with all-in-one nursing care can more effectively improve the neurological and cognitive functions of CH patients. In a previous study, Chen R *et al*. also suggested that the use of ginkgolides could enhance the neurological function of patients with cerebral infarction (R. Chen *et al*., 2022), which is consistent with our research results. The active ingredient of Ginkgolides injection is extracted from the traditional Chinese medicine *Ginkgo biloba*, which is commonly used clinically as an adjunctive treatment for the sequelae of cerebrovascular diseases (Li *et al*., 2021). Meanwhile, modern pharmacological research indicates that bilobalide and ginkgolides A, B and C contained in ginkgolides can inhibit vascular endothelial cell apoptosis, inhibit inflammation to a certain extent, promote blood circulation of the body and remove excess oxygen free radicals (Wang *et al*., 2019). In addition, ginkgolides have the effects of suppressing vascular endothelial cell apoptosis, improving blood circulation, maintaining the integrity of vascular endothelial cells, and facilitating the recovery of damaged blood-cerebrospinal fluid barrier function in patients (Zhang *et al*., 2022). Therefore, the use of ginkgolides is helpful in improving

the neurological and cognitive functions of CH patients more effectively. Furthermore, the results of an animal experiment by Fan XX *et al*. showed that ginkgolide injection could balance the extra cellular matrix, regulate the expression of matrix metalloproteinases and improve blood flow in addition to anti-oxidative stress and anti-inflammatory effects (Fan *et al*., 2021). This also explains the lower levels of inflammatory factors in the research group.

In the comparison of nutritional status, the nutritional protein levels were higher in the research group than in the control group, suggesting that ginkgolides combined with all-in-one nursing care can better promote the recovery of patients' nutritional status. Pharmacological research has confirmed that giankgolides are rich in trace elements needed by the human body, which not only help regulate hemodynamics, but also better promote human endocrine, improve the metabolism of nutrients and activate human immune function, thus promoting the overall recovery of patients' nutritional status (Du *et al*., 2021). In the treatment of asthma, ginkgolides have also been shown to activate the secretion of nutritional proteins and promote the rehabilitation of patients (Kim *et al*., 2024), which can support our findings.

Although no table inter-group difference was found in the comparison of self-care ability, the ESCA scores of both groups increased statistically after care, indicating that all-in-one nursing care also has a positive significance in strengthening patients' self-care ability. The reasons are analyzed as follows: (1) The various forms of health education carried out under the all-in-one care model can help patients understand the related knowledge of CH convalescence from multiple perspectives and effectively reduce the anxiety caused by insufficient awareness (Gil-Garcia *et al*., 2022). (2) Through psychological intervention, patients are actively encouraged to express their inner feelings, which is convenient for medical staff to carry out targeted psychological intervention, effectively alleviate patients' bad psychological status, and help them cultivate hobbies, so that patients can gain a sense of accomplishment from hobbies and maintain good psychological status. Besides, urging relatives and friends to accompany and encourage patients can make patients feel supported by others, thus enhancing patients' self-efficacy (Wang *et al*., 2022). (3) Health education helps patients understand that active rehabilitation exercise can promote limb function recovery, strengthening their confidence in rehabilitation exercise; moreover, the demonstrative role of successful cases can further enhance patients' confidence in rehabilitation. Moreover, utilizing patient-patient communication can increase communication between patients and gain recognition from others, thus enhancing patients' sense of self-concept (Jolink *et al*., 2023). An enhanced sense of self-concept can make patients feel that they are needed

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by their relatives and friends, which promotes them to actively participate in rehabilitation training, strengthens their belief in returning to normal life as soon as possible and enhances their self-responsibility.

CONCLUSION

Ginkgolides combined with all-in-one nursing care can effectively promote neurological function recovery in CH patients and improve their nutritional status, which has extremely high clinical application value. However, the number of cases in this study is small and the study period is short, so it is still necessary to address these limitations to provide more reliable clinical reference and guidance.

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