# MANAGEMENT OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE – A REVIEW

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## ABSTRACT

Spontaneous intracerebral hemorrhage (SICH) is defined as a bleeding into the brain parenchyma which occurs in the absence of trauma or surgery. Medical and surgical management of SICH is complex. Medical management comprises of: treatment of arterial hypertension, treatment of increased intracranial pressure, anticonvulsant agents (recommended in supratentorial SICH). Many randomized studies have been conducted to compare surgical and medical management of SICH and the conclusions were not favourable to surgery. Still, early surgical intervention remains an option in some cases. Surgery should be considered in patients with moderate to large lobar or basal ganglia hemorrhages and those with progressive neurological deterioration. Patients with cerebellar hemorrhages larger than 3 cm, with brainstem compression and hydrocephalus and those exhibiting neurological deterioration should undergo surgical evacuation of the clot. Contraindications for surgery are: brainstem hemorrhages, small hemorrhages, elderly patients with Glasgow Coma Scale score less than 5. Evidence-based recommendations regarding the role of surgery in SICH are needed.

**Key words:** spontaneous intracerebral hemorrhage, management, surgery

## DEFINITION

Spontaneous intracerebral hemorrhage (SICH) is defined as a bleeding into the brain parenchyma which occurs in the absence of trauma or surgery. Intracerebral hemorrhage accounts for about 10-15% of all strokes and is associated with high mortality and morbidity. Depending on the underlying cause of hemorrhage, SICH may be classified as primary or secondary. Primary SICH accounts for approximately 70 to 80% of cases and it is due to spontaneous rupture of small vessels damaged by hypertension or amyloid angiopathy. Secondary SICH is associated with several conditions such as: vascular malformations, abnormal coagulation, vasculitis, tumors, trauma.

Terms such as: spontaneous intracerebral hemorrhage (SICH), primary intracerebral hemorrhage (PIH ), primary intracerebral hematoma are considered synonymous knowing that hemorrhagic phenomenon has a dynamic evolution.

## SICH MANAGEMENT

Guidelines from the American Heart Association/American Stroke Association (AHA/ASA) recommend that patients with SICH should be monitored and treated in an intensive care unit (1,2). This recommendation is based upon the frequent association of ICH with elevations in intracranial pressure and blood pressure, intubation and mechanical ventilation are sometimes needed and multiple medical issues and complications may occur. The treatment of the brain hemorrhage requires a multidisciplinary team.

Currently, there are debating on the appropriate management of SICH center on the issue of a conservative versus a neurosurgical approach.

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## MEDICAL TREATMENT

### General measures

SICH patients demand a correct diagnosis and treatment knowing that early neurologic deterioration is common in the first hours after the hemorrhagic event. Rapid neurological deterioration and ensuing loss of consciousness mandate permanent airway control (in some cases the patient should be intubated). General measures comprise of: maintenance of normothermia, evaluation and treatment of fever if it is neccesary, monitoring the glucose level considering that normoglycemia is recommended, hyperglycemia should be treated with insulin and hypoglycemia should be avoided. Fluids replacement should be initially done with normal saline solution, Dextrose-containing solutions should be avoided. Anticoagulant and antiplatelet drugs should be discontinued acutely after the onset of hemorrhage and anticoagulant effect should be reversed with appropriate agents. Intermittent pneumatic compression is used to prevent venous thromboembolism in patients with ICH. Prevention of aspiration in patients with SICH requires no feed that means nulla per os (NPO) status until swallowing function is evaluated.

### Systemic arterial hypertension treatment

Systemic arterial hypertension (SAH) is common in patients who have suffered a spontaneous intracerebral hemorrhage, since its onset. There is no consensus regarding the mechanism of this hypertension. The major factors involved seem to be the release of catecholamines and Cushing effect. There are limited clinical trial data regarding the correct decision. Outcomes of death and severe disability were found to be similar among patients groups with intensive blood pressure lowering (target systolic blood pressure (SBP) < 140 mmHg within one hour) versus traditional management (target SBP < 180 mmHg) in the INTERACT2 trial (Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial). In this study, 2,839 patients with acute ICH (within 6 hours) and elevated blood pressure were evaluated (3).

Current guidelines (1,2) for managing elevated blood pressure in acute SICH are:

- for patients with SBP > 200 mmHg or MAP >150 mmHg, consider aggressive reduction of blood pressure with continuous intravenous infusion of medication accompanied by frequent (every five minutes) blood pressure monitoring;
- for patients with SBP > 180 mmHg or MAP > 130 mmHg and evidence or suspicion of elevated intracranial pressure (ICP), consider monitoring intracranial pressure and reducing blood pressure using intermittent or continuous intravenous medication to keep cerebral perfusion pressure in the range of 61 to 80 mmHg;
- for patients with SBP >180 mmHg or MAP > 130 mmHg and no evidence or suspicion of elevated ICP, consider a modest reduction of blood pressure (target MAP of 110 mmHg or target blood pressure of 160/90 mmHg) using intermittent or continuous intravenous medication, and clinically reexamine the patient every 15 minutes.

The hemodynamic effect of most of the blood pressure lowering agents on the intracranial pressure is poorly understood. Most vasodilator drugs increase the intracerebral blood flow, thus having the potetial of elevating the intracranial pressure. Short acting lowering BP agents, such as alpha and beta blockers like labetalol, should be initially used. Nitroprusside, the most widely used hypotensive agent in severe blood pressure elevations, is a vasodilator that can increase the cerebral blood flow and subsequently, the intracranial pressure, but this effect hasn't been demonstrated on a clinical trial basis yet.

Arterial vasodilators like hydralazine, angiotensin-converting-enzyme inhibitors and calcium channel blockers have a lower tendency to increase intracranial pressure, to maintain blood flow. Venodilators must not be used in patients with SICH and increased intracranial pressure.

In conclusion, there is no absolute evidence that lowering blood pressure in the acute phase after a recent intraparechymal hemorrhage, has a significant effect on the patient's prognosis. A light reduction in the SBP can be well tolerated by patients with systemic hypertension or patients with an increased risk or rebleeding (such as those suffering from coagulopathies).

### Management of increased intracranial pressure

Increased intracranial pressure due to SICH can result from the hematoma itself and from surrounding edema. Increased intracranial pressure in spontaneous intracerebral hematoma can lead to herniation syndromes and death. Current guidelines recommend to begin the management of elevated intracranial pressure, with simple measures: elevate the head of the bed to 30 degrees after hypovolemia is excluded. Analgesia and sedation (with intrave-

nous propofol, etomidate, or midazolam), particularly in unstable, intubated patients are recommended. (1)

Glucocorticoids should not be used to lower the intracranial pressure in most patients with ICH they rarely improve the patient status.

ICP monitoring and treatment leads to a reduction of secondary lesions. Invasive monitoring and treatment of ICP should be considered for patients with GCS < 8, those with clinical evidence of transtentorial herniation, or those with significant IVH or hydrocephalus (2). Most authors recommend that ICP should be treated when it reaches more than 20 mmHg, thus achieving a cerebral prefusion pressure of above 60-70 mmHg.

Mannitol is frequently used, especially when surgical treatment isn't an option.

It is administered as an initial bolus of 1 g/kg, followed by infusions of 0.25 to 0.5 g/kg every six hours. The goal of therapy is to achieve plasma hyperosmolality (300 to 310 mosmol/kg) and also to maintain an adequate plasma volume. The major side effects include hypovolemia and a hyperosmotic state (7).

Hyperventilation to a $PaCO_2$ of 25 to 30 mmHg causes an important lowering of ICP, but unfortunately the effect only lasts for a few minutes to a few hours.

Cerebrospinal fluid drainage by intraventricular catheter placement (ventriculostomy) is an effective method of lowering ICP. Ventriculostomy will be used in patients with hydrocephalus or intraventricular bleeding. It is preferred to use the prophylactic antibiotics to patients with intracranial pressure monitoring devices. Neuromuscular blockade is sometimes employed to reduce ICP in patients who are not responsive to analgesia and sedation.

Barbituric coma can reduce ICP by decreasing cerebral metabolic activity, which translates into a reduction of the cerebral blood flow and also cerebral blood volume. Pentobarbital should be given in repeated boluses of 5 mg/kg at every 15 to 30 minutes until ICP is controlled. Usually a dose of 10 to 20 mg/kg is required. Then continuously infused at 1 to 4 mg/kg/h. Continuous electroencephalogram monitoring is neccesary.

Decompressive craniectomy may be necessary when all other methods have failed.

### Management of epileptic seizures

Seizures are more common in lobar then in profound hemorrhage. Most seizures occur in the first 24 hours after the onset of bleeding. If a seizure occurs, intravenous fosphenytoin or phenytoin is the most appropriate intravenous antiepileptic drug (AED) treatment that should be administered to prevent recurrent seizures (2). But the choice of the initial antiepileptic agent depends upon individual circumstances and contraindications.

There is no consensus regarding the disruption anticonvulsant therapy after an intracerebral hemorrhage, but in most patients it may be discontinued after the first if they have no electrical activity.

### Hemostatic therapy

The most studied agent that has been for used in ICH is activated recombinant factor VIIa (rFVIIa). Current guidelines have concluded that recombinant factor VIIa treatment for acute ICH that is not associated with warfarin use is investigational and should not be used for treatment of ICH outside the context of a study/trial (1,2).

## SURGERY TREATMENT

In 1883, Macewan reported the first surgical therapeutic success in a SICH.

Surgery has the potential to reduce the volume of intracerebral haemorrhage and there is clinical and experimental evidence that the removal of hematoma can reduce nervous tissue damage, probably by reducing the local ischaemia or removal of noxious chemicals.

Patients with a Glasgow score of 13-15 rarely need surgical treatment, as is also true for patients in a deep coma (Glasgow 3-5). Therefore, surgical treatment is an option in patients with a Glasgow score of 6-12 and in those with a progressively deteriorating neurological status.

There are many international studies with a focus on this matter but they lack the conclusive results needed in order to develop neurosurgical treatment guidelines.

### Supratentorial hemorrhage

Surgical therapy for patients with supratentorial ICH should be individualised. Indications for surgical treatment have not been well defined in these cases.

Current guidelines suggest toperform a standard craniotomy only in cases with lobar clots > 30 mL within 1 cm of the surface. The surgical method is standard craniotomy and no other method is accepted. No other patient group is recommended for surgery. Clinical studies have reported a wide variability in the timing of surgery, ranging from within

4 hours up to 96 hours from the onset of symptoms to time of operation. (1,2).

ISTICH I (International Surgical Trial in Intracerebral Hemorrhage) was the first multicenter randomized trial for the surgical treatment of spontaneous hematomas, it completed the recruitment of new cases in 2003. Investigators randomized 1,033 patients with supratentorial bleeding during the first 72 hours of onset and have included either in the group treated surgically or healthcare. 503 patients were assigned to early surgery and the result was satisfactory at 6 months. The outcome was good compared to those managed with the initial medical conservative treatment (14).

The STICH studies differ from the other trials in that early surgery was compared with the option of delayed surgery for patients who later deteriorate.

The STICH II – Surgical Trial in Lobar Intracerebral Haemorrhage – was done on 601 conscious patients, without intraventricular extension and found that rates of unfavorable outcomes after six months were similar in the 307 conscious patients treated with early (within 48 hours of onset) surgical hematoma evacuation versus the 294 patients initially treated conservatively. The results of the study were published in 2013 and they confirmed that early surgery does not increase the rate of death or disability at 6 months and might have a clinically relevant survival advantage for patients with spontaneous superficial intracerebral hemorrhage without intraventricular hemorrhage (15).

Decompressive craniectomy (DC) is performed to prevent intracranial pressure increase. There are few reports regarding DC in intracerebral hemorrhage and most of them regard the combined treatment of hematoma evacuation plus DC and less on DC, only. Although the effect of DC on perilesional edema remains unknown, it was showed that DC significantly reduces the midline shift, therefore counteracting the mass effects of the hematoma and edema formation (16). The diameter of decompressive craniectomy must be at least 150 mm wide opening of the dura followed by large duralplasty and suture the wound in anatomic planes.

### Minimally invasive surgery

The right moment to perform surgical drainage of intraparenchymatous hematomas is quite controversial and the method of performing it is even more controversial. Less invasive techniques then craniotomy include endoscopic hemorrhage aspiration, use of fibrinolytic therapy to dissolve the clot followed by aspiration, and CT-guided stereotactic aspiration.

### Basal ganglia haematomas

Generally, they don't have a surgical indication, studies showing no difference in outcome between medical and surgical treatment.

However, some spontaneous putamen hemorrhages can benefit from surgical treatment using a transfrontal, transtemporal (through the superior temporal gyrus) or transsylvian approach with the aid of microsurgical techniques.

### Thalamic hemorrhages

Thalamic hemorrhages do not have a surgical indication, most of the cases in which a surgical treatment was attempted, had a fatal outcome.

### Spontaneous cerebellar haematoma

There is a consensus regarding the role of surgical treatment in spontaneous infratentorial haematomas, although there are no controlled randomized trials designed to evaluate the surgical methods in posterior fossa spontaneous haematomas. A cerebellar haematoma of more than 3 cm, associated or not with hydrocephaly and compressing the brainstem, represents a definite indication. Surgery decreases the risk of brainstem compression and obstructive hydrocephalus. (2).

### Pontine haematomas

They rarely benefit from surgical treatment as they have an extremely poor prognosis regardless of treatment. If a surgical procedure is however attempted, an approach through the floor of the fourth ventricle or through the subarachnoid space is recommended (4).

In conclusion, there is no consensus in the literature about the best approach – clinical or surgical – that is applied to the majority of the patients with SICH and further studies are needed. The treatment shall be individualized taking into consideration the clinical feature of the patient, location and size of the hematoma.

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