Tropical Journal of Pharmaceutical Research December 2021; 20 (12): 2645-2651
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v20i12.27

Original Research Article

Combination of lateral ventricular puncture and catheterization with different doses of urokinase in the treatment of ventricular hemorrhage under CT multimodal imaging

Zhifu Song[1], Yulan Gan[2], Xueping Huang[1], Xiaolin Huang[1], Gonghong Liu[1], Bing Kong[1], Wenyou Wu[1]*

[1]Department of Neurosurgery, [2]Department of Neonatology, Luzhou People's Hospital, Luzhou 646000, Sichuan Province, China

For correspondence:* ***Email:* *hdcs2f@163.com;* ***Tel:*** *+86 18090168021*

Sent for review: 17 July 2020 *Revised accepted: 29 November 2021*

Abstract

Purpose: *To study the clinical effectiveness of lateral ventricular puncture and catheterization in combination with urokinase in the treatment of intraventricular hemorrhage (IVH) under computed tomography (CT) multimodal imaging.*
Methods: *Eighty-four IVH patients were selected and assigned to high- and low-dose urokinase groups. The clinical efficacy of the combination of lateral ventricle puncture and drainage at different doses of urokinase under CT multimodal imaging in the treatment of IVH, was determined.*
Results: *Compared with the low-dose urokinase group, postoperative waking time, postoperative extubation time and discharge time in the high-dose group were markedly better in high-dose urokinase group, while GCS score after treatment was lower in the high-dose group, with higher total effectiveness in the high-dose urokinase group. There was a significantly higher hematoma clearance in the high-dose group on the 3rd day of treatment ($p < 0.001$), while the total incidence of postoperative complications were markedly lower in the high-dose group ($p < 0.05$).*
Conclusion: *The combination of lateral ventricular puncture and drainage with high-dose urokinase under CT multimodal imaging enhances the recovery of consciousness in IVH patients. Therefore, the combined treatment has great potentials for clinical application.*

Keywords: *CT multimodal imaging, Lateral ventricular puncture, Catheterization, Urokinase, Ventricular hemorrhage (IVH)*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Intraventricular hemorrhage (IVH) is a type of cerebrovascular disease characterized by acute onset and rapid development. Without timely diagnosis and treatment, it is prone to severe complications such as intracranial hypertension, hydrocephalus and cerebral vasospasm, thereby endangering the lives safety of patients [1,2].

The removal of neuro-endoscopic hematoma is a surgical approach for treating IVH. Neuro-endoscopy provides a clear vision for doctors and enables them to directly visualize the panorama of the ventricles in patients, so as to quickly remove acute hydrocephalus and reduce intracranial pressure.

However, being a minimally invasive treatment method, this surgery has the disadvantages of limited canal diameter, frequent postoperative infection, and ineffectiveness in stopping bleeding in deep operations, all of which affect the therapeutic effect [3,4]. Lateral ventricle puncture and drainage has the advantages of being a simple and fast operation which causes minimal damage to brain tissue. It is a treatment method with relatively advanced technology which is often used in many studies as an emergency measure for the treatment of IVH. However, simple lateral ventricle puncture and drainage has the disadvantages of low hematoma clearance rate and blockage of drainage tube [5]. Urease, an enzyme protein obtained from human kidney tissue culture, is used to prevent thrombosis.

At present, there is no literature on the treatment of IVH with lateral ventricle puncture and drainage in combination with different doses of urokinase under CT multimodal imaging. In this study, the clinical data of IVH patients treated with lateral ventricle puncture and drainage in combination with different doses of urokinase under CT multimodal imaging were analyzed. This was with a view to investigating the therapeutic effect of different doses of urokinase perfusion on IVH so as to provide a new direction for the clinical treatment of the disease.

METHODS

General patient information

Eighty-four IVH patients who received treatment in our hospital from June 2018 to June 2021 served as subjects in this study. They were assigned to high-dose and low-dose urokinase groups, with 42 patients per group. The study was approved by the institutional ethical committee, and followed the guidelines of Declaration of Helsinki [6].

Inclusion criteria

Patients who were diagnosed with IVH after cranial CT, coronal and sagittal reconstruction, and CTA, and patients with no history of trauma before onset were included in this study. The study received approval from the ethical committee of Luzhou People's Hospital (approval No. 20180416). The aim of the investigation was explained to the subjects and their families, and signed informed consent was obtained from them.

Exclusion conditions

Patients with severe coagulation disorders, and subjects whose conditions were complicated with aneurysm or cerebrovascular malformation, cerebral infarction and parenchymal hemorrhage, with no indication for operation, were excluded from the study. Moreover, patients with respiratory and circulatory failure were excluded.

Treatments

Subjects in both groups were treated with lateral ventricle puncture and drainage under CT multimodal imaging. After general anesthesia, the puncture point and puncture angle of the patients were accurately located and marked in line with the three-dimensional reconstruction technology of head CT multimodal imaging. Routine disinfection and draping were performed, and the skulls were drilled. The puncture was performed along the puncture direction made before surgery, and the dura mater was drilled. A brain puncture needle was used to puncture along the imaginary line direction of the external auditory canal to a depth of about 5 cm. When old blood or reddish cerebrospinal fluid showed in the puncture needle, it confirmed that the needle had entered the lateral ventricle.

After withdrawal of the brain puncture needle, a drainage tube was inserted along the positioning channel left by the needle into the lateral ventricle, and the guide wire was removed when bloody cerebrospinal fluid appeared. The drainage was properly fixed at a depth of about 6-7 cm. The brain drainage device was connected, and the tube was linked to a plastic three-way valve placed at 10-15 cm above the lateral ventricle. The hematoma was laterally punctured and catheterized for urokinase injection, and the lateral ventricle needed only a routine puncture to drain the cerebrospinal fluid [7,8]. After successful puncture of the lateral ventricle, the drainage tube was drawn out more than 7 cm away from the puncture point through the subcutaneous tunnel with a teasing needle.

The high-dose group was given intermittent intraventricular injection of urokinase after surgery (6 h after onset), and 5 mL of normal saline mixed with 80,000 U of urokinase was injected into the ventricle. The injector was connected with a three-way valve, and then the

valve was opened. The urokinase solution was slowly injected into the lateral ventricle through the drainage tube. After the injection, the valve was closed. The operations were performed strictly under aseptic conditions, each one for 12 h. In order to ensure adequate contact between the drug and the blood clot, the drainage tube was clamped for 2 h after each injection, and then opened. If blockage was found in the drainage tube, 0.9 % sodium chloride solution was used to rinse the lateral ventricle slowly until the blood color became lighter. The intensity of rinsing was not high (twice a day), and the injection volume used each time was less than 10 ml. After surgery (6 h after onset), 5 mL of normal saline mixed with 20,000 U of urokinase was injected into the ventricle in the low-dose group. The injection and rinsing methods were the same as described above. Both groups were treated continuously for 7 days.

Assessment of treatment indexes

Surgical cost, as well as time lags for postoperative awakening, postoperative extubation, and discharge were determined. *Glasgow Coma Scale (GCS)* [9] was used to evaluate the degree coma in the two groups before and after treatment, with a total score of 15 points. The higher the score, the better the patients' consciousness. Barthel index score [10] was used to evaluate ability of independent living of patients in the two groups at different times. At admission, 3rd day, and 7th day of treatment were designated T1, T2 and T3, respectively. The scale had 100 points as full score, with scores higher than 60 points indicating that the patients could basically take care of themselves, while scores of 40 - 60 points indicated that the patients needed some help in their lives. Patients who scored 20-40 points needed much help in their lives, while scores less than 20 points indicated that the patients could not take care of themselves at all.

Efficacy evaluation

If the GCS scores of patients increased by 45-100 %, the treatment was markedly effective. Increases of 19 - 44 % indicated that the treatment was effective, while an increase no more than 18 %, or aggravation of the condition, indicated ineffective treatment.

$$TE = ME + E \quad \text{.....(1)}$$

where *TE* = total effectiveness; *ME* = markedly effective; *E* = effective.

The percentage hematoma clearance, hematoma clearance time and postoperative complications were determined in both groups on the 1st day and 3rd day of treatment.

Statistical analysis

The SPSS21.0 software was selected for the analysis and processing of the experimental data, while graphics were prepared with GraphPad Prism 7. The count data are presented as [n (%)], and were tested using χ^2. Measurement data are presented as mean ± SD, and were analyzed using *t*-test. Values of $p < 0.05$ indicated statistical significance of differences.

RESULTS

Patient profiles

Table 1 shows that male/female proportion, average age, average BMI value, average bleeding volume, bleeding sites, underlying diseases, educational level and area of residence were comparable between the two groups ($p > 0.05$).

Postoperative waking time and extubation time, surgical cost and discharge time

Table 2 shows that surgical cost was similar in both groups. However, time lags for postoperative awakening, postoperative extubation and discharge were significantly better in the high-dose urokinase patients than in the low-dose urokinase subjects.

GCS score

Table 3 shows that there was no significant difference in the GCS scores between the two groups before treatment ($p > 0.05$). However, post-treatment GCS score was significantly higher in high-dose group than in low-dose group.

Barthel Index

There was no significant difference in Barthel index scores at T1 between the 2 groups. However, Barthel index scores at T2 and T3 were markedly higher in high-dose group than in low-dose group ($P < 0.05$; Figure 1).

Clinical efficacy

As presented in Table 4, there was markedly higher total effectiveness in high-dose group than that in low-dose group.

Hematoma clearance rate and clearance time

Percentage hematoma clearance was similar in the 2 groups of subjects on the 1st day of treatment. However, on the 3rd day, % hematoma clearance was markedly higher in high-dose urokinase subjects than in those given low-dose urokinase ($p < 0.001$; Table 5). Hematoma clearance time in the high-dose group was significantly lower than that in the low-dose group ($p < 0.05$).

Table 1: Comparison of clinical profile the two groups

Item	High-dose group (n = 42)	Low-dose group (n = 42)	χ^2/t	*P*
Gender			0.048	0.826
Male	24(57.14%)	23(54.76%)		
Female	18(42.86%)	19(45.24%)		
Average age (years)	54.27 ± 4.67	54.31 ± 4.69	0.039	0.969
Average BMI value(kg/m^2)	21.32 ± 1.25	21.34 ± 1.27	0.073	0.942
Average bleeding volume (mL)	42.43 ± 5.62	42.46 ± 5.65	0.024	0.981
Bleeding sites				
Thalamus and basal ganglia	13(30.95%)	11(26.19%)	0.233	0.629
Frontotemporal lobe or frontal lobe	16 (38.10%)	17 (40.48%)	0.050	0.823
Parietal lobe	13 (30.95%)	14 (33.33%)	0.055	0.815
Underlying diseases			0.049	0.825
Hypertension	25 (59.52%)	24 (57.14%)		
Diabetes mellitus	17 (40.48%)	18 (42.86%)		
Educational status				
University	12 (28.57%)	10 (23.81%)	0.246	0.620
Middle school	16 (38.10%)	13 (30.95%)	0.474	0.491
Primary school	14 (33.33%)	19 (45.24%)	1.248	0.264
Area of residence			0.449	0.503
Urban area	15 (35.71%)	18 (42.86%)		
Rural area	27 (64.29%)	24 (57.14%)		

Table 2: Surgical cost, and times taken before postoperative awakening, postoperative extubation, and discharge in both groups

Group	Postoperative awakening time (min)	Postoperative extubation time lag (days)	Surgical cost (thousand yuan)	Discharge time lag (days)
High-dose group	23.34 ± 9.47	4.62 ± 0.21	4246.73 ± 253.52	15.24 ± 4.26
Low-dose group	31.25 ± 8.74	5.47 ± 0.34	4253.42 ± 254.15	18.32 ± 4.19
t	3.978	13.785	0.121	3.341
P	0.000	0.000	0.904	0.000

Data are presented as mean ± SD

Table 3: GCS scores before and after treatment in the two groups

Group	n	Before treatment	After treatment
High-dose	42	4.53±1.57	12.54±1.63
Low-dose	42	4.56±1.59	9.26±1.61
T_1		0.087	9.278
P_1		0.931	< 0.001

Data are presented as mean ± SD

Table 4: Total treatment effectiveness in both groups [n (%)]

Group	n	Markedly effective	Effective	Ineffective	Total effectiveness
High-dose	42	22 (52.38%)	17 (40.58%)	3 (7.14%)	92.86% (39/42)
Low-dose	42	17 (40.48%)	15 (35.71%)	10 (23.81%)	76.19% (32/42)
χ^2					4.459
P					＜0.05

Table 5: Percentage hematoma clearance and hematoma clearance time

Group	Hematoma clearance (%)		Hematoma clearance time (day)
	1st day of treatment	*3rd day of treatment*	
High-dose	54.23 ± 8.32	83.34 ± 6.35	3.73 ± 0.62
Low-dose	54.28 ± 8.16	76.32 ± 6.61	5.21 ± 0.58
t	0.028	4.963	11.297
P-value	0.978	0.000	0.000

Table 6: Comparison of postoperative complication incidents between the two groups [n (%)]

Group	Intracranial infection	Hydrocephalus	Re-hemorrhage	Total incidence (%)
High-dose	1 (2.38)	1 (2.38)	0 (0)	4.76 (2/42)
Low-dose	3 (7.14)	2 (4.76)	3 (7.14)	19.05 (8/42)
χ^2				4.087
P-value				0.043

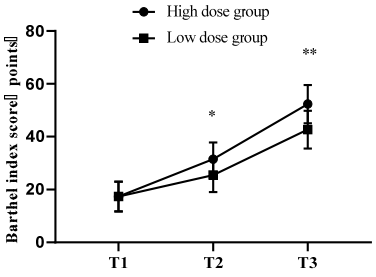

Figure 1: Comparison of Barthel Index scores at different times between the two groups. Values are presented as mean ± SD. *P < 0.05, Barthel index score at T2 in the high-dose urokinase subjects vs Barthel index score at T2 in low-dose urokinase subjects; **p < 0.05, Barthel index score at T3 in the high-dose group vs Barthel index score at T3 in the low-dose urokinase subjects

Incidence of postoperative complications

There were markedly lower incidents of postoperative complications in high-dose urokinase subjects than in the low-dose subjects ($p < 0.05$; Table 6).

DISCUSSION

Intraventricular hemorrhage (IVH), a critical disease seen regularly in clinics, is one of the major causes of disability and mortality in middle-aged and elderly people. The disease (IVH) causes compression of the surrounding brain tissues in patients, impedes cerebral blood circulation, and damages the blood-brain barrier [11]. At the same time, the increase in hematoma decomposition products leads to an increase in intracranial pressure to some extent, and produces a cascade of reactions, thereby aggravating the condition of the patient. In addition, ventricular casting occurs when the ¾ of the ventricular system is filled with blood clot. This will lead to acute expansion of the ventricular system, compression of the brainstem and hypothalamus, and cerebral hernia, in severe cases [12,13].

Lateral ventricle puncture and drainage is better than conservative medical treatment. It quickly removes the hematoma from the ventricles of patients, decreases the compression to the surrounding tissues, effectively reduces the toxic effects of hematoma decomposition products on the brain tissues, and relieves the clinical symptoms of IVH. In addition, lateral ventricle puncture and drainage results in minimal damage to the cerebral cortex and deep nuclei of patients, and it is suitable for patients with combined multiple organ dysfunction, as well as elderly patients.

However, this surgery also has some limitations such as its ineffectiveness in bringing about rapid draining out of hematoma from the brain. If hematoma stays in the brain for a long time, the toxic effects may aggravate secondary brain injury in patients, impair neurological function, and affect treatment outcomes [14].

Due to the limitations of lateral ventricle puncture and drainage, solid hematoma cannot flow out spontaneously through the drainage tube, and its forced removal causes brain parenchymal injury. Therefore, hematoma liquefaction is a necessary operation for efficient and rapid removal of hematoma. Indeed, minimally invasive surgery in combination with hematoma liquefaction has become an inevitable trend in the treatment of IVH [15,16]. Urokinase is a direct activator of fibrinolytic enzyme. It acts directly on the endogenous fibrinolytic system, leading to degradation of fibrin clots, thereby exerting a thrombolysis effect. A study [17] has found that the perfusion property of urokinase is dose-dependent. However, there is no standard for the

use and dose of urokinase at present. Therefore, there is need for further studies on the effective drug concentration of urokinase.

In this study, the IVH subjects were divided into low-dose and high-dose groups, and all patients underwent lateral ventricle puncture and drainage under CT multimodal imaging. In the postoperative urokinase perfusion phase, the high-dose group received 80,000U of urokinase, while the low-dose group received 20,000U of urokinase. In addition, the GCS score after treatment was markedly higher in high-dose urokinase subjects, and % hematoma clearance and hematoma clearance time in the high-dose group were significantly better than those in the low-dose group on the 3rd day of treatment.

In a study involving implementation of puncture and drainage, followed by 60,000U of urokinase perfusion for patients with cerebral hemorrhage, the post-treatment GCS score of patients was significantly higher than that of patients treated with 20,000U of urokinase perfusion after puncture and drainage [18]. This indicated that perfusion with 80,000U of urokinase was effective for IVH patients after lateral ventricle puncture and drainage under CT multimodal imaging.

Limitations of the study

The small sample size used may have a great impact on the results of this study. Therefore, it is necessary to expand the sample size and control the uncertain factors which might have affected the results obtained, so as to provide more reliable reference for clinical applications.

CONCLUSION

The use of lateral ventricular puncture and drainage in combination with high-dose urokinase perfusion therapy under CT multimode imaging improves the activities of daily living of IVH patients, increases hematoma clearance, and shortened hematoma clearance time, with significant efficacy and high safety. Therefore, the combined treatment has potentials for clinical application.

DECLARATIONS

Acknowledgement

This study was supported by Key R & D Program of Luzhou Science and Technology Planning Project (no. 2018-SYF-25); and Sichuan Medical Research Project (no. Q19032).

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Zhifu Song conceived and designed the study, and drafted the manuscript. Yulan Gan, Xueping Huang and Xiaolin Huang collected, analyzed and interpreted the experimental data. Gonghong Liu, Bing Kong and Wenyou Wu revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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