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# Blood pressure control in ultra-early basal ganglia intracerebral hemorrhage

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**Abstract. – OBJECTIVE: We performed this study to investigate the effect of blood pressure control in ultra-early basal ganglia intracerebral hemorrhage.**

**PATIENTS AND METHODS: 120 patients with ultra-early basal ganglia intracerebral hemorrhage were randomly divided into experimental group (strengthened antihypertensive) and control (normal antihypertensive). Each group consists of 60 patients, whose contractive pressure were controlled by intravenous antihypertensive drugs among 130-140 mmHg and 160-180 mmHg respectively for 24h, after 1h of beginning treatment. They were all evaluated by NIH Stroke Scale (NIHSS) before and after the treatment. Cranial CT, hematoma volume, hematoma enlargement, edema volume, serum matrix metalloproteinase-9 level were performed and compared between groups.**

**RESULTS: After 24h, hematoma volume and hematoma enlargement in the experimental group was significantly lower than control ($p < 0.05$). After 14 days, NIHSS score in the experimental group was significantly lower than control ($p < 0.05$). Cerebral edema amount and serum MMP-9 level in the experimental group were significantly lower than control after 5 days and 14 days.**

**CONCLUSIONS: Ultra-early basal ganglia intracerebral hemorrhage can remarkably reduce hematoma enlargement, cerebral edema, serum MMP-9 level, and improve the neurological function.**

*Key Words:*
Intracerebral hemorrhage (ICH), Strengthened antihypertensive, Hematoma expansion, Cerebral edema, Matrix metalloproteinase-9.

## Introduction

Intracerebral hemorrhage (ICH) is a common emergency at the department of neurology. The mortality and morbidity is the highest in stroke diseases. As is shown in current studies, hematoma expansion and peripheral edema are associated with early neurologic deterioration, which is the main reason of disease development or even death[1-4]. Hypertension is also associated with hematoma expansion and peripheral edema, especially systolic blood pressure (SBP). In this study, we investigated blood pressure (BP) control in hematoma expansion, cerebral edema and neurological improvement on ultra-early basal ganglia ICHe.

## Patients and Methods

### Patients

All 120 patients with ICH were obtained from November 2009 to November 2012 in the Department of Neurology of our hospital. We randomly divided them into two groups. The experimental group (strengthened antihypertensive) consists of 37 males and 23 females (58.05 ± 11.55 year-old). Control (normal antihypertensive) consists of 35 males and 25 females (59.47 ± 13.25 year-old). All patients were confirmed as acute spontaneous hemorrhage by cranial CT (bleeding volume < 30 ml, duration < 4 h). Within 1h of invasion, their SBP were over 160 mmHg at least 2 times (1 mmHg = 0.133 kPa). Intracranial artery stenosis, trauma derived hemorrhage, cerebral arteriovenous malformations, bleeding after infarction or thrombolysis were excluded. Ischemic stroke within 30 days, heart, lung, liver, kidney dysfunction or coagulopathy, acute and chronic inflammation, cancer were also excluded. The general data of this study has no significant difference (Table I).

### Treatment

Experimental group was performed intravenous nitroglycerin in 1 h. SBP was less than 140 mmHg and maintained 130-140 mmHg. In control, if SBP was less than 180 mmHg, antihy-



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**Table I.** Comparison of general data of two groups on admission ($x \pm s$, n = 60).

| Group | Age (year-old) | Gender | | SBP (mmHg) | Start time of treatment (h) |
|---|---|---|---|---|---|
| | | Male | Female | | |
| Experiment | 58.05 ± 11.55 | 37 | 23 | 190.75 ± 12.74 | 2.24 ± 1.23 |
| Control | 59.47 ± 13.25 | 35 | 25 | 188.58 ± 12.54 | 2.13 ± 1.05 |
| $t$ or $\chi^2$ value | 0.624 | 0.139 | 0.939 | 0.517 | |
| $p$ value | 0.534 | 0.709 | 0.350 | 0.606 | |

pertensive drugs will not be used. SBP was less than 180 mmHg and maintained 160-180 mmHg. In 24 h of admission, BP was monitored continuously (5 min per time until it reached BP standards; then, 15 min per time). After 24 h of onset, the treatment of all patients was replaced by oral angiotensin converting enzyme inhibitor (ACEI), like enalapril, etc., to slightly increase contractive pressure.

### Neurological Score

We performed U.S. National Institutes of Health neurological deficit (NIHSS) score before and after 24 and 14 d of treatment.

### Cranial CT

Cranial CT was performed before admission and disease aggravated or after 24 h, 5 d, 14 d of admission. Hematoma volume = 1/2 (A × B × C × D). (1) The longest diameter in the largest sectional area of hematoma (cm). (2) At the same area, vertical maximum diameter width of A line (cm). (3) The number of hematoma layers. (4) Thickness of CT slice (cm). During absorption of hematoma, density of peripheral lesions reduced, rendering the hematoma volume decrease. So, we defined hematoma range in the outer edge of the isodense lesion between high-density haematoma and low-density edema, which is similar with the hematoma volume on admission. Lesion volume (range of peripheral edema edge) was valued at the same formula above. Edema volume (surrounding edema volume) = lesion volume – hematoma volume. The hematoma expansion was according to Kazui standard. Hematoma brain CT scans were calculated twice and defined as V1 and V2. If V2/ V1 ≥ 1.4 or V2-V1 ≥ 12.5 ml, we considered it as hematoma expansion[5].

### Serum MMP-9 Levels

We determined it by ELISA. Venous blood was obtained at 24h, 5d, 14d before and after the treatment. The procedure was followed by instruction of ELISA kit (R&D Systems).

### Statistical Analysis

Statistical analysis was performed using the SPSS13.0 software (SPSS Inc., Chicago, IL, USA). Measurement data and enumeration data were compared by $t$ test and $X^2$ test respectively.

## Results

There is no significant difference at 24h before and after treatment according to NIHSS score (Table II). And after 14d of treatment, NIHSS score of the experimental group was obviously lower than control ($p < 0.05$). Hematoma volume, hematoma enlargement, edema volume, serum matrix metalloproteinase-9 (MMP-9) level were compared (Tables III to V). After 24h of treatment, hematoma volume and hematoma enlargement in experimental group was significantly lower and less than control ($p < 0.05$). After 5d and 14d of treatment, edema volume and MMP-9 level were significantly lower than control ($p < 0.05$).

**Table II.** Comparison of NIHSS Score between two groups ($x \pm s$, n = 60).

| Group | Before treatment | 24 h after treatment | 14 d after treatment |
|---|---|---|---|
| Experiment | 9.74 ± 4.49 | 9.25 ± 4.10 | 6.28 ± 3.68* |
| Control | 9.50 ± 4.81 | 9.30 ± 4.46 | 7.82 ± 4.28 |
| $t$ value | 0.274 | 0.075 | 2.126 |
| $p$ value | 0.784 | 0.941 | 0.036 |

**Table III.** Comparison of hematoma volume and expansion ($x \pm s$, n = 60).

| Group | Hematoma volume(ml) | | Hematoma expansion (cases, %) |
|---|---|---|---|
| | Before treatment | 24h after treatment | |
| Experiment | 10.86 ± 5.72 | 11.99 ± 6.90* | 5 (8.33%)* |
| Control | 11.02 ± 5.67 | 14.74 ± 7.75 | 14 (23.33%) |
| $t$ or $\chi^2$ value | 0.160 | 2.049 | 5.070 |
| $p$ value | 0.873 | 0.043 | 0.024 |

**Table IV.** Comparison of edema volume ($x \pm s$, ml, n = 60).

| Group | Before treatment | 24 h after treatment | 5 d after treatment | 14 d after treatment |
|---|---|---|---|---|
| Experiment | 0.91 ± 0.52 | 2.18 ± 1.54 | 4.94 ± 4.23* | 3.52 ± 3.22* |
| Control | 0.97 ± 0.49 | 2.71 ± 1.70 | 7.14 ± 6.41 | 4.89 ± 3.79 |
| $t$ value | 0.583 | 1.801 | 2.219 | 2.140 |
| $p$ value | 0.561 | 0.074 | 0.028 | 0.034 |

**Table V.** Comparison of serum MMP-9 level ($x \pm s$, ng/ml, n = 60).

| Group | Before treatment | 24 h after treatment | 5 d after treatment | 14 d after treatment |
|---|---|---|---|---|
| Experiment | 53.38 ± 12.40 | 88.52 ± 13.85 | 101.89 ± 16.20* | 50.69 ± 11.11* |
| Control | 52.07 ± 11.70 | 89.07 ± 12.19 | 108.99 ± 20.30 | 55.56 ± 14.11 |
| $t$ value | 0.554 | 0.231 | 2.117 | 2.099 |
| $p$ value | 0.593 | 0.818 | 0.036 | 0.038 |

## Discussion

ICH is a primary non-traumatic brain parenchymal hemorrhage, which has a high morbidity and mortality. Its pathophysiological processes mainly include 3 stages: hematoma formation, invasion and peripheral edema. Studies indicated that high BP was associated with hematoma expansion, especially high SBP[6,7]. So, regulating the increasing BP was a crucial clinical intervention.

In antihypertensive treatment of acute cerebral hemorrhage trial (ATACH)[8], nicardipine was used to control SBP in 3 predeterminated levels after l8-24h of ICH: 170-200 mmHg, 140-170 mmHg, l10-140 mmHg. Our results indicate that early antihypertensive regulation is accessible, good tolerance, and able to reduce hematoma expansion, neurological deterioration and mortality remarkably. Meanwhile, Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT)[9] showed that, as for patients with acute cerebral hemorrhage within 6h, rapid antihypertensive therapy (SBP: 130-140 mmHg) could relieve hematoma expansion. In this study, the case number of early hematoma expansion in experimental group is significantly less than control ($p < 0.05$). However, as there is ischemic penumbra or low perfusion around hematoma, strengthened antihypertensive treatment can lead to low perfusion pressure and reduce cerebral blood flow further. In this study, though there is a distinction between two groups after 24h of treatment by NIHSS score, but it is not statistically significant ($p > 0.05$). Disease of the experimental group was not aggravated obviously, proving that early strengthened antihypertensive treatment is safe. And, in 24h of ICH, BP control has no adverse effects. This may be due to the fact that ischemic penumbra or low perfusion around hematoma occur mainly during obvious cerebral edema, rendering neurological damage less.

Cerebral edema is one of the main cause of neurologic impairment deterioration after hemorrhage. Currently, there are fewer studies about the association between hypertension and cerebral edema. Vemmos et al[3,4] found that cerebral edema after hemorrhage was independently associated with ele-

vated BP within 24h. Patients with elevated SBP had a more severe edema. Anderson et al[10] and Koch et al[11] also found the similar conclusion. They considered that patients with SBP ≥ 160 mmHg had a higher risk of hematoma enlargement. And reducing elevated BP can improve hematoma enlargement and peripheral edema, and decrease mortality further. In our study, at 5d and 14d after treatment peripheral edema volume in experimental group was significantly less than control ($p < 0.05$). Matrix metalloproteinase-9 (MMP-9), an important member of matrix metalloproteinases family, is associated with blood-brain barrier damage directly as well as the key factor of vasogenic brain edema and brain tissue damage[12]. After hypertensive ICH, MMP-9 level in serum and brain tissue shoots up[13]. Besides inflammation around the hematoma, hematoma expansion can cause surrounding brain tissue hypoperfusion, ischemia, hypoxia, MMP-9 up-regulation. In this study, serum MMP-9 level had no significant difference among the two groups before and after 24h of treatment. But after 5d and 14d, serum MMP-9 level and peripheral edema in experimental group were less than control ($p < 0.05$). Further, Tan et al[14] found that patients with hypertension had a higher serum MMP-9 level than control. But, whether strengthened antihypertensive treatment can reduce serum MMP-9 level and relieve peripheral edema still needs further studies.

## Conclusions

Our result indicates that early recovery of neurological function in experimental group is faster than control. We also suggest that strengthened antihypertensive treatment can improve the early neurological recovery by inhibiting hematoma volume growth and peripheral edema in ultra-early basal ganglia ICHe.

### Conflict of Interest

The Authors declare that there are no conflicts of interest.

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