Research Paper

Clinical Efficacy of Nimodipine in the Treatment of Patients with Hypertensive Cerebral Hemorrhage and its Impact on Neurological Function

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The clinical efficacy of nimodipine in the treatment of patients with hypertensive cerebral hemorrhage and its effect on neurological function was explored. The data of hypertensive cerebral hemorrhage patients were analysed, and were randomly divided into observation group and control group each with 59 cases. The control group was given conventional treatment, and the observation group was given intravenous nimodipine. After 14 d of continuous treatment, the clinical treatment effect, National Institutes of Health Stroke Scale score, intracranial hematoma and edema volume, mean arterial pressure, increased intracranial pressure and endothelin-1 levels were observed. Changes in indicators such as Glasgow outcome score and quality of life questionnaire-C30 scores were observed. After treatment, the total effective rate of the observation group was 94.9 %, which was better than that of the control group, 76.3 %. The neurological deficit score, hematoma and edema volume, mean arterial pressure, increased intracranial pressure and endothelin-1 levels of the observation group were significantly improved compared with those before treatment, and were better than the control group where the difference was statistically significant ($p<0.05$). Similarly, Glasgow outcome score and quality of life questionnaire-C30 scores of the observation group and the control group were both higher after treatment, and comparatively, the observation group was higher than the control group, with a statistical difference $p<0.05$. Adverse reactions occurred between both the groups were observed and no significant difference was found ($p>0.05$). Nimodipine treatment for hypertensive cerebral hemorrhage patients can improve the degree of neurological deficit, promote the absorption of cerebral hematoma, reduce intracranial pressure with low adverse reactions and definite clinical effects, and is worthy for application.

Key words: Hypertensive cerebral haemorrhage, nimodipine, neurological function, blood pressure

Hypertensive Cerebral Hemorrhage (HCH) refers to a serious cerebrovascular bleeding disease caused by high blood pressure. Its mechanism is that long-term high blood pressure leads to atherosclerosis, which reduces the strength of the blood vessel wall and then causes, rupture and bleeding[1]. HCH is a disease with high mortality and disability rates[2], among middle-aged and elderly people which is commonly considered to be the majorly affected group. Studies have reported that HCH will not only cause neurological deficits in patients, leading to serious consequences such as cerebral ischemia and cerebral edema, but even after the intracerebral hematoma is removed through surgery or minimally invasive methods, the harm of cerebral edema will still exist, seriously threatening the patients, their life and health. The main cause of HCH is established when patients with high blood pressure experience mood swings, physical labor, excessive mental work or fatigue, that affects cerebral blood vessel rupture and bleeding. The amount of bleeding increases as the condition worsens; it will compress the brainstem, cranial nerves or cerebral blood vessels. It causes the patients to suffer from a series of symptoms such as hemiplegia, aphasia, confusion and even coma. In severe cases, it can endanger the patient's life.

Clinical treatment of HCH mainly focuses on controlling cerebral hemorrhage and reducing intracranial blood pressure. One of the applications of mannitol is to reduce intracranial pressure and dehydration therapy. Mannitol is an osmotic diuretic that can quickly increase plasma osmotic pressure,

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achieve the effect of dehydration and quickly reduce intracranial pressure, with minimal damage to the kidneys. Side effects are caused by the long-term use, which can easily cause symptoms such as hyponatremia and hyperkalemia; moreover, if the systolic blood pressure is >180 mmHg during the acute onset period, nifedipine, edaravone, triamterene, etc., must be immediately used for reducing the blood pressure. In severe cases, intravenous antihypertensive drugs are used to achieve rapid blood pressure reduction; additionally, neuroprotective agents and drugs which help to correct coagulation function are used. Edaravone can effectively relieve the symptoms of cerebral hemorrhage and promote the recovery of neurological function; tranexamic acid can inhibit hematoma, avoid compression of nerve blood vessels, and can effectively reduce early mortality. When HCH is severe or the amount of bleeding is enormous, surgical therapy is often used to remove the hematoma. However, surgery is a traumatic therapy that can cause great damage to the body, whose general prognosis is not ideal. And if Minimally Invasive Surgery (MIS) is adopted, its clinical efficacy and safety should be compared with conservative treatment and surgery has yet to be determined[3]. At present, conservative treatment is mostly used in clinical practice for HCH patients whose bleeding volume is <30 ml. Commonly used long-acting antihypertensive drugs include calcium ion antagonists such as amlodipine, nifedipine sustained-release tablets and controlled-release tablets and as well as felodipine. Similarly, angiotensin-converting enzyme inhibitors include indopril and enalapril. Although these drugs can reduce intracranial pressure and control cerebral hemorrhage, their long-term effects are poor, and the degree of neurological deficit, which is generally measured using National Institutes of Health Stroke Scale (NIHSS). The score is also low and the prognosis is not ideal. Nimodipine is a new type of calcium channel blocker. It has a good effect on improving blood circulation and reducing cerebral vasospasm, especially cerebral vasospasm which is caused after subarachnoid hemorrhage, in the acute or recovery stage of vascular disease. It can protect neuronal cells and effectively improve patients' quality of life. This study explored the treatment using nimodipine among HCH individuals admitted in Panan County People's Hospital. The treatment effect was significant and the prognosis was good. The clinical data has been reported in this study.

MATERIALS AND METHODS

General information:

118 individuals with HCH, who were admitted to Panan County People's Hospital were selected and were divided into observation group and control group, each with 59 individuals. Among the 118 individuals, 72 were males and 46 were females. All the individuals were aged between (35.6-75.2) y, with an average age of (52.4±6.5) y. All the patients were diagnosed with cerebral hemorrhage by cranial Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). The duration of hypertension ranged from (2-14) y, with an average of (6.7±0.5) y. This study was approved by the Hospital's Ethics Committee.

Inclusion criteria:

Patients whose condition complies with the clinical diagnostic criteria for hypertensive disease; patients whose time from the onset to admission is <24 h; patients whose bleeding volume of cerebral haemorrhage is <30 ml and patients having signed consent, were included in this study.

Exclusion criteria:

Patients who were observed to have ruptured cerebral vascular malformation; patients having severe abnormal liver and kidney function; severe mental disorder and poor compliance; coagulation dysfunction and malignant tumors and patients having infectious diseases and autoimmune system diseases were excluded from this study.

Medication method:

Patients in the control group were subjected to conventional therapies such as dehydration to reduce intracranial pressure, Electrocardiogram (ECG) monitoring, continuous low-flow oxygen inhalation for protecting brain cells, controlling blood sugar, correcting acid balance, maintaining water and electrolyte balance, supplementing nutrition and vitamins, and following symptomatic treatment. It is advised to stop using other vasodilator drugs during treatment[4]. On this basis, the observation group was treated injecting 10 mg of nimodipine was diluted in 400 ml of 5 % glucose solution, and was pumped at a speed of 5 ml/h, once a day. Nimodipine injection was produced by the Chenxin Pharmaceutical Co., Ltd., approved by the national drug standard H20059048, whose specification is 50 ml:10 mg. Both the groups

were treated for 14 d and the changes in the patient's blood pressure and blood pressure fluctuations were dynamically monitored.

Research indicators:

Clinical efficacy: It was measured according to different grades such as, markedly effective, significantly improved and ineffective. When blood pressure returned to normal, NIHSS was significantly reduced, and the disability level was 0. This phenomenon was considered to be markedly effective. If the blood pressure dropped significantly and NIHSS was alleviated, with disability level range from 1 to 3, was considered to be significantly improved. When blood pressure did not drop, NIHSS neither decreased nor increased, and the disability level was level 3 or above such condition was considered to be ineffective.

Total effective rate=(number of improved cases+number of markedly effective cases)/total number of cases×100 %

NIHSS score: NIHSS was used to measure the score of neurological deficits. The total score of NIHSS is 100 points. Higher score denotes more serious NIHSS defect and is categorized into 3 levels. NIHSS score <91 %-100 % is considered as level I. NIHSS score <46 %-90 % is considered to be level II. While NIHSS score <8 %-18 % is level III. The degree of neurological deficit is positively correlated with NIHSS score.

Cerebral hematoma volume and edema volume: Hematoma volume and edema volume before and after treatment were measured based on the CT examination results and were recorded in detail to observe the improvement of cerebral hematoma and edema.

Changes in Mean Arterial Pressure (MAP), Increased Intracranial Pressure (ICP) and Endothelin-1 (ET-1) levels: Serum MAP=diastolic blood pressure+1/3 pulse pressure; ICP assessment mainly uses the German Spiegelberg intracranial pressure detector and ET-1 is detected by enzyme-linked immunoassay. During the test, 3 ml of fasting venous blood was drawn in the morning and the serum was separated and tested at high speed. The above indicators were collected and tested before and after 14 d of treatment.

Glasgow Outcome Score (GOS) and Quality of Life Questionnaire (QLQ-C30) scoring: The study used the GOS scoring[5] to evaluate the improvement effect of patients after treatment, with a complete score of 5 points. According to international standards, a score of 5 indicates clear consciousness, 4 to 4.9 indicates mild impairment of consciousness, 3 to 3.9 indicates moderate impairment of consciousness, 2 to 2.9 indicates severe impairment of consciousness, and a score of 2 or <2 indicates poor prognosis. The total score of QLQ-C30 is 100 points, and the score is positively correlated with the QLQ to determine the patient's prognosis.

Adverse reactions: The adverse reactions of patients in the two groups after treatment were observed. Adverse drug reactions include gastrointestinal reactions such as nausea, vomiting, and loss of appetite that occurs after treatment. Similarly, circulatory system adverse reactions include dizziness, headache, rash, cyanosis of the lips, hypotension, and other reactions.

Statistical analysis:

Statistical Package of Social Sciences (SPSS) version 22.0 statistical software was used to analyze the research data obtained where $p<0.05$ was considered to be statistically significant difference between the groups.

RESULTS AND DISCUSSION

Patient general conditions such as average age, average bleeding rate and average disease duration were compared between both the groups. There was no significant difference in the general conditions between the two groups ($p>0.05$) (Table 1).

Drug efficacy and total effective rate after the treatment was compared between both the groups. After treatment, the total effective rate of the observation group was 94.9 %, which was significantly better than that of the control group, which was 76.3 %. There was a significant difference between the two groups ($p<0.05$) (Table 2).

Further, NIHSS score, hematoma volume and edema volume between both the groups was observed. After medication, the NIHSS score of the observation group was significantly lower than that of the control group, with significant difference ($p<0.05$); the hematoma and edema volume of the observation group were significantly reduced, when compared with the control group before treatment with a significant difference ($p<0.05$) (Table 3).

MAP, ICP, and ET-1 levels between both the groups were observed. The levels of MAP, ICP and ET-1 in the observation group after treatment were significantly

lower than the control group before treatment, and there were significant differences between the two groups ($p<0.05$) (Table 4).

QLQ-C30 and GOS scores were compared. After treatment, the QLQ-C30 and GOS scores of both the groups were improved comparatively, before treatment. Especially, the observation group was better than the control group, and there was a significant difference ($p<0.05$) (Table 5).

Adverse drug reactions were also compared between both the groups. After treatment, 1 patient was observed to have gastrointestinal discomfort, 1 patient had dizziness, and 1 patient with headache was observed in the observation group. The total incidence rate was 5.08 %, and 8.47 % in observation and control groups respectively. There was no significant difference between the two groups ($p>0.05$) (Table 6).

TABLE 1: COMPARISON OF THE GENERAL CONDITIONS OF THE PATIENTS IN TWO GROUPS, n (%) (x±s)

Group (n=59)	Gender		Average age (y)	Average disease duration	Average bleeding rate	Bleeding site		
	Male	Female				Ventricle	Thalamus	Subretinal space
Observation	38	21	45.6±6.5	6.7±3.7	16.33±2.6	15 (25.43)	13 (22.03)	31 (52.54)
Control	34	25	47.0±6.2	6.4±3.9	16.29±2.8	17 (28.82)	11 (18.64)	31 (52.54)
χ^2	0.062	0.341	0.003	0.032	0.059	0.047	0.497	0.346
p	0.541	0.573	1.225	1.065	0.625	0.875	0.421	0.565

TABLE 2: COMPARISON OF TREATMENT EFFECTS BETWEEN THE PATIENTS OF TWO GROUPS, n (%)

Group	n	Effective	Efficient	Invalid	Total effective rate
Observation	59	42 (71.2)	14 (23.7)	3 (5.1)	56 (94.9)
Control	59	36 (61.0)	9 (15.3)	14 (23.7)	45 (76.3)
χ^2					7.213
p					0.008

TABLE 3: COMPARISON OF NIHSS SCORES AND HEMATOMA VOLUME AND EDEMA VOLUME BETWEEN THE TWO GROUPS (x±s)

Group (n=59)	NIHSS score		Hematoma volume (ml)		Edema volume (ml)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Observation	28.81±4.28	8.12±2.15	30.22±9.73	16.79±8.24*	8.69±1.83	2.41±0.64*
Control	29.17±4.43	18.34±2.16	29.70±9.84	24.46±8.95*	8.81±1.89	4.52±1.76*
t	0.328	21.327	0.137	3.451	8.513	2.41
p	0.897	0	0.718	0.02	0.231	0.592

Note: *p<0.05 with respective comparison with control group before medication

TABLE 4: COMPARISON OF MAP, ICP AND ET-1 LEVELS BETWEEN THE PATIENTS OF TWO GROUPS (x±s)

Group (n=59)	MAP (mmHg)		ICP (mmHg)		ET-1(ng/l)	
	Before medication	After medication	Before medication	After medication	Before medication	After medication
Observation	97.14±7.22	72.14±6.51*	5.04±2.15	2.84±0.95*	128.34±11.75	72.94±8.25
Control	98.09±7.20	84.39±6.59*	4.97±1.28	4.59±0.89*	129.72±11.80	85.47±8.97*
t	0.062	3.341	0.112	2.324	0.137	3.451
p	0.844	0.023	0.569	0.052	0.718	0.02

Note: *p<0.05 with respective comparison with control group before medication

TABLE 5: COMPARISON OF QLQ-C30 AND GOS SCORE LEVELS BETWEEN THE PATIENTS OF TWO GROUPS (x±s)

Group (n=59)	QLQ-C30 (mmHg)		GOS (mmHg)	
	Before medication	After medication	Before medication	After medication
Observation	72.14±6.51	97.14±7.22	2.14±0.55	4.64±0.25
Control	84.39±6.59	98.09±7.20	2.30±0.43	4.27±0.18
t	3.341	0.062	2.324	0.112
p	0.023	0.844	0.052	0.569

TABLE 6: COMPARISON OF ADVERSE DRUG REACTIONS BETWEEN THE PATIENTS OF THE TWO GROUPS, n (%)

Groups (n=59)	Gastrointestinal discomfort	Dizziness	Headache	Hypotension	Overall incidence
Observation	1 (1.69)	1 (1.69)	1 (1.69)	0 (0)	3 (5.08)
Control	0 (0)	2 (3.39)	2 (3.39)	1 (16.9)	5 (8.47)
χ^2					2.217
p					6.732

HCH is a common, frequent and extremely serious cerebrovascular disease in clinical practice. Its pathogenesis is that small blood vessels in the brain are affected by hypertension and cerebral arteriosclerosis, resulting in abnormally elevated blood pressure and reduced vascular compliance. It depicts glassy or fibrous changes, focal hemorrhage or even necrosis appearance in the wall of the arteries at the base of the brain[6]. Hypertension is an important cause of cerebral hemorrhage, and uncontrolled increase in blood pressure is the most common cause of spontaneous cerebral hemorrhage[7]. When blood pressure suddenly rises, it is easy to cause cerebral blood vessel rupture and bleeding[8]. When the amount of bleeding accumulates to a certain extent it forms hematoma, which causes compression symptoms on the brain tissue. Pathophysiological changes such as hematoma rupture and cerebral edema will occur, which may compress the cranial nerves and cause serious damage to the body[9]. HCH patients account for more than 50 % of the total number of spontaneous cerebral hemorrhages[10] and this disease usually starts suddenly. 33 % of people with long-term hypertension may probably develop cerebral hemorrhage, and a few patients will have precursors, such as headaches, slow movement or blurred speech[11]; the effect of treatment in the acute phase or preventive treatment is not ideal[12]. According to relevant statistics, the 6 mo mortality rate of this disease is 30 %-50 %[13]. Timely and effective treatment of HCH is the key to improving the prognosis of patients.

There are 3 main stages in the pathogenesis of HCH namely, cerebral artery rupture stage, hematoma formation and cerebral edema stage. The latter 2 stages are the most serious stages and can easily lead to pathological reactions such as blood toxicity attacks, acute inflammatory reactions, and tissue ischemia and hypoxia, causing irreversible damage to brain tissue[14]. Mostly HCH bleeding will be complicated by cerebral edema or cerebral hematoma, which will compress the cranial nerves and cause serious consequences to the body[9]. Inflammation produces a large amount of inflammatory factors, which further aggravates the symptoms of cerebral ischemia and cerebral edema[15]. Currently and clinically, HCH patients with intracranial bleeding volume <30 ml, brain midline shift <1 cm, stable vital signs, no pressure deformation of the ventricles and cisterns are mainly treated conservatively to reduce blood pressure and intracranial pressure. It is crucial to improve the therapeutic effect[16].

Nimodipine is a new generation calcium channel blocker which is currently the most fat-soluble antihypertensive drug among similar drugs. It can pass through the blood-brain barrier smoothly, by selectively acting on cerebral blood vessels, and greatly improves cerebral blood circulation[17], maintains stable vascular osmotic pressure, reduces ET-1 levels by ensuring cerebral blood supply, and maintaining its balance.

Nimodipine is a calcium ion antagonist, which can inhibit the vasoconstriction of calcium ion mediators, preventing the influx of calcium ions into cells, inhibiting smooth muscle contraction, effectively reduce neuron necrosis, protect the nervous system, reduce neurological damage, alleviate cerebral vasospasm and promote the restoration of cerebral

blood flow[18], thereby reducing blood pressure and intracranial pressure; it ultimately achieves this effect of inhibiting HCH[19]. By promoting the cerebral blood perfusion and restoring blood supply to brain tissue, it can effectively prevent and treat ischemic damage to brain tissue[20]. At the same time, once nimodipine binds to specific receptors in the central nervous system, it can antagonize cerebral vasospasm and brain tissue ischemia caused by the antiplatelet drug 5-Hydroxytryptamine (5-HT), the vasoconstrictor thromboxane, and subarachnoid hemorrhage[21]. The advantage of nimodipine is that it can selectively act on cerebral blood vessels, has rapid clinical and antihypertensive effects, does not damage cerebral blood vessels, and significantly acts by improving blood circulation during the recovery period of acute cerebrovascular disease[22]. Modern pharmacological research has confirmed that because nimodipine mainly acts on cerebral blood vessels and nerve cells, it can effectively relieve cerebral vasospasm, improve cerebral circulation, promote the dissolution and absorption of cerebral hematoma that has stopped bleeding, thereby effectively reducing the risk of cerebral edema[23].

Nimodipine is commonly used clinically to treat hypertensive diseases such as acute cerebrovascular disease and ischemic neurological disorders[24]. A study found that the application of nimodipine in the treatment of HCH can effectively improve the patient's neurological function, reduce vasoconstriction, and reduce the risk of recurrence. Studies found that the total effective rate of nimodipine in the treatment of HCH patients was significantly higher than that of the control group, and the patients' NIHSS score, intracranial hematoma volume, and brain edema volume were significantly better than those of the control group ($p<0.05$). Naibing *et al.*[25] in related studies found that when nimodipine was used to treat HCH patients, the NIHSS scores of both groups of patients were reduced after treatment, and the reduction was more significant in the observation group, which is consistent with the results of this study. Related studies depict that nimodipine treatment can reduce ET-1 levels in HCH patients. ET-1, a polypeptide substance which is vascular can promote the relaxation of vascular smooth muscles, enhance the excitement of the nervous system, release of neurotransmitters, and promote vasoconstriction in HCH patients. Elevated ET-1 will greatly affect therapeutic effects of cerebrovascular disease. Because nimodipine can inhibit the influx of calcium ions into cells, dilate blood vessels, block and control the spasm or contraction of blood vessels, thereby improving the intravascular environment, regulating vascular osmotic pressure, restoring blood supply to the brain and reduce ET-1 levels, to maintain its balance. In this study, ET-1 reducing effect in the patients of observation group was significantly better than that of the control group, indicating that nimodipine has an obvious effect on reducing ET-1. In addition, MAP and ICP levels have a significant impact on the therapeutic effect of HCH patients. A decrease in MAP will lead to insufficient perfusion of organs and tissues, causing risks such as brain dysfunction and cardiac dysfunction; too high pressure will cause cerebral edema. Elevated ICP is a cause of cerebral blood vessel rupture and cerebral hematoma. By comparing the changes in MAP and ICP, it was found that the patient's MAP and ICP levels decreased more significantly when treated with nimodipine.

The results of this study showed that the treatment effect of the observation group was significantly higher than that of the control group ($p<0.05$). The NIHSS scores, intracranial hematoma volume, and edema volume of the two groups were improved compared with those before treatment, and the observation group was significantly better than before treatment. In the control group, the difference was statistically significant ($p<0.05$). In the observation group, the levels of MAP, ICP and ET-1 were significantly lower before treatment and the control group denoted difference which was statistically significant ($p<0.05$). In the observation group GOS, QLQ-C30 scores and other indicators were better than those in the control group, and the difference was statistically significant ($p<0.05$); 3 patients in the observation group and 5 patients in the control group were having adverse reactions and there was no significant difference between the two groups ($p>0.05$). It can be seen that the clinical efficacy of nimodipine in the treatment of HCH patients is confirmed. Nimodipine can effectively improve neurological function, reduce the volume of hematoma and edema, is conducive to prognosis and recovery, has a low incidence of adverse reactions, and can greatly improve the health level and QOL of HCH patients.

In summary, the application of nimodipine in the treatment of HCH patients has a significant effect. It not only significantly improves the patient's neurological function, reduces intracranial hematoma

and cerebral edema, but also greatly reduces the degree of neurological deficit, and has a significant antihypertensive effect, effectively improving the patient's neurological function. The patient's QOL whose curative effect is accurate and stable.

However, due to the small sample size of this study, limited clinical conditions, and possible omissions and errors in the observations, the research results might inevitably have some errors and deficiencies. In the next step of the research, the sample size shall be further enriched, observation indicators will be added, and various indicators will be closely observed during the research process to ensure the accuracy of each data, so as to provide more accurate research results for clinical use.

Conflict of interests:

The authors declared no conflict of interests.

REFERENCES

1. Jiyao L. Effect of edaravone and nimodipine in the treatment of hypertensive cerebral hemorrhage. J Cardiovasc Surg 2018;7(4):629-30.
2. Nianbao W, Wei W. The clinical effect of Yunnan Baiyao combined with nimodipine in treatment of hypertensive cerebral hemorrhage. Clin Res Pract 2021;6(8):57-9.
3. Tang Y, Yin F, Fu D, Gao X, Lv Z, Li X. Efficacy and safety of minimal invasive surgery treatment in hypertensive intracerebral hemorrhage: A systematic review and meta-analysis. BMC Neurol 2018;18(1):136.
4. Chao L, Jinjian G. The study of nimodipine in the treatment of hypertensive cerebral hemorrhage. Contemp Clin Med J 2020;33(3):201-2.
5. Sheng Y. Method and effect analysis of nerve function rehabilitation in patients with hypertensive cerebral hemorrhage. China Rural Health 2021;3:78-81.
6. Yuxing Y, Weihao H, Zhifeng D. Efficacy of nimodipine in the treatment of ischemic brain injury after cerebral hemorrhage. Jilin Med J 2018;39(9):1673-4.
7. Dastur CK, Yu W. Current management of spontaneous intracerebral haemorrhage. Stroke Vasc Neurol 2017;2(1):21-9.
8. Hong-jian Y, Qiang S, Yunfeng Y. Clinical study of Shilong Qingxue granule combined with edaravone in the treatment of hypertensive cerebral hemorrhage. Mod Med Clin 2019;34(8):4.
9. Shi HY. Clinical study of edaravone and nimodipine in the treatment of hypertensive cerebral hemorrhage. Cardiovasc Dis Prev Treat Knowl 2022;12(17):24-6.
10. Zhao Q, Wu J. Effect of nimodipine in the treatment of hypertensive cerebral hemorrhage and its influence on the degree of neurological impairment in patients. Essays Contemp Med 2020;18(15):139-40.
11. Shang-kang W. Effect of ganglioside combined with nimodipine in the treatment of hypertensive cerebral hemorrhage and its influence on nerve function. Chin Pract Med 2022;17(6):25-8.
12. Gil-Garcia CA, Alvarez EF, Garcia RC, Mendoza-Lopez AC, Gonzalez-Hermosillo LM, Valadez ER. Essential topics about the imaging diagnosis and treatment of hemorrhagic stroke: A comprehensive review of the 2022 AHA guidelines. Curr Probl Cardiol 2022;47(11):101328.
13. Mei L, Fengqun M, Xiaozhuo L, Qing W, Mingming F, Zhengyao Z, *et al.* Effect Western medicines combined with Nao-Xue-Shu in patients with hypertensive intracerebral hemorrhage: A network meta-analysis. Front Pharmacol 2022;13:1-9.
14. Liu H, Wang L. Efficacy of edaravone combined with nimodipine in the treatment of hypertensive cerebral hemorrhage. J Clin Ration Drug Use 2019;12(2):35-6.
15. Guan X, Xie Z, Yang L. Effect of edaravone combined with nimodipine in the treatment of hypertensive cerebral hemorrhage. Chin Pract Med 2021;16(35):112-5.
16. Wu J. Effects of nimodipine on neurological function, oxidative stress and recurrence risk in patients with hypertensive cerebral hemorrhage. Jilin Med J 2022;43(6):1562-3.
17. Luo J, Shen Y, Wu A. Clinical study of nimodipine combined with ganglioside in the treatment of patients with acute cerebral hemorrhage. Chin J Clin Pharmacol 2019;35(1):6-9.
18. Bing X, Xiaoqian G, Qinghua L. Effect of edaravone combined with nimodipine on inflammatory factors and nerve function in patients with hypertensive cerebral hemorrhage. Clin Misdiagn Mistreat 2019;32(3):36-9.
19. Lei X. Effect of edaravone combined with nimodipine on neurological recovery and plasma ET-1 level in patients with hypertensive cerebral hemorrhage. Med Theory Pract 2020;33(13):2110-2.
20. Wang Y, Yao W, Wang L, Xv D. The effect of butylphthalide injection on the cognitive function and the TLRs/NF-κB pathway in hypertensive intracerebral hemorrhage. Am J Transl Res 2021;13(8):9578-85.
21. Yang B, Wang J, Xia S. Effect of compound musk injection combined with nimodipine in the treatment of patients with hypertensive cerebral hemorrhage after minimally invasive removal. J Hunan Univ Chin Med 2019;39(9):1153-6.
22. Li Y, Fang W, Tao L, Li M, Yang Y, Gao Y, *et al.* Efficacy and safety of intravenous nimodipine administration for treatment of hypertension in patients with intracerebral hemorrhage. Neuropsychiatr Dis Treat 2015;11:1231-8.
23. Ping S. Clinical effect of nimodipine combined with ganglioside in the treatment of cerebral hemorrhage. J Clin Ration Drug Use 2021;14(27):67-9.
24. Bing X, Xiaoqian G, Qinghua L. Effect of edaravone combined with nimodipine on inflammatory factors and nerve function in patients with hypertensive cerebral hemorrhage. Clin Misdiagn Mistreat 2019;32(3):36-9.
25. Naibing X. Effects of nimodipine on neurological function and serum hs-CI, IL-6 and IL-13 levels in patients with hypertensive cerebral hemorrhage. Mod Med Health Res 2019;4(19):14-6.

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