Hypertension in acute stroke: a management dilemma

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Hypertension in acute stroke

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A 55-year-old patient presented to the emergency department with acute right-sided hemiparesis and drowsiness. His pulse was 100 bpm and blood pressure (BP) was 220/120 mmHg. He had no history of ischemic heart disease or renal impairment and was not diabetic.

What would be the initial approach in view of this marked elevation in BP?

To manage any patient with acute stroke you have to answer two important questions:

(1) Does this patient have ischemic or hemorrhagic stroke?
(2) If the patient has ischemic stroke, is he a candidate for thrombolytic therapy or not? and if he has a hemorrhagic stroke, what are the indications for surgery?

Management of hypertension in acute ischemic stroke

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The treatment of arterial hypertension immediately after stroke is problematic. Observational studies have found that a rapid and steep reduction in BP during the first 24 h after stroke onset might be harmful [1,2].

Pathophysiologic basis

Two important pathophysiologic processes should be considered during management of acute stroke. These are:

(1) Impaired cerebral autoregulation.
(2) Increased intracranial pressure (ICP).

(a) Impaired cerebral autoregulation

$$CBF=(CAP-JVP)/CVR,$$

where CBF is the cerebral blood flow, CAP is the carotid artery pressure, JVP is the jugular venous pressure, and CVR is the cerebrovascular resistance.

CBF is maintained relatively constant through autoregulation of CVR. Autoregulation of CVR can become dysfunctional during stroke. Under this condition, the brain will be very sensitive to even minor changes in cerebral perfusion pressure (CPP) [3,4].

Another important consideration is that the set-point for cerebral autoregulation is altered in chronic hypertension and the cerebral autoregulation curve is shifted toward the right. This means that CBF can be maintained at a constant level at higher BPs. Acute reductions in BP, even if in within the normal ranges, will lead to a decrease in CBF [as mean arterial pressure (MAP) will lie on the steep part of the cerebral autoregulation curve] and the development of ischemic symptoms in patients with chronic hypertension [3].

(b) Increased ICP

ICP is often increased in cases of intracerebral hemorrhage, large infarction, or brain edema. An increase in MAP may be the only means of maintaining CPP above 60–70 mmHg, the level necessary to maintain perfusion [5].

$$CPP=MAP-ICP,$$

where CPP is cerebral perfusion pressure, MAP is the mean arterial pressure, and ICP is the intra-cranial pressure.

In patients with ischemic stroke, perfusion pressure distal to the obstructed vessel is low, and the distal vessels are dilated. Thus, elevated BP is necessary to maintain brain perfusion in borderline ischemic areas [6]. Lowering of BP in patients with acute ischemic stroke has been associated with clinical deterioration.

The guidelines

For patients with acute ischemic stroke who are not eligible for thrombolytic therapy, the November 2010

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American Heart Association/American Stroke Association guidelines [7] are as follows:

(1) For patients with a systolic blood pressure (SBP) of 220 mmHg or less and a diastolic blood pressure (DBP) of 120 mmHg or less, BP should 'not' be treated acutely unless hypertension is extreme (SBP > 220 mmHg or DBP > 120 mm Hg) or the patient has active ischemic coronary disease, heart failure, aortic dissection, hypertensive encephalopathy, acute renal failure, or preeclampsia/eclampsia.
(2) For patients with SBP greater than 220 mmHg or DBP between 121 and 140 mmHg, a cautious attempt at lowering the BP by ~15% during the first 24 h after stroke onset should be made. Guidelines suggest that antihypertensive medications should be restarted at ~24 h after stroke onset in patients with pre-existing hypertension who are neurologically stable.

Further management

If BP is not maintained at or below 185/110 mmHg, do not consider administering recombinant tissue plasminogen activator (rtPA).

During and after thrombolytic therapy, BP should be maintained below 180/105 mmHg for at least 24 h.

Thrombolytic therapy [7]:

The sooner the rtPA is initiated the more likely it is to be beneficial.

Indications for thrombolytic therapy in acute stroke

(1) Acute ischemic stroke within 4.5 h of symptom onset.
(2) Exclusion of hemorrhage through a baseline computed tomography scan obtained before initiation of therapy.
   (a) The only Food and Drug Administration-approved thrombolytic therapy for ischemic stroke is rtPA at a dose of 0.9 mg/kg (max. 90 mg): 10% as an intravenous bolus, followed by 90% as a 60-min infusion. Antiplatelets and anticoagulants should be avoided for 24 h after lytic therapy.
   (b) The main concern as regards thrombolytic therapy is the risk for bleeding, and the most feared complication is symptomatic intracranial hemorrhage. Before lytic therapy is initiated, treatment is recommended so that BP is less than 185/110 mmHg.
   (c) Criteria for thrombolytic therapy are restrictive, and only 1–2% of patients with acute stroke receive thrombolytic therapy.

Remember

(1) BP management in the acute phase of stroke is different from chronic therapy.
(2) Acute BP lowering due to impaired cerebral autoregulation and, often, increased ICP should be avoided.
(3) BP should be cautiously reduced by ~15% within the first 24 h after stroke onset.
(4) Short-acting nifedipine should be avoided because it can cause a prolonged and precipitous decline in BP [8].

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Management of hypertension in hemorrhagic stroke

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In reference to the above-mentioned presented case:

(1) The patient presented to the emergency department with acute right-sided hemiparesis, drowsiness, and a marked elevation in blood pressure (BP).
(2) The differential diagnosis in the presence of lateralization is usually either hemorrhagic stroke or ischemic stroke.
(3) Elevation of the BP frequently occurs in patients with acute intracerebral hemorrhage (ICH). The degree of elevation in BP is usually greater than that seen in patients with ischemic stroke [1].
(4) Potential pathophysiologic mechanisms for this marked elevation in BP include stress activation of the neuroendocrine system (sympathetic nervous system, renin–angiotensin axis, or glucocorticoid system) and increased intracranial pressure [2].
(5) In view of the marked BP elevation in the present case; the diagnosis may be a hemorrhagic stroke. However, until brain computed tomography (CT) is performed, there is no clear evidence that will help us differentiate between hemorrhagic and ischemic stroke.

Pathophysiologic basis

Mechanisms of brain injury in ICH

Several mechanisms contribute to brain injury:

(1) Primary direct mechanical injury to the brain parenchyma by the expanding clot.
(2) Increased intracranial pressure (ICP).
(3) Herniation secondary to mass effect.

Both clot volume and secondary perilesional edema contribute to the mass effect [3].

Serial CT scans in patients with hypertensive hemorrhage have shown that the hemorrhage enlarges in the first 6 h after presentation in a subset of patients. In a prospective series of 103 patients with ICH, significant hematoma growth (a >33% volume increase) occurred in 38% of patients over the first 24 h.

Pathologic studies before CT scanning found that bleeding points occurred at the rim of the hemorrhage and postulated that this new recruitment of bleeding sites would lead to enlargement of the clot. As the clot expands, surrounding vessels are stretched, causing new sites of vessel rupture. Although the precise mechanism of hematoma enlargement is not yet defined and may be heterogeneous; blood-brain barrier breakdown and dysregulation of hemostasis through inflammatory cascade activation is common. Overexpression of IL-6 and matrix metalloproteinases, are probably important pathways.

In addition, the volume of the clot is very important in determining the outcome in patients with ICH, especially during the first 24 h [4].

The conflict:

(1) Severe elevations in BP may worsen ICH by causing bleeding and hematoma enlargement [5].
(2) Enlargement of the hematoma is associated with neurologic deterioration and worse outcomes. These observations indicate that significant improvements in patient outcome from ICH can be achieved by minimizing hematoma enlargement [6].

However,

(1) An increased mean arterial pressure may be necessary to maintain cerebral perfusion in some patients, and lowering the arterial pressure [e.g. to a systolic blood pressure (SBP) < 130 mmHg] may cause ischemic changes in the area surrounding the hematoma and worsen neurologic injury. Decreased blood flow to the area surrounding the clot causes local neuronal ischemia, which leads to further cytotoxic edema and release of toxic excitatory amino acids and inflammatory mediators [7,8].

Studies have been carried out in that respect:

(1) Limited prospective data are available on BP management in ICH.
(2) In a randomized controlled trial [INTensive Blood Pressure Reduction in Acute Cerebral Hemorrhage trial (INTERACT)] on 404 patients with acute spontaneous ICH, intensive BP lowering treatment (target SBP 140 mmHg), compared with traditional management (target SBP 180 mmHg), was associated with a reduction in hematoma growth at 24 h (14 vs. 26%). The study showed that SBP greater than 140–150 mmHg within 12 h of ICH is associated with more than double the risk of subsequent death or dependency [9,10].
(3) The Antihypertensive Treatment in Acute Cerebral Hemorrhage (ATACH) trial further confirmed these findings [11].
(4) Smaller, nonrandomized studies have also found that more aggressive BP lowering is associated with strong trends toward reduced hematoma enlargement. Some studies also showed trends toward reduced perilesional edema and better clinical outcomes [12].

The guidelines

The INTERACT and ATACH studies now represent the best available evidence to help guide decisions on BP lowering in ICH. Although these studies have shown that intensive BP lowering is clinically feasible and potentially safe, the BP pressure target, duration of therapy, and whether such treatment improves clinical outcomes remain unclear (Table 1).

(1) These guidelines also concluded that in patients presenting with an SBP of 150–200 mmHg, acute lowering to 140 mmHg is probably safe. They stated that the target for SBP should be 140 mmHg. However, this recommendation was labeled as Class IIa; Level of Evidence: B [13].

Further management of acute hemorrhagic stroke:

(1) Antihypertensive drugs: labetalol is the drug of choice [14].

Table 1 Suggested recommended guidelines for treating elevated BP in spontaneous ICH

1. If SBP is greater than 200 mmHg or MAP is greater than 150 mmHg, then consider aggressive reduction of BP with continuous intravenous infusion and frequent BP monitoring every 5 min.
2. If SBP is greater than 180 mmHg or MAP is greater than 130 mmHg and there is a possibility of elevated ICP, then consider monitoring ICP and reducing BP, using intermittent or continuous intravenous medications, while maintaining a cerebral perfusion pressure of 60 mmHg or more.
3. If SBP is greater than 180 mmHg or MAP is greater than 130 mmHg and there is no evidence of elevated ICP, then consider a modest reduction of BP (e.g. MAP of 110 mmHg or target BP of 160/90 mmHg), using intermittent or continuous intravenous medications to control BP, and clinically re-examine the patient every 15 min.

Note that these recommendations are Class C.
BP, blood pressure; ICH, intracerebral hemorrhage; ICP, intracranial pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

(2) Surgical management: the indications for surgery in patients with ICH vary with the site of the bleed. Intracerebral hemorrhage may be:
  (a) Cerebellar.
  (b) Supratentorial.
  (c) Intraventricular.

Cerebellar hemorrhage

(1) Surgical removal of the hemorrhage by cerebellar decompression should be performed under the following conditions:
  (a) If the hemorrhage is greater than 3 cm in diameter.
  (b) If there is clinical deterioration.
  (c) If there is brainstem compression and/or hydrocephalus due to ventricular obstruction [13].

Surgery decreases the risk for brainstem compression and obstructive hydrocephalus [13].

Supratentorial hemorrhage

(1) Surgery is controversial.
(2) It should not be considered either for patients who are fully alert or for those who are deeply comatose.
(3) It should only be considered as a life saving procedure to treat refractory increases in intracranial pressure; even under these circumstances, decisions should be addressed on a per patient basis [15].

Features that support performance of surgery include:

(1) Recent onset of hemorrhage.
(2) Ongoing clinical deterioration.
(3) Location of the hematoma near the cortical surface.

Features in favor of less aggressive therapy include:

(1) Serious concomitant medical problems.
(2) Advanced age.
(3) Stable clinical condition.
(4) Remote onset of hemorrhage.
(5) Inaccessibility of the hemorrhage.

Open craniotomy is the method of choice [16].

Intraventricular hemorrhage

Patients with neurologic deterioration in the setting of ventricular enlargement may be candidates for ventriculostomy and external ventricular drainage [17].

Conclusion

The management should be rapid and decisive. As stated before 'time is brain'. The management dilemma on whether to lower the BP or keep it as such will continue until we perform CT scanning of the brain for this patient to determine whether he has ischemic (do not lower the BP) or hemorrhagic stroke (aggressively lower the BP).

Diagnosing intracranial hemorrhage on clinical grounds is very imprecise; hence, neuroimaging studies using CT or MRI are critical to help guide BP therapy in stroke patients. According to the 2010 American Heart Association/American Stroke Association guidelines, CT should be performed within 25 min and CT interpretation should be available within 45 min of the patient's arrival at the emergency room [7].

The question on whether we are allowed to intervene or manage BP before obtaining a CT scan of the brain remains. In this case, the marked elevation in BP points toward a high possibility of a hemorrhagic rather than an ischemic stroke. Besides, all the previously mentioned guidelines still had their level of evidence 'B'. However, obtaining an answer to this question requires further studies.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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