Revista Argentina de Clínica Psicológica
2020, Vol. XXIX, N°3, 504-508
DOI: 10.24205/03276716.2020.749

Clinical Efficacy Study of Edaravone on the Treatment of Severe Acute Cerebral Infarction

Xiang Chen[a], YuQin Wang[a], Yeerkebayi.Ashabaiyi[b],YueChun Wang[a] ,YuanYuan Zhang[a*],YuQing Liu[b*]

Abstract

Background: Nowadays, cerebral infarction is becoming a more and more frequently-occurring disease in clinical practice, it is characterized by acute onset and rapid disease progression in clinical practice, the high disability rate and mortality of this kind of disease highlights the significance of the treatment. Edaravone, which is newly developed and considered as a free radical scavenger, has a significant protective effect on neurons.

Objective: To study the efficacy of Edaravone in clinical on the treatment of severe acute cerebral infarction.

Method: Patients (n = 62) with severe acute cerebral infarction and received treatment in our department from February 2015 to August 2017 were included. They were divided into a treatment group and a control group, conventional treatment like intracranial pressure drop, water-electrolyte imbalance correction, intravenous thrombolysis therapy was used for the control group; Edaravone was given to the treatment group on the basis of the treatment for the control group. The clinical efficacy, the incidence of adverse reactions, ADL score and NIHSS score before and after treatment were compared and observed between the two groups.

Result: The total effective rate in treatment group was obviously higher compared with that of the control group ($P < 0.05$); but no difference in NIHSS and ADL score was found before treatment ($P > 0.05$), while the NIHSS and ADL score of treatment group were higher ($P < 0.05$) compared with that of reference group after the treatment.

Conclusion: Edaravone was effective on the of patients with severe acute cerebral infarction, which significantly improved the clinical symptoms, the condition and daily living quality of patients with neurological deficit, it is worthy of clinical application and promotion.

KeyWords：Acute Cerebral Infarction, daily living scale, ADL

1. Introduction

Cerebral infarction is a common and frequently-occurring disease in clinical practice and usually caused by regional brain tissue blood supply disorders, leading to brain tissue hypoxicischemic necrosis and thus resulting in clinical manifestations of neurological deficits. Cerebral infarction can be divided into different categories, such as cerebral thrombosis, cerebral embolism and lacunar infarction according to different pathogenesis.

a Department of Neurology, Affiliated Hospital of Nan Tong University, Nan Tong 226001, China
b Department of Neurology, The Friendship Hospital of Ili Kazakh Autonomous Prefecture Yining 835000, China
#Co-authors: These authors contirbute same to this work.
**Corresponding Author: Yuan Yuan Zhang, YuQing Liu*
Address: No. 20, Xisi Road, Nantong City, Jiangsu Province
Email: winter_sun0101@126.com; doctorlyq@sina.com

Cerebral thrombosis is considered one of the most frequent cerebral infarctions, occupied about 60% of the total, which is associated with diabetes, obesity, hypertension and rheumatic heart arrhythmia (Wang X. et al., 2018). The disease frequently occurs in the middle-aged and elderly people (50~60 years old) with a slightly higher incidence in men than in women. Cerebral infarction is usually associated with risk factors such as arteriosclerosis, hypertension, hyperlipidemia, or diabetes or corresponding systemic nonspecific symptoms. The ischemic cascade after cerebral infarction allows calcium ions to accumulate in brain cells and generate oxygen free radicals in large amounts at the same

time. The prodromal symptoms of cerebral infarction are not specific, and some patients may have the manifestations of transient ischemic attack such as dizziness, temporary limb numbness, and weakness. However, these symptoms are often ignored by patients and their families due to their short duration and mild degree. It is characterized by acute onset and rapid disease progression in clinical practice, the high disability rate and mortality of this kind of disease highlight the significance of the treatment.

The drug treatment of cerebral infarction mainly includes two aspects: first, it mainly includes the drug treatment for controlling blood pressure, blood glucose and blood lipid level; second, it includes thrombolytic therapy, anti-platelet aggregation and anticoagulant therapy, neuropathy-protective agent, endovascular intervention therapy and surgical treatment. It was first suggested in the literature that cerebral ischemia plausibly activates the free-radical reactions pathologically in the central nervous systems (CNS) (Ewelina G. et al., 2017). The mechanism of the above finding was further discussed, at present, thrombolytic therapy and neuroprotection are mainly used in the treatment (Zheng M. et al., 2020), the efficacy, as well as safety, has been confirmed by clinical studies.

Previous studies have indicated that Edaravone can serve as the latest brain-protective agent in the cure of acute cerebral infarction (Takei K. et al., 2017). Clinical studies have suggested that N-acetylaspartate (NAA) can work as a maker of surviving nerve cells, and the concentration of N-acetylaspartate has a sudden decrease at the beginning of cerebral infarction. Edaravone could inhibit the decrease of part of the cerebral blood flow in the treatment cerebral infarction, and the NAA content in the brain was obviously higher compared with that of the control group twenty-eight days after onset. Preclinical studies suggest that intravenous administration of Edaravone to rats after ischemia/ischemia-reperfusion not only prevents the progression of cerebral infarction, but also alleviates the concomitant neurological symptoms, plus inhibits delayed neuronal destruction. Mechanistic studies suggest that Edaravone may clear out the free radicals thus to activate the effect of lipid peroxidation, result in inhibiting oxidative damage in cells inside related to the brain (Takei K. et al., 2017) (Bhandari R. et al., 2018). In addition, Edaravone also has a significant protective effect on neurons (Okamura K. et al., 2014) (Sun Z. et al., 2019). Based on this, a comparison study was carried out to analyze the curative effect of Edaravone on acute cerebral infarction.

Herein, the collected data of sixty-two patients with acute cerebral infarction from February 2015 to August 2017 in our hospital were studied to figure out the clinical effects of Edaravone in the hospital treatment of patient cerebral infarction but in different conditions.

2. Information and Methods

2.1 General information

Patients (n = 62) with severe acute cerebral infarction treated in our department from 2015 to 2017 were included here. They are divided into two groups: a treatment group and a control group, and each group included thirty-one cases. There were 20 males and 11 females in the control group, who were at the age of 46−74, with a mean of 54.34 ± 4.62; the number of case in the treatment group is 22 and 9 for men and women and the patients were at the age of 47−76, with a mean of 56.45 ± 4.73. The general data showed strong inter-group comparability ($P > 0.05$).

Inclusion criteria: All the patients here were diagnosed in line with the diagnostic criteria established by WHO, and all of them voluntarily signed the informed consent and none of them was combined with other serious organ diseases such as heart, liver, and kidney. Exclusion criteria: patients who do not conform to the diagnostic criteria established by WHO; Onset time greater than 72 hours; patients who were completely unconscious; patients who do not adapt to Edaravone treatment; patients with other severe organ diseases and patients who refuse to sign the consent form and refuse treatment.

2.1. Method

Conventional treatment like intracranial pressure drop, water-electrolyte imbalance correction, and intravenous thrombolysis therapy was used for the control group, Edaravone (SFDA approval number: H20080495; drug specification: chemical medicine; 20 mL: 30 mg; Kunming Jida Pharmaceutical Co., Ltd., Kun'ming, China) was given to the treatment group based on the treatment for the control group. In particular, 30 mg of Edaravone added into normal saline (NS) was intravenously injected twice per day, both treatments were given two weeks other cerebral protective agents and anticoagulants were prohibited during the treatment.

2.2. Observational indexes

Efficacy evaluation included: marked effect: the clinical symptoms and performance of the patients were significantly improved after treatment, the NIHSS score was reduced to 90% or above than before treatment, and no disability occurred; effective: the clinical symptoms and performance of the patients were improved after treatment, the NIHSS score was reduced to 45% or above than before treatment, and the disability level reached grade 1-3; ineffective: after treatment, the patient's condition has no change, or even showed signs of aggravation.

The National Institutes of Health Stroke Scale (NIHSS) and activities of daily living scale (ADL) were used to evaluate the nerve defect score and the activities of daily living scores, respectively. The NIHSS score included visual field, gaze, sensation, language, level of consciousness, facial paralysis, limb disorder, etc. Each item was assigned a score of 0-2 or 0-3. The higher the score, the more severe the degree of neurological deficit was. The ADL score covered 14 scoring items. A total score of less than 16 was considered to be completely normal, otherwise, it indicates that the existence of various degrees of decline in body function.

2.3. Statistical Analysis

SPSS 21.0 was employed to carry out the analysis. The total effective rate and the incidence rate of adverse reactions were analyzed by the χ^2 test using enumeration data. ADL and NIHSS scores were measured by the t-test. It is identified as a significant difference if $P < 0.05$.

3. Results

3.1 Comparison of the total treatment efficiency

The total effective rates of the control group and the treatment group were 48.38% and 96.77%, respectively. Their intergroup differences were significant ($P < 0.05$), as shown in Table 1.

3.2. Comparison of the NIHSS and ADL scores

The results of the analysis showed no distinct inter-group difference in NIHSS and ADL score before treatment (P > 0.05); but after treatment, the NIHSS and ADL score in the treatment group were significantly higher compared with those of the reference group (P < 0.05), as shown in Table 2 and Table3.

3.3 Comparison of the adverse reaction rates of the two groups

The adverse reaction rates of 12.9% and 19.35% was calculated for the control group and the treatment group, respectively. No obvious inter-group difference (P > 0.05) was found in the adverse reaction rates, as shown in Table 4.

Table 1: **Comparison of Edaravone efficacy [n (%)]**

Edaravone efficacy	Partially efficient	Excellent efficient	Ineffective percentage	Total treatment
Control (31)	10 (32.25)	5 (16.13)	16(51.61)	15(48.38)
Treatment (31)	21(67.74)	9 (29.03)	10(32.25)	30(96.77)
χ2				13.821
P				0.000

Table 2: **Comparison of the NIHSS scores (□ s, score)**

Treatments	Before treatment	After treatment
Control (31)	22.27 ± 9.45	19.56 ± 4.83
Treatment (31)	22.21 ± 6.23	13.65 ± 2.14
t	0.0215	2.5643
P	0.8213	0.000

Table 3: **Comparison of the ADL scores of (□ s, score)**

Treatments	Before treatment	After treatment
Control (31)	12.56±2.23	6.21±2.62
Treatment (31)	12.75±2.42	4.34±2.21
t	0.954	2.591
P	0.213	0.014

Table 4: **Comparison of the adverse reactions [n (%)]**

Adverse reactions	Nausea	Vomiting	Dizziness	Adverse reaction
Control (31)	2(6.45)	1(3.22)	1(3.23)	4(12.9)
Treatment (31)	3(9.68)	2(6.45)	1(3.23)	6(19.35)
χ^2				0.4421
P				0.5230

4. Discussion

Cerebral infarction, previously called cerebral arterial thrombosis. Cerebral infarction was previously called cerebral arterial thrombosis. It represents the ischemic necrosis or softening of localized brain tissue, which is resulted from cerebral blood supply disorder, ischemia, and hypoxia. The common clinical types of cerebral infarction are cerebral thrombosis, lacunar infarction, and cerebral embolism. Cerebral infarction occupies 80% of all strokes. The ischemic cascade after cerebral infarction allows calcium ions to accumulate in brain cells and generate oxygen free radicals in large amounts at the same time. The main clinical features were sudden collapse, unconsciousness, hemiplegia, speech disorder and mental retardation. Cerebral infarction not only causes a big threat to human health and life but also brings great pain and heavy burden to patients, families and society. Cerebral infarction is a common disease in cerebrovascular disease, its acute onset, and rapid disease progression often cause great harm to the health of patients. In addition, cerebral infarction has a high mortality and disability rate, which may endanger the life safety of patients, therefore, it is critical to perform treatment for this disease as soon as possible (Coutts S.B. et al., 2018). Cerebral infarction is a kind of highly risky disease that might lead to disability or even death. General therapeutic principles are as follows: strong recommendation for early-stage treatment, intravenous thrombolytic therapy as far as possible within 4.5 hours of onset, and appropriate acute phase endovascular intervention in hospitals with conditions within 6-8 hours of onset; determine individualized and integrated treatment plan, adopt corresponding targeted treatment according the genetic risk factors, order of severity, and so on. When those efforts were combined with help from other sections, such as rehabilitation and nursing to reach a cooperative and integrated therapy so that the further improvements in the therapeutic effect can be achieved.

Thrombolytic therapy and neuroprotection are often used while treating the severe acute cerebral infarction in the hospital (Yamashita T. et al., 2015). Edaravone has a low molecular weight and therefore it is easy to crosses the blood-brain barrier (Li Q. et al., 2017) and as a free radical scavenger, Edaravone can supply electrons to free radical after intravenous infusion, then remove the active hydroxyl group in the brain, give regulation and inhibition to lipid peroxidation of dying genes and cells and protect cerebrovascular endothelial cells, so that cerebral ischemia symptoms, cerebral edema and brain tissue damage caused by cerebral ischemia can be alleviated (Ren Y. et al., 2015).

The analysis in this work told that no obvious inter-group difference can be found ($P > 0.05$) for the adverse reaction's incidence, but the ALD, FMA, NIHSS scores and total treatment efficiency are significantly improved after the treatment of Edaravone ($P < 0.05$). These findings indicate that Edaravone has a good clinical effect in curing severe acute cerebral infarction thus to improve the condition and daily living quality of patients with neurological deficits, moreover, Edaravone has high safety and fewer adverse reactions, is worthy of clinical promotion.

References：

Wang X, Shen B, Sun D, Cui X. (2018). Aspirin ameliorates cerebral infarction through regulation of TLR4/NFkappaBmediated endoplasmic reticulum stress in mouse model. *Molecular medicine reports*, 17(1):479-487.

Ewelina G, Krzysztof S, Marek M, Krzysztof K. (2017). Blood free Radicals Concentration Determined by Electron Paramagnetic Resonance Spectroscopy and Delayed Cerebral Ischemia Occurrence in Patients with Aneurysmal Subarachnoid Hemorrhage. *Cell biochemistry and biophysics*, 75(3-4), 351-358.

Zheng M, Wang X, Yang J, Ma S, Wei Y, Liu S. (2020). Changes of complement and oxidative stress parameters in patients with acute cerebral infarction or cerebral hemorrhage and the clinical significance. *Experimental and therapeutic medicine*, 19(1), 703-709.

Takei K, Watanabe K, Yuki S, Akimoto M, Sakata T, Palumbo J. (2017). Edaravone and its clinical development for amyotrophic lateral sclerosis. *Amyotrophic lateral sclerosis & frontotemporal degeneration*, 18(sup1), 5-10.

Bhandari R, Kuhad A, Kuhad A. (2018). Edaravone: a new hope for deadly amyotrophic lateral sclerosis. *Drugs of today (Barcelona, Spain*: 1998), 54(6), 349-360.

Okamura K, Tsubokawa T, Johshita H, Miyazaki H, Shiokawa Y. (2014). Edaravone, a free radical scavenger, attenuates cerebral infarction and hemorrhagic infarction in rats with hyperglycemia. *Neurological research*, 36(1), 65-69.

Sun Z, Xu Q, Gao G, Zhao M, Sun C. (2019). Clinical observation in edaravone treatment for acute cerebral infarction. *Nigerian journal of clinical practice*, 22(10), 1324-1327.

Coutts SB, Berge E, Campbell BC, Muir KW, Parsons MW. (2018). Tenecteplase for the treatment of acute ischemic stroke: A review of completed and ongoing randomized controlled trials. *International journal of stroke: official journal of the International Stroke Society*, 13(9), 885-892.

Yamashita T, Sato T, Sakamoto K, Ishii H, Yamamoto J. (2015). The free-radical scavenger edaravone accelerates thrombolysis with alteplase in an experimental thrombosis model. *Thrombosis research*, 135(6), 1209-1213.

Li Q, Ding S, Wang YM, Xu X, Shen Z, Fu R, Liu M, Hu C, Zhang C, Cao Q, et al. (2017). Age-associated alteration in Th17 cell response is related to endothelial cell senescence and atherosclerotic cerebral infarction. *American journal of translational research*, 9(11), 5160-5168.

Ren Y, Wei B, Song X, An N, Zhou Y, Jin X, Zhang Y. (2015). Edaravone's free radical scavenging mechanisms of neuroprotection against cerebral ischemia: review of the literature. *The International Journal of Neuroscience*, 125(8), 555-565.