Bleeding Brain Intraparenchymal

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ABSTRACT
Despite the diagnostic and therapeutic advances, intraparenchymal hemorrhage (HIP) continues to present high Indices of mortality and disability. Its clinical differentiation with ischemic stroke from neuroimaging examination is fundamental. There is no specific treatment for a HIP. Its management consists of support and approach measures on intracranial hypertension, being reserved for the intervention Surgical in selected cases. Minimally invasive surgical techniques are underway. This study aims to review and discuss the approach of intraparenchymatous hemorrhages in medical practice.

KEYWORDS: brain hemorrhage, brain parenchymal hemorrhage, brain hemorrhage, cerebrovascular accident, cerebrovascular stroke, brain vascular accident.

INTRODUCTION
According to the Brazilian Society of Cerebrovascular Diseases, hemorrhagic stroke is the whole event caused by spontaneous (non-traumatic) rupture of a vessel, with extravasation of blood to the inside of the brain (hemorrhage intraparenchymal), for the ventricular system (intraventricular hemorrhage) and/or subarachnoid space (subarachnoid hemorrhage)¹.

Intraparenchymal hemorrhage (HIP) is a common disease, responsible for 10-20% of cerebrovascular accidents. It is more incident with the increase of age, doubling every ten years after the 35 years, in males and influenced by racial factors, being more frequent in Afro, Hispanic, Latin and Asian when compared to the Caucasian population²,³. In general, 30-day mortality of these patients is up to approximately 45% and mortality in 1 year is about 63%⁴,⁵.

Etiology
The spontaneous HIP may be classified as primary or secondary depending on the underlying cause⁶-⁸:
- Primary: It represents about 80-85% of cases and occurs due to spontaneous rupture of small vessels damaged by uncontrolled chronic hypertension or angiopathy amyloid (AAC), causing the so-called aneurysms of Charcot-Bouchard. It is also differentiated as to the location in Lobar (commonly resulting from AAC) and not Lobar (often due to long-standing arterial hypertension) and, in the latter, Putamen, Thalamus, subcortical white matter, bridge and cerebellum, the most common sites.
Secondary: Corresponds to 15-25% of cases and is associated with a series of congenital and acquired conditions, such as vascular pathologies (arteriovenous malformations, Moyamoya, Cavernomas, Venous Angiomas and Telangiectasias), tumors, hemorrhagic transformation of cerebral ischemia, leukemia, coagulation disorders, use of anticoagulants and thrombolytic agents, cerebral vasculitis, drug abuse, cerebral venous thrombosis, among other causes.

Risk Factors
Non-modifiable

- Advanced age;
- Black and Oriental breed;
- Male.

Modifiable

- Hypertension: is the main risk factor, being present in 70 to 80% of patients with HIP;
- Angiopathy Amyloid: is characterized by deposits of the beta peptide Amyloid within small and medium vessels of the cortex and leptomeningeal. It may occur as a sporadic disorder, sometimes in association with Alzheimer’s disease, or as a specific familial syndrome. It is a significant cause of HIP lobar primary in the elderly, especially in the parietal and occipital lobes;
- Smoking: Smokers have a higher risk of stroke, including HIP than in non-smokers;
- Alcohol: Consumption of moderate or large quantities of alcohol in the 24h preceding the ictus seems to precipitate HIP;
- Coagulopathies: Both the coagulopathies primary and secondary, such as the use of oral anticoagulants; antplatelet drugs, thrombolytics for the treatment of acute ischemic stroke or acute myocardial infarction (AMI) are associated with increased risk of the HIP;
- Sympathomimetics Medicines or drugs with sympathomimetic activity, (Phenylpropanolamine, cocaine, amphetamines, or ephedrine) also increase the risk of the HIP;
- Cholesterol and triglyceride Status: There may be an inverse relationship between the levels of total cholesterol, LDL and triglycerides and the risk of a HIP;
- Other: Less established factors, such as obesity and genetic factors, are also pointed out as relevant to the risk of the HIP.

Clinical picture

HIP is usually characterized by the sudden focal neurological deficit, dependent on the bleeding topography, sudden onset and rapidly progressive. Although frequent, the headache is not present in all cases, only when the HIP is accompanied of meningeal irritation due to intraventricular hemorrhage or subarachnoid associated, or increased intracranial pressure. For this last reason or by distortion of brain structures, the vomiting is associated. Convulsive seizures may occur, especially in bleeding Lobar.

Bleeding in the Putamen occurs in approximately 35% of the cases, subcortical in 30%, cerebellum in 16%, thalamus in 15% and bridge in 5-12%. They manifest themselves with:

- **Putamen:** Hemiplegia, loss hemisensory, hemianopsia homonymous, gaze paralisis, torpor, and coma.
- **Cerebellar:** Imbalance, vomiting, headache (usually occipital), stiffness nuchal, paralysis of the gaze, facial paresis or even torpor due to compression of the brainstem. It is a crucial diagnosis since these patients frequently deteriorate and require surgery.

- **Thalamic:** hemiparesis, loss hemisensory and occasionally hemianopsia transient homonymous, and there may be pupils miotic non-reactive. Aphasia can occur if bleeding affects the dominant hemisphere or neglect in the non-dominant hemisphere.

- **Pontina:** Usually leads to deep coma in the first few minutes after hemorrhage, probably due to rupture of the reticular activation system. The motor examination is marked by total paralysis. The pupils are reactive, but the ocular movements are absent, and there may be ocular oscillation, facial paralysis, deafness, and dysarthria. When the patient is awake.

It is also essential that all patients with suspected HIP are evaluated by the Glasgow Coma Scale and by NIHSS (National Institutes Of Heath Stroke Scale) in the evaluation neurological. By hard clinical differentiation with ischemic stroke, a neuroimaging test for diagnostic confirmation of HIP is essential.

Complementary exams

In addition to a rapid clinical history and neurological examination, computed tomography without hire (TCSC) of the skull is highly sensitive and specific for hemorrhagic stroke and is the key to early diagnosis.

In the HIP, it will reveal not only the location and size of the hemorrhage but also the intraventricular extension, the mass effect, the hydrocephalus and the first signs of herniation. The volume of the hematoma can be estimated using the ABC/2 method, where:  

- A - Is the maximum diameter of the hematoma (in cm);
- B - Is the largest perpendicular diameter A (in cm);
- C - Is the sum of the points obtained with the 10mm cuts, in which the main axis of the hematoma presents:
  - 75% to 100% of a = 1 point for each cut;
  - 25% to 50% of a = 0.5 point each cut;
  - ≤ 25% of a = Do not score;

**Hematoma Volume (mL) = A x B x C / 2**

This calculation of the hematoma volume, although variable among the examiners, proved to be sufficient for clinical decision making since hematomas with more than 30mL have a worse prognosis.

MRI can be as sensitive as CCTSC to determine the presence of hemorrhage, but rarely offers additional information in the acute situation, and may be performed when there is suspicion of non-hypertensive etiology (Cavernomas, Angiopathy Amyloid, Neoplasms, among others). As a general rule, the hyperacute hematoma is isointense in T1, hyperintense in T2 and hypointense in T2. After the seventh day, it becomes hyperintense on T1 and T2 due to hemoglobin degradation in Methemoglobin, and in the chronic phase, the low signal of hemosiderin is better visualized in T2 or T2*

Angiography is indicated for investigation of secondary causes such as AVM, aneurysms, fistulas, venous sinus thrombosis and vasculitides in patients with atypical HIP localization or aged below 45 years (regardless of the presence of SAH). The method of choice is conventional catheter angiography, but CT or MRI angiography with use of
Despite the diagnostic and therapeutic advances, HIP continues to present high indices of mortality and disability. The main factors related to the poor prognosis in the short term (in 30 days) of these patients are initial volume of hemorrhage more significant than 30cm³, lowering of the level of consciousness at admission, intraventricular bleeding, advanced age, and localization primarily infratentorial hemorrhage more significant than 30cm³, lowering of the level of consciousness at admission, intraventricular hemorrhage, advanced age, and localization primarily infratentorial hemorrhage.

**Prognosis**

Despite the diagnostic and therapeutic advances, HIP continues to present high indices of mortality and disability. The main factors related to the poor prognosis in the short term (in 30 days) of these patients are initial volume of hemorrhage more significant than 30cm³, lowering of the level of consciousness at admission, intraventricular bleeding, advanced age, and localization primarily infratentorial.

For stratification of the risk of mortality in 30 days, the HIP scale is the most used. Scores between 0 and 2 are associated with low mortality and scores ≥ 3 are associated with a high mortality rate (Table 1).

**Table 1. HIP Scale**

| Components                        | Points |
|-----------------------------------|--------|
| Glasgow Scale                     |        |
| 3-4                               | 2      |
| 5-12                              | 1      |
| 13-15                             | 0      |
| Hematoma Volume (cm³)             |        |
| ≥ 30                              | 1      |
| < 30                              | 0      |
| Ventricular flooding              |        |
| Yes                               | 1      |
| No                                | 0      |
| Origin Infratentorial             |        |
| Yes                               | 1      |
| No                                | 0      |
| Age (years)                       |        |
| ≥ 80                              | 1      |
| < 80                              | 0      |
| Total                             | 0-6    |

Source: Hemphill et al. (2001)

**Treatment**

There is no specific treatment for the HIP. The initial approach should be focused on airway evaluation, respiratory and hemodynamic parameters, temperature, capillary glycemia and detection of focal and external neurological signs of trauma and its complications. Airway stabilization, respiration, and circulation (ABC) are essential to prevent secondary injuries caused by hypoxemia, uncontrolled hypertension, and hematoma expansion. Intubation for airway protection is indicated in patients with Glasgow Scale (GCS) ≤ 8 or significant respiratory distress. Ideally, after performing the neuroimaging exam, patients with HIP should be quickly referred to beds monitored in a stroke unit or intensive care beds.

**Temperature**

Fever is an independent risk factor for poor prognosis. In about 20% of patients, there is no infection and fever is attributed to inflammatory responses to extravasated blood, predominating in those with a poor clinical condition at admission and in those with an intraventricular extension of hemorrhage. It is suggested that hyperthermia (axillary temperature ≥ 37.5°C) is treated in the acute phase of HIP usually with acetaminophen or dipyrone. In refractory cases, it may be associated with anti-inflammatory non-steroidal, external physical methods and internal active cooling (intravascular cooling catheters), although there are no studies proving efficacy and safety of cooling in patients with hemorrhagic stroke.

**Glucose**

Care should be taken to avoid hyperglycemia and hypoglycemia. Insulin therapy is recommended in order to reach blood glucose levels between 100-140mg/dL. For patients with hemorrhagic stroke, it is recommended to Nitroprusside of sodium IV, paying attention to a potential increase in ICP. For more severe or refractory cases, it is recommended to Labetalol And Nicardipine are not available for use in Brazil. Associated with mechanical prophylaxis, the prophylactic doses of non-fractioned subcutaneous heparin or LMWH may be initiated after the first 48h in patients with documented stable hematoma.

**Blood pressure (BP)**

In the HIP, the elevation of systolic blood pressure (SBP) is associated with the expansion of the hematoma, neurological deterioration, and lower prognosis. Thus, treatment is suggested if SBP > 180mmHg and mean BP (map) > 130mmHg, aiming to reach a BP close to 160x90mmHg (or Pam < 110 mmHg) in patients with intracranial hypertension, SBP should be maintained above 90mmHg and ideally, intracranial pressure (PIC) monitoring should be used to maintain cerebral perfusion pressure (CPP) above 60-80mmHg (PPC = PAM – PIC).

The medications antihypertensive generally used in the acute phase of the HIP are Metoprolol, Diltiazem or Esmolol since the Labetalol And Nicardipine are not available for use in Brazil. For more severe or refractory cases, it is recommended to Nitroprusside of sodium IV, paying attention to a potential increase in ICP. Oral antihypertensive medicinal products should be instituted as soon as possible (Tables 2 - 3).
Intracranial hypertension
Increased intracranial pressure (ICP/PIC) due to HIP may result from the hematoma itself and the surrounding edema, which may contribute to brain injury and neurological deterioration. A graded approach is recommended starting with simple measures that include2,3:
- Elevation of the headboard in 30° and positioning of the head, avoiding excessive flexion or rotation of the neck;
- Analgesia (Morphine or Fentanyl) and Sedation (Propofol, Etomidate Or Midazolam) particularly in unstable and intubated patients;
- Keep the Euvolemia: If necessary, isotonic fluids (e.g., saline solution 0.9%) should be administered.
- BP control;
- Treatment of fever and seizures;
- Invasive monitoring and specific treatment of PIC should be considered for patients with GCS<8, with clinical evidence of herniation transtentorial or with significant intraventricular hemorrhage or hydrocephalus. The goal should be to keep the PIC< 20mmHg. More aggressive therapies to obtain this control include osmotic diuretics (e.g., mannitol and hypertonic saline solution), neuromuscular blockade, hyperventilation, hypothermia, and Ventriculostomy.

Table 2. Blood pressure control in HIP

| Blood pressure          | Conduct                                                                 |
|-------------------------|--------------------------------------------------------------------------|
| SBP >200 mmHg or PAM >150 mmHg (two readings with a 5-minute interval) | Initiate aggressive BP reduction by continuous infusion of intravenous antihypertensive medication with BP monitoring every 5 minutes. |
| PAS>180 mmHg or PAM>130 mmHg Suspected increase in ICP | Consider ICP monitoring. Initiate BP reduction by continuous or intermittent infusion of intravenous antihypertensive medication with BP monitoring every 5 minutes. Keep PPC>60-80 mmHg. |
| PAS>180 mmHg or PAM>130 mmHg No suspected increase in ICP | Initiate moderate BP reduction by continuous or intermittent infusion of antihypertensive medication. With BP monitoring every 15 minutes (target BP 160×90 mmHg or PAM target 110×70 mmHg). |
| PAS<90 mmHg             | Expansion with Crystalloids intravenously and infusion of vasoactive amines: Dopamine 2 – 20 mg/Kg/min. / noradrenaline 0.05 – 0.2 mg/Kg/min. |

BP: blood pressure; PAM: mean arterial pressure; ICP: Intracranial pressure; PPC: Cerebral perfusion pressure.

Table 3. Antihypertensive medications used in HIP

| Drug       | Intravenous Dose                      | Contraindications                                                                 |
|------------|---------------------------------------|----------------------------------------------------------------------------------|
| Metoprolol | 5mg-1 ML/min every 10 min, up to a maximum of 20 min. | Severe HF, COPD, asthma, hypotension, bradycardia. |
| Enalapril  | 0.625-1.25 mg in 5 min every 6 h.     | Sudden BP drop in renin-increasing states. ARF if renal artery stenosis.         |
| Diltiazem  | 0.25-0.35 mg/kg at 10 min Infusion 5-15 mg/h. | Sinus node disease or atrioventricular node. Severe HF. |
| Nitroprusside Sodium | 0.25-10 mg/Kg/min. | Potential increase in ICP, variable response, cyanide poisoning and Thiocyanate. |
| Esmolol    | 250-500 mg/Kg/min in bolus every 10 min or infusion 25-300 mg/Kg/min. | Severe HF, COPD, asthma, hypotension, bradycardia. |

HF: Heart failure; ARF: acute renal failure; COPD: Chronic obstructive pulmonary disease; BP: blood pressure; ICP: Intracranial pressure. Source: Modified de Pontes-Neto et al. (2009).
concentrate of factors II, IX and X, with variable amounts of factor VII, its concentration of coagulation factors dependent on vitamin K is about 25 times greater than that of fresh frozen plasma (FFP) and can reverse the coagulopathy rapidly, with lower volume and lower risk of infection, pulmonary edema, transfusion-related acute lung injury (Trali) and cardiac overload associated with transfusion (COAT).

If the use of unfractionated heparin: administer sulfate Protamine (IV) 1mg for each 100 units of heparin administered in the last 2-3 hours (maximum 50mg). Repeat half of the initial dose if ttpa remains elevated3.

If symptomatic HIP associated with the use of thrombolytics: administer fresh frozen plasma, cryoprecipitate, and platelets19.

Seizures
HIP patient has up to 16% risk of clinical seizures within a week, Particularly In those where there is hemorrhage Lobar With intraventricular flooding. Therefore, prophylactic treatment with anticonvulsants is recommended in patients with torporuous and comatose with activity Epileptiform HIP patient has up to 16% risk of clinical seizures within a week, Particularly In those where there is hemorrhage Lobar With intraventricular flooding. Therefore, prophylactic treatment with anticonvulsants is recommended in patients with torporuous and comatose with activity Epileptiform.

Phenobarbital, which should be maintained at therapeutic serum levels for one month and subsequently withdrawn20.

In cases of hydrocephalus, an external ventricular shunt may already reveal patterns that identify patients who benefit most from minimally invasive surgeries. And neuroprotection studies in surrounding areas of the lesion confirm the benefit of correct measures of intracranial hypertension, glycemic control, and body temperature.

The treatment of intracranial hemorrhage continues to be directed towards the reduction of disability and morbidity and mortality. However, prevention measures are widely studied and disseminated in clinical practice. In this area of prevention, adequate blood pressure control is of paramount importance.

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