Journal of Hainan Medical University

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Influence of minimally invasive hematoma evacuation combined with nerve growth factor preparation on neurological function injury in patients with hypertensive cerebral hemorrhage

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ARTICLE INFO

Article history:
Received 14 Apr 2017
Received in revised form 16 Apr 2017
Accepted 19 Apr 2017
Available online 24 May 2017

Keywords:
Hypertensive cerebral hemorrhage
Minimally invasive hematoma evacuation
Nerve growth factor
Neurological function injury

ABSTRACT

Objective: To study the influence of minimally invasive hematoma evacuation combined with nerve growth factor preparation on neurological function injury in patients with hypertensive cerebral hemorrhage. **Methods:** A total of 112 patients with hypertensive cerebral hemorrhage who were treated in our hospital between July 2013 and February 2016 were collected, and according to random number table, they were divided into the control group (n=56) who underwent minimally invasive hematoma evacuation therapy and the observation group (n=56) who underwent minimally invasive hematoma evacuation combined with nerve growth factor preparation therapy. Serum contents of inflammatory mediators, nerve injury indexes and neurotransmitters were compared between two groups of patients before and after treatment. **Results:** Before treatment, there were no significant differences in serum contents of inflammatory mediators, nerve injury indexes and neurotransmitters between the two groups. After treatment, serum contents of inflammatory mediators such as CRP, PCT, IL-1β and IL-6 in observation group were lower than those in control group; serum contents of nerve injury indexes such as NSE, S100B, GEAP and MBP were lower than those in control group; serum contents of neurotransmitters such as SP, NPY, Glu and Asp were lower than those in control group while GABA and Gly were higher than those in control group. **Conclusion:** Minimally invasive hematoma evacuation combined with nerve growth factor preparation can effectively reduce neurological function injury, and has positive clinical significance.

1. Introduction

Hypertensive cerebral hemorrhage is one of the most serious complications of hypertension diseases, it mainly occurs under rage, excessive mental/physical activity and other conditions, the bleeding part is the most commonly in lenticulostriate artery, the main clinical manifestations include severe pain, nausea and vomiting as well as lateral limb dysfunction, and severe cases can cause central failure[1,2]. Minimally invasive hematoma evacuation is the main therapy for patients with hypertensive cerebral hemorrhage, which can early remove local brain hematoma and restore the blood supply to neurons[3]. Statistics show that there can still be different levels of intelligence, swallowing and limb dysfunction in the vast majority of patients after surgical treatment, and the root cause is nerve tissue damage. Nerve growth factor preparation is an important neurotrophin that can promote growth and differentiation of neurons, and adding exogenous nerve growth factor after hypertensive cerebral hemorrhage is considered to be the reliable means to reduce brain injury severity and accelerate the neural function repair[4]. In the research, minimally invasive hematoma evacuation combined with nerve growth factor preparation was used for the treatment of patients with hypertensive cerebral hemorrhage, and its role was explored from the aspects of neural function damage.

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Fund Project: Scientific Research Project of Deyang Science and Technology Bureau No: DYCC20160054.

2. Information and methods

2.1 General information

A total of 112 patients with hypertensive cerebral hemorrhage who were treated in our hospital between July 2013 and February 2016 were selected, and the patients and their families signed informed consent forms. According to random number table, the enrolled patients were divided into the control group (n=56) who received minimally invasive hematoma evacuation and the observation group (n=56) who received minimally invasive hematoma evacuation combined with nerve growth factor preparation. Control group included 30 male cases and 26 female cases that were 48-71 years old; observation group included 29 male cases and 27 female cases that were 49-73 years old. The gender and age distribution of the two groups were not statistically significant (P>0.05), and the hospital ethics committee discussed and approved the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) acute onset of consciousness loss and physical impairment; (2) diagnosed with cerebral hemorrhage by imageological examination; (3) with noninvasive systolic pressure ⩾160 mmHg; (4) time interval between onset and admission ⩽4 h. Exclusion criteria: (1) with history of cerebral hemorrhage and traumatic brain injury; (2) associated with neurological impairment diseases such as Alzheimer's or Parkinson's disease; (3) with history of nerve growth factor allergy; (4) associated with severe liver, liver and kidney dysfunction.

2.3 Therapy

Control group of patients received conventional minimally invasive hematoma evacuation, and the observation group of patients received nerve growth factor preparation therapy on the basis, specifically as follows: mouse nerve growth factor for injection (Wuhan Hitech Biological Pharmaceutical Co., Ltd., approved by S20060051) 30 μg dissolved in saline 2 mL, by intramuscular injection, 1 time/d, for 4 consecutive weeks.

2.4 Observation indexes

Before and after treatment, 2.0-3.0 mL cubital venous blood was extracted from two groups of patients at the same point in time, anti-coagulated and centrifuged at 4 ℃ to get supernatant and freeze it in the deep cryogenic refrigerator (Shanghai Juncheng Biotechnology Co., Ltd., the article number STC-156E) for test. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of inflammatory mediators, including C-reactive protein (CRP), procalcitonin (PCT), interleukin-1 β (IL-1 β) and interleukin 6 (IL-6). RIA was used to determine the contents of serum nerve damage indexes, including neuron-specific enolase (NSE), S100B protein (S100B), glial fibrillary acidic protein (GEAP) and myelin basic protein (MBP). ELISA was used to detect the serum contents of peptide neurotransmitters, including substance P (SP) and neuropeptide Y (NPY) as well as the contents of amino acid neurotransmitters, including glutamate (Glu), γ-aminobutyric acid (GABA), aspartic acid (Asp) and glycine (Gly).

2.5 Statistical methods

Professional statisticians were selected for data statistics in the study, and statistical software was SPSS 20.0. Inflammatory mediators, nerve injury indexes, neurotransmitters and other measurement data were in terms of mean ± standard deviation, comparison within group was by paired t test and comparison between groups was by grouping t test. P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Inflammatory mediators

Before and after treatment, comparison of serum inflammatory mediators CRP (mg/L), PCT (pg/mL), IL-1 β (pg/mL) and IL-6 (pg/mL) contents between two groups of patients was as follows: before treatment, differences in serum CRP, PCT, IL-1 β and IL-6 contents were not statistically significant between two groups of patients (P>0.05); after treatment, serum CRP, PCT, IL-1 β and IL-6 contents in both groups were lower than those before treatment, serum CRP, PCT, IL-1 β and IL-6 contents in observation group were lower than those in control group, and differences were statistically significant (P<0.05), shown in Table 1.

Table 1.

Comparison of serum inflammatory mediator contents before and after treatment.

Groups	n	Time	CRP	PCT	IL-1 β	IL-6
Control group	56	Before treatment	34.27±4.19	183.29±21.74	71.38±8.95	92.48±10.53
		After treatment	20.38±2.95*	79.34±9.15*	43.27±6.39*	50.71±6.32*
Observation group	56	Before treatment	34.38±4.08	182.68±20.85	71.49±9.12	92.74±10.39
		After treatment	9.62±1.15$^{*\#}$	41.66±5.92$^{*\#}$	18.35±2.18$^{*\#}$	29.34±4.15$^{*\#}$

Note: compared with same group before treatment, $^{*}P$<0.05; compared with control group after treatment, $^{\#}P$<0.05.

3.2. Nerve injury indexes

Before and after treatment, comparison of serum nerve injury indexes NSE (μg/L), S100B (μg/L), GEAP (ng/L) and MBP (μg/L) contents between two groups of patients was as follows: before treatment, differences in serum NSE, S100B, GEAP and MBP contents were not statistically significant between two groups of patients (P>0.05); after treatment, serum NSE, S100B, GEAP and MBP contents in both groups were lower than those before treatment, serum NSE, S100B, GEAP and MBP contents in observation group were lower than those in control group, and differences were statistically significant (P<0.05), shown in Table 2.

3.3 Neurotransmitters

Before and after treatment, comparison of serum neurotransmitters SP (μg/mL), NPY (μg/L), Glu (μmol/L), GABA (μmol/L), Asp (μmol/L) and Gly (μmol/L) contents between two groups of patients was as follows: before treatment, differences in serum SP, NPY, Glu, GABA, Asp and Gly contents were not statistically significant between two groups of patients (P>0.05); after treatment, serum SP, NPY, Glu and Asp contents in both groups were lower than those before treatment while GABA and Gly contents were higher than those before treatment, serum SP, NPY, Glu and Asp contents in observation group were lower than those in control group while GABA and Gly contents were higher than those in control group, and differences were statistically significant (P<0.05), shown in Table 3.

4. Discussion

Minimally invasive hematoma evacuation is the main operative method for clinical treatment of hypertensive cerebral hemorrhage, which can maximize the removal of intracranial hematoma as well as reduce the edema oppression to surrounding normal tissue and inhibit further progress of nerve injury[5]. But minimally invasive hematoma evacuation alone is weak for regeneration and repair of already damaged nerve tissue, which leaves behind different degree of postoperative nerve function damage in a significant portion of patients. Nerve growth factor (NGF) plays an important role in the process of nerve growth, and cell experiments in vitro have confirmed that after neuron damage, NGF can effectively reduce the apoptosis rate and alleviate nerve function damage[6,7]. Mouse nerve growth factor is the NGF preparation extracted from mouse submandibular gland, and in vivo rat experiment results have confirmed that it can improve the limb dysfunction caused by toxic peripheral neuropathy[8]. In the research, minimally invasive hematoma evacuation combined with mouse nerve growth factor was used for the treatment of patients with hypertensive cerebral hemorrhage in order to clarify the relief on nerve injury.

After cerebral hemorrhage, excessive release of inflammatory mediators is involved in neuron damage process, CRP belongs to the acute phase protein, it is released into the blood early after cerebral hemorrhage and detected, and it is a sensitive index to reflect nerve function damage degree[9]. PCT is a new type of inflammatory factor, its content remains stable in the mild infectious diseases, but after severe infection or traumatic event happens, PCT is massively secreted and becomes the important auxiliary index for judging the damage degree[10]. IL-1 β and IL-6 are the typical pro-inflammatory factors, and massive CRP synthesis can accelerate the increase of their secretion, induce mononuclear macrophage accumulation in the damaged area and further the damage neuron membrane. In the study, serum levels of inflammatory mediators were compared between the two groups before and after treatment, and it was found that serum CRP, PCT, IIL-1 β and IL-6 levels of both groups after treatment were lower than those before treatment, and the above serum levels of observation group were lower than those of control group, it indicates that adding mouse nerve growth factor on the basis of minimally invasive hematoma evacuation can effectively reduce the inflammatory response, and this could be the one of the

Table 2.

Comparison of serum nerve injury index contents before and after treatment.

Groups	n	Time	NSE	S100B	GEAP	MBP
Control group	56	Before treatment	51.27±6.09	1.46±0.19	22.37±3.18	7.39±0.84
		After treatment	27.84±3.41*	1.05±0.13*	13.28±2.05*	4.11±0.49*
Observation group	56	Before treatment	50.53±6.27	1.43±0.18	22.49±3.09	7.34±0.82
		After treatment	15.92±2.18*#	0.68±0.08*#	7.16±0.85*#	2.09±0.31*#

Note: compared with same group before treatment, *P<0.05; compared with control group after treatment, #P<0.05.

Table 3.

Comparison of serum neurotransmitter contents before and after treatment.

Groups	n	Time	Peptide neurotransmitters		Amino acid neurotransmitters			
			SP	NPY	Glu	GABA	Asp	Gly
Control group	56	Before treatment	6.38±0.79	254.38±30.19	89.34±10.18	4.12±0.45	40.27±5.18	61.48±7.53
		After treatment	4.11±0.53*	150.36±21.28*	42.94±5.61*	7.09±0.85*	21.46±3.04*	85.82±9.17*
Observation group	56	Before treatment	6.31±0.78	251.47±29.53	89.48±9.74	4.09±0.41	39.85±4.79	61.39±7.28
		After treatment	2.09±0.31*#	94.37±10.19*#	26.46±3.41*#	11.19±1.56*#	10.78±1.95*#	97.64±10.83*#

Note: compared with same group before treatment, *P<0.05; compared with control group after treatment, #P<0.05.

important mechanisms for it to protect the brain.

After nerve injury occurs, a variety of factors pecifically existing in the central nervous system can be abnormally secreted into the blood circulation and become the specific indexes to judge the neural function. NSE is mainly secreted and synthesized by neurons and neuroendocrine cells, S100B is the marker protein of the glial cells, and after the nerve cell membrane damage, NSE and S100B leak out from the cells, cross the blood-brain barrier and enter into the systemic circulation, leading to the increase in above index contents in serum[11,12]. GEAP is an acidic protein that monitors the neuropathy of the central nervous system and its generation increases in damaged neurons. MBP is the strongly basic membrane protein synthesized by oligodendrocytes in central nervous system, it is massively released into the cerebrospinal fluid when the nerve damage caused by trauma involves myelin, and a few enters into the blood stream[13]. In the study, serum levels of above nerve damage indexes were compared between the two groups before and after treatment, and it was found that serum NSE, S100B, GEAP, and MBP levels of both groups after treatment were lower than those before treatment, and serum NSE, S100B, GEAP and MBP levels of observation group were lower than those of control group, explaining that joining mouse nerve growth factor therapy can further optimize the nerve function and reduce the damage to neurons and the surrounding tissue.

Neurotransmitter is closely associated with the nervous system function, previous study points out that the peptide neurotransmitter contents increase significantly in patients with acute phase of cerebral hemorrhage, and the degree of specific increase is consistent with nerve damage degree[14,15]. Amino acid neurotransmitters include excitatory amino acids and inhibitory amino acids, and the excitatory amino acids Glu and Asp content increase while the inhibitory amino acids GABA and Gly content decrease inpatients with acute phase of cerebral hemorrhage, which can further cause nerve damage[16,17]. In the study, serum neurotransmitter levels were compared between two groups of patients before and after treatment, and it was found that the serum peptide neurotransmitters SP and NPY as well as excitatory amino acids Glu and Asp levels decreased while inhibitory amino acids GABA and Gly contents increased in both groups after treatment, and the changes in serum levels of above neurotransmitters in observation group were greater than those in control group, it confirms that minimally invasive hematoma evacuation combined with mouse nerve growth factor treatment can effectively optimize the balance of neurotransmitter levels in patients, and this also is the essential reason why it ultimately improves patients′ neural function.

Thus it is clear that minimally invasive hematoma evacuation combined with mouse nerve growth factor preparation helps to reduce the systemic inflammatory response and nerve damage, and optimize the neurotransmitter levels in patients with hypertensive cerebral hemorrhage, it is a kind of practical therapy, and it is worthy of popularization and application in clinical practice in the future.

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