Blood Pressure in Acute Stroke: Causes and Consequences

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Patients with acute stroke often have high blood pressure levels the first days after hospital admission. The causes of high blood pressure in patients with acute stroke are incompletely known. In stroke patients with large cerebral lesions and impaired consciousness, high blood pressure seems to be secondary to high intracranial pressure and in these patients high blood pressure indicates a worse prognosis. In the majority of patients, alert on hospital admission, high blood pressure increases from hospitalization stress and is not related to a worse prognosis. (*Hypertens Res* 1994; 17 Suppl. I: S77-S82)

Key Words: antihypertensive drugs, blood pressure, cerebrovascular disorders

Patients with acute stroke often have high blood pressure levels the first days after hospital admission (1, 2). In an population-based study, 20% of all patients had an admission blood pressure of 220/115 mmHg or higher (3). These high blood pressure levels are the result of a blood pressure elevation compared with prestroke blood pressures (4), and in most patients, the blood pressure will normalize without treatment within a few days in hospital (1, 3, 5) (Fig. 1). The causes of high blood pressure in patients with acute stroke are incompletely known and the literature contains various recommendations regarding acute antihypertensive treatment to patients with acute stroke. This article will review possible mechanisms causing high blood pressure in patients with acute stroke and the prognostic value of high blood pressure in these patients.

Why High Blood Pressure after Stroke?

Hypertension

About 50% of all stroke patients have a previously known hypertension (1-3, 6-9). A history of hypertension affects the absolute blood pressure level in acute stroke, but the blood pressure course follows the same pattern in previously normotensive patients as in hypertensive patients (3, 5), Fig 1.

Cushing-Reflex

High intracranial pressure may increase blood pressure through the Cushing-reflex (10). This well-known mechanism is probably not of importance in the majority of stroke patients with small lesions. The vasogenic edema is maximal at the end of the first week after the stroke (11), but at that time the blood pressure is most often normalized.

Homeostatic Response

The elevated blood pressure has been proposed to be a beneficial homeostatic response aimed to increase blood flow in the ischemic penumbra (3). The mechanisms underlying this putative homeostatic response are not understood.

Lesions in Cardiovascular Control Areas

In experimental animals it is possible to increase or decrease blood pressure by stimulation or ablation in many regions of the nervous system, such as nucleus tractus solitarius in the medulla, the parabrachial nucleus of the pons, the hypothalamus, etc. (12, 13). In man, tumors at such locations have induced hypertension, and the hypertension has been cured after removal of the tumour (14). An autopsy study found patients with infarctions or hemorrhages in the pons to have had higher blood pressures before death than patients with lesions at other localisations (15). In a study including also survivors, patients with brainstem infarctions or TIA had no higher blood pressures than patients with cerebral hemispheric lesions (16). The importance of this type of blood pressure elevating mechanism in the total population of patients with acute stroke is unknown.

Mental Stress

The blood pressure course after stroke is more related to the time after hospitalization than to the time after onset of symptoms (5, 17). Patients with large neurological deficits do not have higher blood pressures than patients with small deficits or TIA (5). Therefore, mental stress at hospitalization has been proposed to be a significant blood pressure elevating factor in many patients with acute stroke. Hypertensive subjects without stroke have a blood pressure course after hospitalization that is similar

Fig. 1. Systolic (SBP) and diastolic (DBP) blood pressure course in stroke patients with previous hypertension (■) and without previous hypertension (□), at hospital admission (Adm), the first day in the ward (1), the 4th day in the ward (4) and on discharge from hospital (Dis). The bars indicates 95% confidence intervals of the group mean values. From ref.5.

to the course in patients with acute stroke (18).

Sympathetic Activation

The blood pressure elevation in patients with acute stroke is thought to be mediated through sympathetic activation. Patients with acute stroke are hemodynamically characterised by an increased peripheral resistance (19). High catecholamine levels are found in plasma and urine during the first days or weeks after stroke (20). Catecholamine levels have been related to blood pressure levels in some (21, 22), but not in all studies (23). Patients with impaired consciousness and high blood pressure refractory to antihypertensive treatment have very high catecholamine excretion (24). However, the secretion rate of norepinephrine and epinephrine seems to remain high for a longer period after stroke than blood pressure does (21, 22).

Animal Studies

It is difficult to reproduce a stroke in an elderly human in animal models. The use of anesthetics makes it difficult to study the "normal" blood pressure course after cerebral infarctions in animals. In many animal stroke models, blood pressure does not increase after middle cerebral artery occlusion (25-29) but this finding is not entirely consistent (30). There may also be different blood pressure responses after occlusion of the left compared to the right middle cerebral artery (31). The results from animal studies are probably not immediately transferable to stroke patients.

High blood pressure after stroke may thus have multiple etiologies. In patients with large cerebral lesions, especially intracerebral hemorrhages, the Cushing-reflex is the most important blood pressure-elevating mechanism. In patients with small lesions or TIA, hospitalization stress is probably the most important mechanism for the blood pressure course and the blood pressure level is dependent on the prestroke blood pressure level.

Is High Blood Pressure Shortly after Stroke Associated with a Worse Outcome?

A history of hypertension has been related to increased 30-day case fatality rate (32) and increased risk of stroke recurrence during the first 30 days after stroke (33). Other studies did not find a history of hypertension to result in a worse prognosis in the acute stage (34).

Studies on the association between initial blood pressure levels and short-term outcome in patients with acute stroke are summarized in Table 1. A majority of the studies found a worse prognosis in patients with high initial blood pressure levels. The relation between blood pressure levels and stroke prognosis is different in different subsets of stroke patients. Patients with impaired consciousness have a worse prognosis with higher blood pressure levels (40) (Fig. 2) probably reflecting high intracranial pressure. In alert patients, high blood pressure is not associated with worse outcome.

Shall We Treat Hypertension in the Acute Phase of Stroke?

The recommendations in the literature regarding treatment of high blood pressure in the acute phase of stroke are variable. Many advocate avoiding treatment (45-52), while others prefer to treat high blood pressures, e.g. $\geq 180/105$ mmHg (53-59). There are a number of concomitant disorders that definitely increase the need for acute treatment. Dissection of an aortic aneurysm where the dissection obstructs the flow to the brachiocephalic artery or the left common carotid artery is an unusual cause of stroke but necessitates acute antihypertensive therapy. The high blood pressure should be treated if overt heart failure, unstable angina or myocardial infarction is present. In patients with increased risk of hemorrhage from anticoagulant or thrombolytic therapy it may also be advantageous to lower high blood pressures. Other severe

Table 1. Observational Studies Investigating the Association between Initial Blood Pressure Levels and Short-Term Outcome in Patients with Acute Stroke

No. of pat.	Diagnosis	Endpoint	Blood pressure cut-off level	Results	Authors
92	I+H	mortality	SBP $\geq$ 220 or DBP $\geq$ 120	—*	Harmsen <i>et al</i> (35)
148	I+H	ADL + mortality	SBP	+	Allen (36)
6,395?	I+H	mortality	SBP $\geq$ 200 DBP $\geq$ 115	—* —*	Hatano (37)
388	I+H	mortality	$\geq$ 220/115	—	Britton <i>et al</i> (38)
98	I	deterioration	SBP	—	Dávalos <i>et al</i> (39)
1,273	I	recurrence	SBP $\geq$ 160 DBP $\geq$ 100	= —	Sacco <i>et al</i> (33)
831	I	mortality	MAP	—/0#	Carlberg <i>et al</i> (40)
94	H	mortality	SBP PP $>$ 65	= —	Turhim <i>et al</i> (41)
77	H	mortality	n.p.	=*	Dollberg <i>et al</i> (42)
85	H	mortality	MAP	—/0#	Carlberg <i>et al</i> (40)
244	Hx	mortality	n.p.	=*	Nath <i>et al</i> (43)
75	Hc	deterioration	SBP $\geq$ 200	—	Dunne <i>et al</i> (44)

I, ischemic stroke; H, hemorrhagic stroke; Hx, the study also included cerebral hemorrhage of non-stroke origin; Hc, cerebellar hemorrhage; SBP, systolic blood pressure, mmHg; DBP, diastolic blood pressure, mmHg; MAP, mean arterial blood pressure; PP, pulse pressure; n.p., not presented; +, better outcome with high blood pressure; —, worse outcome with high blood pressure; =, no association between outcome and blood pressure; —/0#, increased mortality in patients with impaired consciousness, but not in alert patients; *, statistics of the results not presented. Where no cut-off level is presented, blood pressure was used as a continuous variable.

Fig. 2. Thirty-day case fatality rate in 831 stroke patients with different blood pressures at hospital admission. Filled circles, patients with impaired consciousness. Open circles, alert patients. The calculated regression lines for patients with impaired consciousness are inserted. From ref. 40.

hypertensive vessel disease, especially hypertensive encephalopathy, should also be treated.

In the more ordinary stroke patient, arguments

for acute treatment are the edema around a hemorrhage or an infarction that may increase if blood pressure is high (60). In experimental animals, a cerebral infarction may be transformed into a hemorrhagic infarction if the blood pressure is high (61). In stroke patients, hypertension may not involve a similar risk for hemorrhagic transformation (62).

On the other hand, in a patient with acute ischemic stroke, acute antihypertensive therapy may involve a substantial risk. The cerebral circulation may already be compromised by stenoses in the carotid arteries and other vessels. Autoregulation is impaired and therefore a blood pressure reduction may directly decrease blood flow in the already ischemic areas surrounding the infarct (63). Also, case reports in the literature describe patients who have deteriorated or died after acute blood pressure-lowering therapy (46, 64). Also, the spontaneous blood pressure decline after hospitalisation most often makes such therapy unnecessary. A study designed to evaluate the effect of acute antihypertensive therapy in patients with acute stroke and a diastolic blood pressure of 115–135 mmHg was stopped because the spontaneous blood pressure fall during the 3 h of observation before randomisation was so common that only 18 out of 684 patients could be randomized (65). Acute antihypertensive therapy thus seems not to be indicated in most patients with acute ischemic stroke. The

opposite, pharmacologically induced hypertension has been tested in patients with acute stroke. Some patients react with an immediate regression of symptoms, but the positive effect seems to be of short duration (66). In animal models, the beneficial effect of induced hypertension after experimental stroke (67, 68) is inconsistent with the deterioration after induced hypertension found in other studies (69). Induced hypertension may increase the cerebral edema and increase the risk for hemorrhage. Therefore, such therapy is probably not feasible in most patients with stroke (70).

The situation is somewhat different in patients with acute intracerebral hemorrhage. Intracerebral edema and high intracranial pressure are more pronounced than in cerebral infarctions. High blood pressure increase the edema (60), but the subsequent blood pressure elevation from the Cushing-reflex helps to maintain cerebral perfusion pressure despite this high intracranial pressure. Rebleedings in the hematoma have been reported to occur mainly in patients with very high blood pressure (71, 72). The frequency of rebleedings is unknown and rebleedings diagnosed from clinical signs are very rare (71). With early and repeated CT-scans, rebleeding may be detected more commonly, especially among aspirin users (72).

On the other hand, the brain tissue around the hemorrhage may be hypoperfused if blood pressure is lowered and may result in infarction (46). In one study cerebral blood flow decreased if blood pressure was lowered more than 20% (equal to pre-stroke levels in the study patients) in patients with acute intracerebral hemorrhage (73). With current information a cautious modest blood pressure reduction may be advantageous to prevent rebleeding and decrease the edema, but the total net gain of such therapy is unknown. It is difficult to perform and control such therapy in non-intensive stroke units.

Treatment of High Blood Pressure in Patients with Acute Stroke

If acute antihypertensive drug therapy has to be administered to a patient with acute stroke, the cerebrovascular effects of the drug must be taken in consideration.

Intracranial pressure may increase after acute administration of many antihypertensives. This has been shown with nifedipine (74), nitroglycerine (75), nitroprusside (76), dihyralazine (77), chlorpromazine (74) and reserpine (74).

Cerebral blood flow decreases after acute administration of diazoxide (78), clonidine (79) and betablockers (80-81).

Diuretics (mainly furosemide for acute therapy) is preferable to patients with volume overload such as cardiac or renal failure. In other patients, diuretic therapy should be avoided as dehydration increase blood viscosity. Furosemide decreases elevated intracranial pressure (74) but the effect on blood pressure is usually small.

After acute administration of betablockers, cere-

bral blood flow decreases and the acute effect on blood pressure is usually very modest. Combined alpha- and betablockers such as labetalol do not seem to have a similar deleterious effect on cerebral blood flow (78) and can be used if acute antihypertensive therapy is needed in stroke patients.

Calcium antagonists are widely used to patients with ischemic or hemorrhagic stroke. They may, however, increase intracranial pressure in patients with cerebral hemorrhage (74), and reduce cerebral blood flow in patients with cerebral infarction (63). Calcium antagonists should therefore be used with caution shortly after stroke.

ACE-inhibitors do not decrease cerebral blood flow (82). In patients with acute stroke, cerebral blood flow does not change after administration of captopril (83). ACE-inhibitors are therefore possible to use in patients with acute stroke. Low initial doses should be used to avoid hypertension in patients with activated renin-angiotensin system.

Central acting drugs like clonidine and alphas-methyl-dopa should also be avoided because of the sedative effect.

If acute antihypertensive therapy is necessary in a patient with acute stroke, a combined alpha- and betablocker such as labetalol or ACE-inhibitors seems to be most advantageous. If the antihypertensive drug is given orally in low doses and after the first days in hospital, the acute effects on cerebral vessels are probably of less importance.

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