Effects of Prostaglandin E1 on Perihematomal Tissue after Hypertensive Intracerebral Hemorrhage

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Abstract-

Purpose: To observe the effects of Prostaglandin E1 (PGE1) on hematoma, perihematomal tissue and the impairment of neurological function in patients with hypertensive intracerebral hemorrhage (HICH).

Methods: A total of 40 patients with HICH were enrolled according to the inclusion criteria and randomly divided into two groups: the control group (n=20) and the PGE1 treatment group (n=20). In each group, ^{99m}Tc-ethyl cysteinate dimer (ECD) SPECT brain perfusion imaging was performed on days 5 and 20 after stroke, and the regional cerebral blood flow of the hematoma area, the proximal and distal regions of the hematoma surrounding tissue and the frontal and parietal lobe areas were calculated with semi-quantitative methods (the Ra value was shown as an uptake ratio). The volumes of hematoma and perihematomal tissue of the subjects (low-density areas around the hematoma as observed in the skull CT) were recorded by skull CT scan. Meanwhile, the NIHSS score for each patient was assessed upon admission and on the 5th, 12th, and 20th days of hospital stay. The mRS scores of each patient were recorded on the 1st and 20th days of admission. The NIHSS and mRS assessments were also performed three months following admission.

Results: In the PGE1 treatment group, the Ra values of the proximal and distal regions of the perihematomal tissue were significantly higher than those in prior treatment ($p<0.01$), and were significantly higher than the values in control group ($p<0.01$). The Ra values in the frontal and parietal lobes showed no significant differences before and after treatment ($p>0.05$). The volumes of hematomas in the PGE1 group were obviously reduced on the 12th and 20th days when compared with the 1st day and the 5th day, and these differences showed statistical significance ($p<0.01$). The volumes of hematomas in the control group were obviously reduced on the 20th when compared with the 1st day. On the 20th day, volumes of hematomas were significantly reduced in the PGE1 group than in control group ($p<0.01$). Moreover, the volume of perihematomal tissue in the PGE1 group was significantly reduced on the 20th day when compared with on the 5th day and the control group (all $p<0.01$). NIHSS scores showed statistically significant differences on the 20th day of admission and the follow-up three months later when the PGE1 treatment group and control group were compared ($p<0.05$). mRS scores in the three-month follow-up also showed statistically significant differences between the two groups ($p<0.01$).

Conclusion: The application of PGE1 therapy for patients with hypertensive intracerebral hemorrhage started on the 5th day after stroke was capable of enhancing rCBF of perihematomal tissue. This treatment significantly improved the prognosis of and recovery from neurological deficits in HICH patients.

Key Words: hypertensive intracerebral hemorrhage, perihematomal tissue, PGE1, treatment, prognosis

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INTRODUCTION

A series of pathological and physiological variations occurs in the organic and local brain tissue after hypertensive intracerebral hemorrhage, except in patients with surgical indications, and the therapy is mainly confined to maintain homeostasis and control symptoms. In fact, after cerebral hemorrhage, local brain tissue suffers from aggravated impairment induced by the decrease of regional cerebral blood flow (rCBF), inflammatory reaction, toxicity of neurotransmitters, increased levels of free radicals and various blood components such as thrombin[1-4]. Currently, how to suppress these factors to ensure maximum protection for the perihematomal tissue after the hypertensive intracerebral hemorrhage is a problem that warrants further focus and investigation for the treatment of intracerebral hemorrhages. PGE1 was generated in blood vessel endothelial tissue and was characterized by the expansion of small vessels as well as the inhibition of platelet aggregation and inflammatory reactions. Previous studies revealed the targeting of PGE1 to the region of pathological inflammatory and spastic blood vessels[5], which was able to specifically affect the local ischemia tissue and improve the ischemia and hypoxia of brain tissue so as to promote neurological function. Therefore, based on these pharmacological features of PGE1, it was applied in the patients with hypertensive intracerebral hemorrhage, and then its effects on the perihematomal tissue and the improvement of neurological impairment were observed.

Subjects

Between November 2007 and January 2009, a total of 40 patients with hypertensive intracerebral hemorrhage were admitted to our department and were selected for this study according to the diagnostic criteria formulated in the National Academic Conference of Cerebrovascular Disease in 1995. CT examination indicated hemorrhage of the basal ganglia with a volume of 10 to 30 mL. To be considered for the study, patients must have been experiencing this illness for the first time, without any case history of chronic liver disease or hemorrhagic disease as well as having a thrombocyte measurement greater than 100×10^9/L and normal blood coagulation. A history of cerebroventricular hemorrhage, subarachnoid hemorrhage and other cerebral hemorrhage of any systemic disease precluded patients from the study, as well as severe functional defects in cardiac, liver, or kidney systems, etc. The patients presented with aggravated pathogenic conditions, hematoma ruptures into the ventricles of the brain or subarachnoid hemorrhage were terminated from therapy. This study was approved by the Ethics Committee of Affiliated Hospital of Nangtong University. Informed consent was obtained from all the participants.

The patients were randomly assigned into two cohorts according to admission date. A cohort of 40 subjects was divided into a PGE1 group and a control group, consisting of 10 males and 10 females in the PGE1 group with an average age of 50.2 ± 12.2 and an average course of disease 10.2 ± 12.2h, as well as 10 males and 10 females in the control group with an average age of 52.1 ± 5.59 and an average course of disease 11.8 ± 5.35h.

Medication methods

According to their disease conditions, All patients admitted accepted regular therapy, including 1) dehydration and lowering intracranial pressure (mannitol, glycerol + fructose or albumin according to the intracranial pressure); 2) If systolic blood pressure ≥200 mmHg and/or diastolic blood pressure ≥110 mmHg, slow intravenous infusion of sodium nitroprusside (for acute phase) and oral antihypertensive agents (benazepril, valsartan or nifedipine extended release tablets, etc); 3) Antibiotics were used to control infection. Based on the regular therapy, on the 5th day after stroke, the patients in the PGE1 group accepted intravenous bolus injection of PGE1 at a dose of 10 μg/d continuously for 15 days.

SPECT imaging of rCBF (cerebral blood flow)

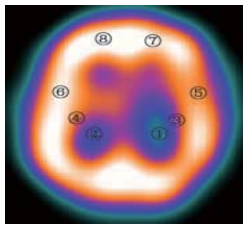
SPECT imaging of the rCBF of each patient was performed on the 5th and 20th days after stroke. Observation of patients was terminated upon the detection of rCBF, hematoma and volume of perihematomal tissues on the 20th day of admission.

SPECT methods

The SPECT (single photon emission computed tomography) instrument used was a Forte SPECT meter manufactured by the PHILIP company. The imaging agent was a (99m)Tc-ethyl cysteinate dimer (ECD) kit provided by the Jiangyuan Pharmaceutical factory of the Jiangsu Institute of Nuclear Medicine. The subjects received 400 mg potassium chlorate administered orally, followed by quiet rest for 30 min and avoidance of phono- and photostimulation for 5 to 10 min. After this, patients received intravenous elbow injections of 20 mCi of a developing agent (radiochemical purity >95%). Data acquisition was performed 15 to 30 min later with a 360-degree rotation and one frame per 6 degrees (acquisition matrix 128×128 and magnification 1.46). The horizontal coronal, sagittal and canthomeatal lines (OM) were manipulated in the reconstruction, and the thickness of each layer was approximately 10 mm.

Image manipulation: The image was treated with SPECT Multiview 1.0 postprocessing software.

Image analysis: 1) Visualization: The analysis was performed by two experienced doctors of nuclear medicine according to criteria that stipulated that areas with reduced or enhanced radioactivity and more than two layers and fault styles, as discerned by the unaided eye, were regarded as positive. 2) Semi-quantitative methods (6): The region of interest (ROI) model was applied to the following layers: the maximum hematoma area, the central region of the hematoma, proximal regions of the perihematomal tissue, the distal regions of normal surrounding tissues and the frontal and parietal lobes as well as the opposite side of the mirror imaging region. Uptake counts of the above areas were obtained using the regular 9-pixel cycle frame, and the uptake ratio (Ra) was defined as the index of observation. The rCBF was also calculated by semi-quantitative methods. Ra was calculated using the following equation: Ra = ROI radiocounting in the diseased side of region / ROI radiocounting in the opposite side of mirror imaging region. Ra values of ≤0.9 or ≥1.1 showed clinical significance. See Figure 1 (The ROI model analysis).



Graph 1. The region of interest (ROI) model analysis (basal ganglia region)

Calculation of the volume of hematoma and perihematomal tissue (Skull CT indicated low density areas of perihematomal tissue)

The calculation of hematoma volumes was accomplished by 1/2 ABC methods [7]. Absolute value of the volume of perihematomal tissue was calculated using the following equation: Absolute value of the volume of perihematomal tissue = CT scan indicated total focal zone (mixing volume of hematoma and perihematomal tissue)-volume of hematoma. The measurements of the volume of total focal zone were the same as those of the hematoma. Skull CT scans were performed on the 1st, 5th, 12th (7th day after PGE1 treatment), and 20th (20th day after PGE1 treatment) days after stroke.

Assessment of clinical neurological function and prognostic evaluation

The NIHSS (National Institutes of Health Stroke Scale) scores were recorded on the 5th, 12th, and 20th days of admission, respectively. The mRS scores were recorded by modified Rankin scale on the 1st of admission and after the therapy. The NIHSS and mRS assessments were also performed in the follow-up three months later.

Statistical methods

Measurements were expressed as mean±SEM ($\bar{x}\pm$S). Paired Student's t test and Pearson correlation analysis were applied with the SPSS 13.0 statistical package. Statistical significance was defined as $p<0.05$.

RESULTS

Baseline conditions of patients before enrollment in study groups (Table 1)

The comparison of sex, age, volume of hematoma and perihematomal tissues in two groups showed no statistically significant differences before treatment ($p>0.05$). Also, there was no difference in neurological defect scores. (Figure 2)

Results of SPECT brain perfusion imaging

Visualization

A total of 40 patients were first evaluated by SPECT brain perfusion imaging, which revealed that the radioactive distribution of ischemia in the hematoma, proximal regions and distal regions of perihematomal tissue was diminished when compared with the uninjured side. Regional cerebral blood flow (rCBF) was less than the uninjured side. The radioactive padding of the hematoma, proximal regions and distal regions of the

Table 1. *Baseline conditions of patients before enrollment in study groups*

Item	PGE1treatment group		Control group	
	Male	Female	Male	Female
Sex ratio	10(50%)	10(50%)	10(50%)	10(50%)
Age	50.2 ± 12.2		52.1 ± 10.2	
Ra value in the central area of hematoma	0.42 ± 0.06		0.41 ± 0.06	
Ra value in the proximal regions of perihematomal tissue	0.54 ± 0.06		0.53 ± 0.06	
Ra value in the distal regions of perihematomal tissue	0.67 ± 0.05		0.67 ± 0.06	
The frontal and parietal lobe area	0.95 ± 0.06		0.96 ± 0.05	
Volume of hematoma	23.82 ± 4.61		23.85 ± 4.53	
Volume of perihematomal tissue	6.01 ± 2.71		5.80 ± 2.28	
NIHSS scoring	11.85 ± 5.99		11.50 ± 5.76	
mRS scoring	3.30 ± 0.73		3.20 ± 0.86	

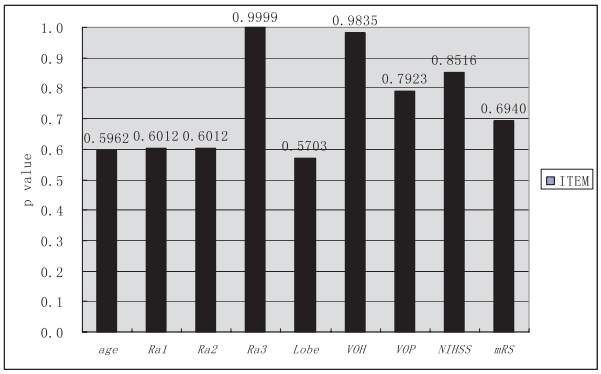
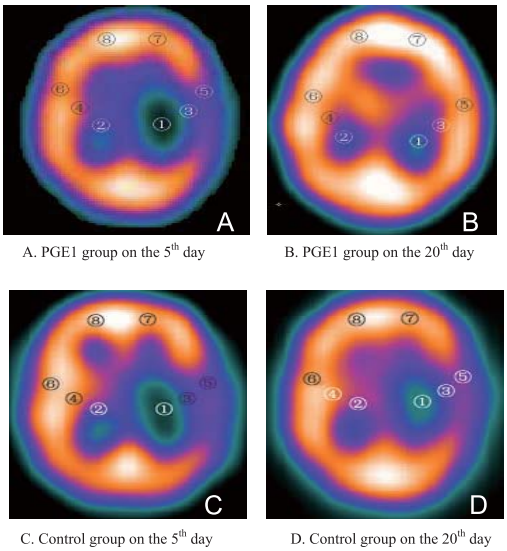


Figure 2 : The comparison of age, volume of hematoma and perihematomal tissue in two groups before treatment *Ra1:* Ra value in the central area of hematoma; *Ra2:* Ra value in the proximal regions of perihematomal tissue; *Ra3:* Ra value in the distal regions of perihematomal tissue; *Lobe:* The frontal and parietal lobe area; *VOH:* Volume of hematoma; *VOP:* Volume of perihematomal tissue



A. PGE1 group on the 5th day
B. PGE1 group on the 20th day
C. Control group on the 5th day
D. Control group on the 20th day

Graph 2. rCBF of patients in the two study groups on the 5th and 20th days

perihematomal tissue in the control group was not significant after treatment. The improvement of rCBF was also not significant; however, the radioactive padding of the hematoma, proximal regions and distal regions of the perihematomal tissue in the treatment group showed significant differences compared with before-treatment samples, and rCBF values were significantly improved (Graph 2).

Semi-quantitative analysis On the 20th day, in the PGE1 treatment group, the Ra values of the proximal and distal regions of the perihematomal tissue were significantly higher than those in prior treatment ($p<0.01$), and were significantly higher than the values in control group ($p<0.01$). (Table 2)

Hematoma volumes (cm^3) The volumes of hematomas in the PGE1 group were obviously reduced on the 12th and 20th days when compared with the 1st day and the 5th day, and these differences showed statistical significance ($p<0.01$). The volumes of hematomas in the control group were obviously reduced on the 20th when compared with the 1st day. On the 20th day, volumes of hematomas were significantly reduced in the PGE1 group than in control group ($p<0.01$). (Table 3)

Volume of perihematomal tissue The volume of perihematomal tissue in the PGE1 group was significantly reduced on the 20th day when compared with on the 5th day and the control group (all $p<0.01$). (Table 4)

Scoring of neurological function (NIHSS scoring, mRS scoring)

NIHSS scores showed statistically significant differences on the 20th day and the follow-up three months later when the PGE1 treatment group and control group were compared ($p<0.05$). mRS scores in the three-month follow-up also showed statistically significant differences between the two groups ($p<0.01$). (Table 5, 6)

The correlation between Ra values in the perihematomal region and hematoma volumes as well as the volume of perihematomal tissue The results indicated that the central region of the hematoma and the proximal and distal Ra values of the perihematomal region as well as the hematoma and perihematomal tissue volumes showed a negative correlation. (Figure 2, 3; Table 7)

Adverse effects and safety evaluation

Adverse effects similar to those observed with Alprostadil administration, such as hemorrhage, erythrema, and hypoleukocytosis,etc. were not observed in the PGE1 treatment group during or after treatment.

Table 2. *The variation of Ra value in the two groups before and after treatment ($\bar{x}\pm S$, n=20)*

Region	PGE1 treatment group (Ra value)		Control group (Ra value)	
	The 5th day	The 20th day	The 5th day	The 20th day
Central area of hematoma	0.42 ± 0.06	0.44 ± 0.06	0.41 ± 0.06	0.44 ± 0.05
Proximal regions of perihematomal tissue	0.54 ± 0.06	0.68 ± 0.06*#	0.53 ± 0.06	0.52 ± 0.06
Distal regions of perihematomal tissue	0.67 ± 0.05	0.78 ± 0.06*#	0.67 ± 0.06	0.65 ± 0.06
The frontal and parietal lobe area	0.95 ± 0.06	0.97 ± 0.05	0.96 ± 0.05	0.95 ± 0.05

*: P<0.01 The comparison of PGE1 group before and after treatment; #:P<0.01 The comparison of PGE1 group and control group on the 20th day.

Table 3. *Comparison of the hematoma volumes in the two groups at each time point ($\bar{x}\pm S$, cm^3, n=20)*

Group	The 1st day	The 5th day	The 12th day	The 20th day
PGE1 group	23.82 ± 4.61	27.82 ± 8.43	15.07 ± 7.05*△#	5.40 ± 4.11*△#
Control group	23.85 ± 4.53	27.92 ± 8.80	22.31 ± 8.98	13.82 ± 8.02*

*: P<0.01 The comparison of the volume on the 1st day; △: P<0.01 The comparison of the volumes in the PGE1 group on the 12th and 5th days; #: P<0.01 The comparison between the PGE1 group and the control group at 20th day.

Abnormal phenomena such as blood in urine or feces, liver and renal dysfunction, blood coagulation defects, or abnormal electrocardiograms were not observed.

The comparison of SPECT brain perfusion imaging and skull CT scanning between the two study groups (see accompanying graph)(Graph 3,4)

Graphs A-D show skull CT scans on the 1st, 5th, 12th, and 20th days of admission, respectively. According to the graphs, the hematoma on the 12th day

Table 4. *The comparison of the volumes of perihematomal tissue in the two groups (χ±S, cm³, n=20)*

Group	The 1st day	The 5th day	The 12th day	The 20th day
PGE1 group	6.01 ± 2.71	23.44 ± 8.20	18.70 ± 7.78	5.38 ± 3.13*#
Control group	5.80 ± 2.28	23.96 ± 8.71	20.16 ± 7.90	12.16 ± 6.05*

* Comparison on the 5th day P <0.01; # Comparison with control group P <0.01

Table 5. *NIHSS scoring in the two study groups (χ±S, n=20)*

Group	The 1st day	The 5th day	The 12th day	The 20th day	The 90th day
PGE1 group	11.85 ± 5.99	14.45 ± 6.17	12.2 ± 5.28	5.55 ± 3.32*	1.50 ± 1.00*
Control group	11.50 ± 5.76	14.05 ± 6.02	13.35 ± 5.40	9.80 ± 4.21	4.05 ± 2.95

The comparison between the PGE1 treatment and the control group * P <0.05

Table 6. *mRS scoring in the two study groups (χ±S, n=20)*

Group	The 1st day	The 20th day	The 90th day
PGE1 group	3.03 ± 0.73	2.65 ± 0.93	0.35 ± 0.49*
Control group	3.20 ± 0.86	2.60 ± 1.05	1.70 ± 0.73

* The comparison between the PGE1 group and the control groups P <0.05

Table 7. *The correlation between hematoma volume and perihematomal tissue volume*

Ra value	Volume of hematoma	volume of perihematomal tissue
Central area of hematoma	r = -0.679*	r = -0.671*
Proximal regions and distal regions of perihematomal tissue	r = -0.669*	r = -0.204*

* p<0.01

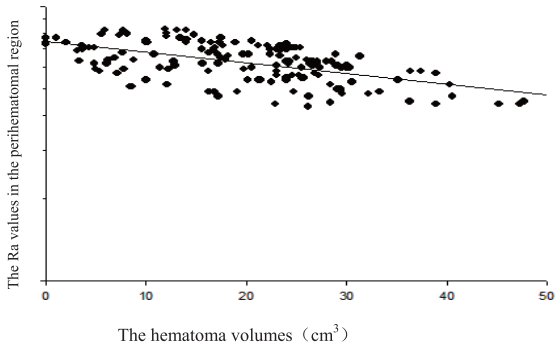


Figure 2. The correlation between hematoma volume and Ra value in the perihematomal region

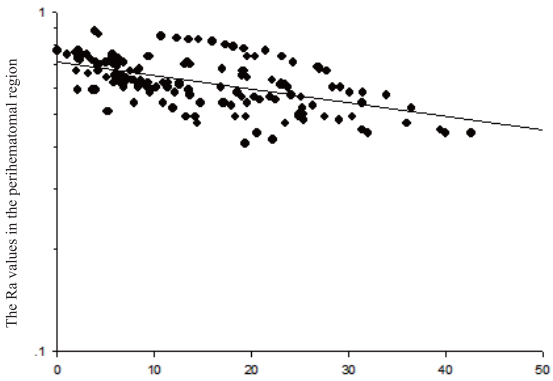
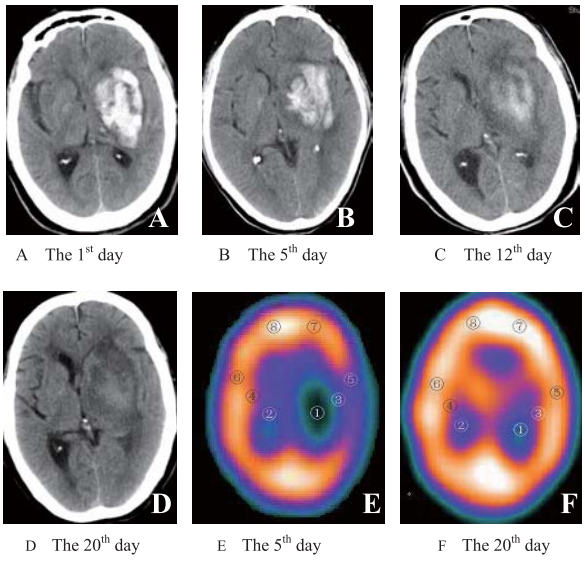
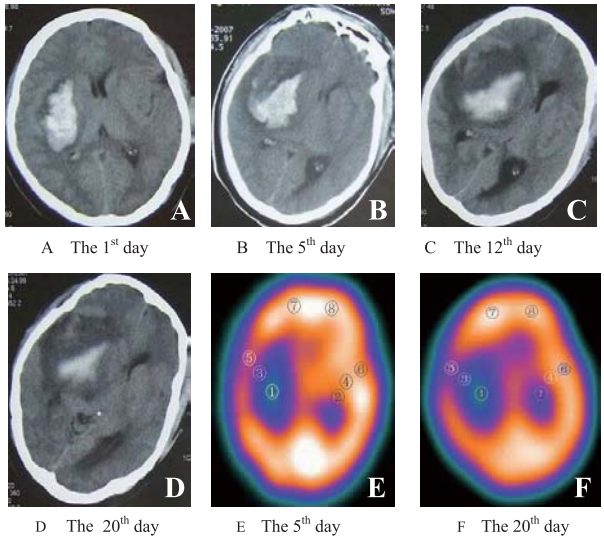


Figure 3. The correlation between volume of the perihematomal tissue and Ra values in the perihematomal region



Graph 3. PGE1 group



Graph 4. Control group

was significantly diminished and fundamentally absorbed on the 20th day.

Graphs E and F show SPECT brain perfusion imaging on the 5th and 20th days of admission, respectively. Graph E shows impairment of radioactive distribution in hematoma as well as the proximal and distal regions of the perihematomal tissue, which was reduced in distinct degree when compared to the uninjured side. However, rCBF was significantly reduced when compared to the opposite side. Graph F shows significant padding of radioactive distribution in the proximal and distal regions of the perihematomal tissue compared with that of admission Additionally, rCBF was also significantly improved. The semi-quantitative analysis was shown as follows: In graph E, the Ra value in the central region of the hematoma was 0.40; in the proximal region of perihematomal tissue, it was 0.52; in the distal region of perihematomal tissue, it was 0.60; and in the frontal and parietal lobes, it was 0.95. In graph F, the Ra value in the central region of the hematoma was 0.45; in the proximal region of the perihematomal tissue, it was 0.65; in the distal region of perihematomal tissue, it was 0.76; and in the frontal and parietal lobes, it was 0.96. These data indicate that Ra values in the perihematomal tissue were significantly increased after the application of Alprostadil.

Graphs A-D show skull CT scans on the 1st, 5th, 12th, and 20th days of admission, respectively.

Graphs E and F show SPECT brain perfusion images on the 5th and 20th days of admission, respectively. Graph E shows impairment of radioactive distribution in hematoma as well as radioactive distribution in the proximal and distal regions of the perihematomal tissue, which was reduced in distinct degree when compared to the uninjured side. However, rCBF was significantly reduced compared with the opposite side. Graph F shows no significant padding of the radioactive distribution in the proximal and distal regions of the perihematomal tissue. The semi-quantitative analysis was shown as follows: In graph E, the Ra value in central region of hematoma was 0.44; in the proximal region of the perihematomal tissue, it was0.56; in the distal region of the perihematomal tissue, it was 0.67; and in the frontal and parietal lobes, it was 0.95. These data indicate that the rCBF in the perihematomal tissue was significantly reduced after cerebral hemorrhage. In graph F, the Ra value in the central region of hematoma was 0.44; in the proximal region of the perihematomal tissue, it was 0.55; in the distal region of the perihematomal tissue, it was 0.65; and in the frontal and parietal lobes, it was 0.94.

DISCUSSION

One of the most critical reason for patients' developing aggravated or deteriorated conditions was recurrent hemorrhage in the acute stages following hematencephalon. The most common time of the recurrent hemorrhage was usually in the first 3 hours of the invasion, and the risk of the recurrent hemorrhage was obviously reduced after 24 hours. The variation of blood flow in the perihematomal tissue was conducive to the pathophysiological variations in the diseased regions in the subacute stages, which was induced by factors such as the toxic effect of materials generated by the decomposition and destruction of the hematoma as well as the compression of the hematoma and cerebral edema. In this study, we focused on the group treated with PGE1 for intracerebral hemorrhage on the 5th day. After the patients' hypertensive intracerebral hemorrhage, the volume of blood flow was reduced in the perihematomal tissue due to distinct sampling time [8-11]. However, the amount of research concerning the variation of blood flow in the perihematomal tissue 24 h following the traumatic event is quite limited. In this study, we observed the blood flow in the perihematomal tissue that was reduced on the 5th and 20th days following hypertensive intracerebral hemorrhage as well as the duration of the event and the effect of PGE1 on rCBF and prognosis. Furthermore, SPECT imaging follow-up was used to observe regional brain tissue, and this technology demonstrated many advantages for the evaluation of rCBF in the perihematomal tissue after the intracerebral hemorrhage .

The results indicate that the Ra uptake ratios in patients with hypertensive intracerebral hemorrhage in the central regions of the hematoma as well as the proximal region and the distal regions of the perihematomal tissue all showed significant decreases in blood flow on the 5th day in both the treatment group and the control group. However, decreases in the frontal and parietal lobes were not significant. Nevertheless, the blood flow in the proximal and distal regions of the perihematomal tissue was still in the low range on the 20th day of recheck, indicating that rCBF in the perihematomal tissue was continually reduced on the 5th day of the hypertensive intracerebral hemorrhage and was maintained the low level for about 20 days. This also suggests that facilitating the enhancement of rCBF in this region in this period plays a critical role in the cellular activity of the perihematomal tissue and the recovery of tissue function after intracerebral hemorrhage. The negative correlation between Ra values in the perihematomal tissue and NIHSS as well as mRS scores also confirms this point. Thus, it also indicates that the neurological functional recovery and prognosis after hypertensive intracerebral hemorrhage were positively correlated with rCBF values in the perihematomal tissue. The lesser values of rCBF in the perihematomal tissue led to the less neurological functional recovery and prognosis. The improvement of rCBF in the perihematomal tissue facilitated positive neurological functional recovery and prognosis after hypertensive intracerebral hemorrhage.

The 1/2 ABC method was able to measure the volume of the hematoma and the perihematomal tissue after intracerebral hemorrhage rapidly and feasibly. In this study, we adopted the 1/2 ABC measurement method to measure the patients' volume of hematoma and perihematomal tissue on the 1st, 5th, 12th, and 20th days of admission. The results showed that the volume of the hematoma was significantly diminished on the 20th day compared to the 1st day. Moreover, the volume of the perihematomal tissue was gradually formed and enlarged with the liquefaction of hematoma and the appearance of occupation effect. The volumes of the hematomas in the PGE1 treatment group showed significant statistical differences on the 12th day compared with those on the 5th day, which indicated that PGE1 could shorten physiological pathogenesis of hypertensive intracerebral hemorrhage, facilitate the absorption of the hematoma, and relieve the successive impairment in the perihematomal tissue. The correlation analysis also indicated that the volume of perihematomal tissue showed positive correlation with the volume of the hematoma, and the uptake ratio Ra was even smaller. This proved that impairment of the perihematomal tissue after hypertensive intracerebral hemorrhage was correlated with a decrease in rCBF.

PGE1 was generated by vascular endothelial tissue that was characterized with vasodilation and antiplatelet aggregation and inhibition of inflammatory reaction. The

previous literature reported that PGE1 shows targeted effects to inflammatory and spastic vascular position [5]. Many groups indicate that the inflammatory effect is related to the cellular defect caused by intracerebral hemorrhage [12,13,14], and it also directly affected the nerve cells and caused some impairment through inflammatory factors. Therefore, in this study, application of PGE1 treatment was able to relieve the impairment of the perihematomal tissue, as it was correlated not only with the improvement of blood flow in the perihematomal tissue but also with the inhibition of inflammation in this area. In our investigation, no adverse effects such as PGE1-related hemorrhage, erythema, and hypoleukocytosis etc. were observed, nor were any related lab abnormal variation was appeared. This treatment was shown to be very safe in this study, but, due to limited numbers of selected cases, further safety and availability evaluation with a larger sample size is still needed.

The degree of negatively affected perihematomal tissue after hypertensive intracerebral hemorrhage was correlated with a series of factors, such as the volume of the hematoma, inflammatory reaction, and rCBF. The degree of affected perihematomal tissue showed a close relationship with the pathogenesis following intracerebral hemorrhage and the recovery of neurological function. Moreover, applying PGE1 treatment on the 5th day following hypertensive intracerebral hemorrhage was capable of enhancing rCBF in the perihematomal tissue, reducing the inflammatory reaction of the perihematomal tissue, improving neurological functional scoring, and improving prognosis when compared to control groups.

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