

Supplementary materials

Inclusion and exclusion criteria.

Inclusion criteria

1. Aged >18 and no more than 80 years old
2. Randomization within 24 h after symptom onset
3. No fever or evidence of infection on admission
4. NIHSS score ranging 11-25
5. Supratentorial parenchymal hematoma ≥ 10 ml
6. GCS ≥ 8
7. Patients or family members sign informed consent forms

Exclusion criteria

1. Infections within the last 4 weeks.
2. Use of antibiotics within the last 2 weeks.
3. Known pre-ICH dysphagia.
4. Planning to receive surgical treatment (including surgical removal of hematoma, removal of bone flap, minimally invasive hematoma aspiration, and ventricular shunt or lateral ventricular drainage for intracerebral hemorrhage).
5. Patients with cerebral hemorrhage or primary ventricular hemorrhage caused by trauma, vascular malformation, aneurysm, coagulopathy, anticoagulant or antiplatelet drugs, thrombolysis, post-infarction hemorrhage transformation, hematopathy, moyamoya disease, primary or metastatic tumor, venous sinus thrombosis, vasculitis, and other definite causes.
6. Previous history of stroke or pre-onset disability of limb motor function (mRS ≥ 1).
7. Pregnancy or within 30 d of delivery.
8. Previous use (within 1 month) of beta-blockers or reserpine.
9. Bronchial asthma or COPD.

10. Cardiogenic shock.
11. Degree II-III atrioventricular blocks.
12. Severe or acute heart failure.
13. Heart rate < 65 beats/min.
14. Known to be allergic to propranolol.
15. Severe liver or renal insufficiency.
16. History of malignant tumors.
17. Currently participating in other interventional clinical trials.
18. Currently, immunosuppressants and immunotherapies are being administered.

*Symptom onset is defined by the “last known normal” principle.

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; GCS, Glasgow Coma Scale; COPD, chronic obstructive pulmonary disease.

The algorithm of SAP is as follows:

C1: Fever $> 38^{\circ}\text{C}$ (if present, recorded as "C1=1", this value can be accumulated, hereinafter referred to as "1") or white blood cell count $< 4000/\text{mm}^3$ (1) or white blood cell count $> 12000/\text{mm}^3$ (1);

C2: New or worsen cough or difficulty breathing or respiratory rate > 25 breaths/minute (1) or presence of purulent sputum (1) or rales, crackles, or bronchial breath sounds (1);

*C3: New/progressive persistent infiltrates, consolidation, or cavities on two consecutive chest CT imaging (1).

If $C1 \geq 1$ and $C2 \geq 1$, and $C3=1$, then the diagnosis is "SAP".

*Outcome of chest CT imaging was determined by two independent radiologists.

The algorithm is implemented by computer and adjudicated by an independent incident adjudication committee.

Detailed dosing guidelines:

An initial dose of 5 mg per day, consisting of 5 mg (5 mL) propranolol hydrochloride injection diluted in 45 mL normal saline to yield a total volume of 50 mL for infusion via a pump at 2 mL/h intravenously over 7 days. Continuous cardiac monitoring is implemented throughout the administration period. In cases of tachycardia (heart rate > 100 beats per minute), the infusion rate can be increased (up to 8 mL/h) or metoprolol can be additionally administered to further control heart rate. If heart rate drops below 55 beats per minute, propranolol infusion is paused until recovery to above 65 beats per minute before resuming (initially at 2 mL/h). The total intervention duration, including pauses, is 7 days. Administration will be ceased immediately if heart rate falls below 40 beats per minute or blood pressure drops to $\leq 90/60$ mmHg.

Updated protocol

Study protocol was first registered in February 2023. After which, considering the actual situation of enrolled patients and following discussions by the Executive Committee and subsequent approval by the Ethics Committee, the inclusion and exclusion criteria were revised in April 2023 after enrolled of 13 patients. And re-estimated sample size was 168. The population keep consistent.

Original version and updated version of inclusion and exclusion criteria listed below:

Original version	Updated version
<p>Inclusion</p> <p>1.Aged 18-80 years old</p> <p>2.Randomization within 24 h after symptom onset</p> <p>3.No fever or evidence of infection on admission</p> <p>4.NIHSS≥11 or 5≤GCS≤12</p> <p>5.Supratentorial parenchymal hematoma≥20ml</p> <p>6.Patients or family members sign informed consent forms</p>	<p>Inclusion</p> <p>1.Aged>18 and no more than 80 years old</p> <p>2.Randomization within 24 h after symptom onset</p> <p>3.No fever or evidence of infection on admission</p> <p>4.NIHSS score ranging 11-25</p> <p>5.Supratentorial parenchymal hematoma≥10ml</p> <p>6.GCS≥8</p> <p>7.Patients or family members sign informed consent forms</p>
<p>Exclusion</p> <p>1. Time of symptom onset cannot be reliably assessed.</p> <p>2. Subjects is considered a candidate for immediate surgical intervention by the neurosurgery service.</p> <p>3. Pregnancy or parturition within previous 30 days or active lactation.</p> <p>4. Use of beta blockers (propranolol, metoprolol, sotalol, carvedilol, bisoprolol,</p>	<p>Exclusion</p> <p>1. Infections within the last 4 weeks.</p> <p>2. Use of antibiotics within the last 2 weeks.</p> <p>3. Known pre-ICH dysphagia.</p> <p>4. Planning to receive surgical treatment (including surgical removal of hematoma, removal of bone flap, minimally invasive hematoma aspiration, and ventricular shunt or lateral ventricular drainage for intracerebral hemorrhage).</p> <p>5. Patients with cerebral</p>

<p>atenolol, esmolol, and etc.) or antibiotics within the last 30 days.</p> <p>5. Use of reserpine within the last 30 days.</p> <p>6. Pre-stroke dementia or disability.</p> <p>7. With severe liver, kidney disease, or malignancy, life expectancy is less than 14 days.</p> <p>8. Bronchial asthma or COPD.</p> <p>9. Cardiogenic shock or severe or acute heart failure.</p> <p>10. Degree II-III atrioventricular block or sinus bradycardia (heart rate $\leq 75/\text{min}$).</p> <p>11. Known sensitivity to propranolol.</p> <p>12. Currently participating in other interventional clinical trials.</p> <p>13. Immunosuppressant therapy or known immunosuppression.</p>	<p>hemorrhage or primary ventricular hemorrhage caused by trauma, vascular malformation, aneurysm, coagulopathy, anticoagulant or antiplatelet drugs, thrombolysis, post-infarction hemorrhage transformation, hematopathy, moyamoya disease, primary or metastatic tumor, venous sinus thrombosis, vasculitis, and other definite causes.</p> <p>6. Previous history of stroke or pre-onset disability of limb motor function ($\text{mRS} \geq 1$).</p> <p>7. Pregnancy or within 30 d of delivery.</p> <p>8. Previous use (within 1 month) of beta-blockers or reserpine.</p> <p>9. Bronchial asthma or chronic obstructive pulmonary disease.</p> <p>10. Cardiogenic shock.</p> <p>11. Degree II-III atrioventricular blocks.</p> <p>12. Severe or acute heart failure.</p> <p>13. Heart rate $< 65 \text{ beats/min}$.</p> <p>14. Known to be allergic to propranolol.</p> <p>15. Severe liver or renal insufficiency.</p> <p>16. History of malignant tumors.</p> <p>17. Currently participating in other interventional clinical trials.</p> <p>18. Currently, immunosuppressants and immunotherapies are being administered.</p>
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