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Acute controlled hypotension and EEG in patients with hypertension and cerebrovascular disease

P. HARMSEN, J. KJÆRULFF, AND E. SKINHØJ

From the Neurological Department N, and the Medical Department C, Bispebjerg Hospital, Copenhagen, Denmark

SUMMARY Forty-seven patients with hypertension and/or cerebrovascular disease were examined by an acute controlled hypotension test. This was performed by intravenous administration of the ganglionic blocking agent pentholonium and head-up tilting on a pivoted table with observation of the clinical neurological state and simultaneous EEG recording. Blood pressure was reduced by approximately 55% and brought to the point where signs of general cerebral ischaemia developed. By tilting back to horizontal the blood pressure returned to near the normal level. No change in focal neurological symptoms or changes in the EEG were observed, and it is concluded that the majority of hypertensive patients with or without previous stroke do tolerate normalization of their blood pressure. Controlled hypotension with tilting seems a simple and valuable test for excluding those few subjects who might not tolerate a blood pressure reduction. Whether EEG monitoring during the test increases the value of the test has not been answered.

Cerebrovascular accidents and mortality are increased in hypertensive patients (Leishman, 1959, and others) and in hypertensive stroke survivors (Marshall and Kaeser, 1961; Baker, Ramseyer, and Schwartz, 1968a; Baker, Schwartz, and Ramseyer, 1968b; Marquardsen, 1969). There is at present very little doubt about the beneficial effect of hypotensive therapy in patients with hypertension even when cerebrovascular disease is present. Several studies have shown that mortality is reduced, partly due to a reduction of the number of further strokes causing death, and that the overall number of cerebrovascular incidents is decreased (Marshall, 1964; Hood, Aurell, Falkheden, Olanders, and Bjork, 1966; Carter, 1970). This is supported by the findings of Cole and Yates (1968) by the demonstration of a 50% incidence of cerebrovascular lesions in consecutive post mortem studies of 100 hypertensive patients against a 25% incidence in 100 normotensive patients. Hamilton, Thompson, and Wiśniewski (1964) found that the diastolic blood pressure must be kept at 110 mm Hg or less in order to obtain a reduction in the number of strokes.

However, often the question arises of how much the pressure in a hypertensive patient should be reduced without this reduction involving a risk for cerebral ischaemia, and further whether this risk may be more pronounced in the patient with cerebrovascular disease. It is known that some hypertensive patients apparently do not tolerate the reduction of blood pressure which is desirable if the long term risk for cerebral complications is to be avoided. Two examples of this type of patient are described by Shanbrom and Levy (1957). Neurological deficits occurred when blood pressure was reduced and were reversed by restoring blood pressure to the original levels. Many others have reported cerebral focal or generalized symptoms occurring during hypotensive therapy. This was often a complication of the use of ganglionic blockers (Grimson, Orgain, Rowe, and Sieber, 1952; Corday, Rothenburg, and Putnam, 1953), but even the present use of thiazides and methyldopa has been reported to cause similar side-effects (Böttiger, Malmborg, and Michaeli, 1964). Fazekas, Kleh, and Parrish (1955) inferred that hypotension was the cause of cerebral complications in these patients.

When considering this category of patients and in particular the hypertensive patients with cerebrovascular disease, the following observations might be of importance:

1. When blood pressure is lowered over a period

of minutes (acute hypotension) it has been established that hypertensive patients develop signs of cerebral ischaemia at a higher blood pressure level (Kety, King, Horvath, Jeffers, and Hafkenschiel, 1950; Finnerty, Witkin, and Fazekas, 1954; Kleh and Fazekas, 1954; Stevens and Fazekas, 1955) than do normal subjects (Moyer and Morris, 1954; Karp, Weissler, and Heyman, 1961) (the critical blood pressure). The various clinical symptoms that develop during this induced acute hypotension have been reported by a number of workers (among others Bessman, Alman, and Fazekas, 1952; Finnerty, Guillaudeu, and Fazekas, 1957).

2. By combining clinical observations with simultaneous EEG recording during acute hypotension it has been shown that focal or global changes appear in the EEG in relation to the occurrence of clinical symptoms of cerebral ischaemia (Stevens and Fazekas, 1955; Meyer, Leiderman, and Denny-Brown, 1956; Weiss and Froelich, 1958; Karp *et al.*, 1961).

3. Severe stenosis of the extracranial major arteries endangers the cerebral circulation and universal or local ischaemia would be likely to develop at hypotension (Marshall, 1968). Angiography with demonstration of the extracranial parts of the caroticovertebral systems might reveal these cases.

4. Regional cerebral blood flow studies with functional tests (Skinhøj, Høedt-Rasmussen, Paulson, and Lassen, 1970) have demonstrated that focal or global loss of cerebrovascular autoregulation is only found shortly after a cerebral vascular accident, but never in between the attacks in patients with repeated strokes. The conclusion of these studies is that haemodynamic crises (Denny-Brown) cannot be responsible for the majority of repeated strokes. This implies that the theoretical contraindication for prophylactic treatment of hypertension in such patients cannot be accepted as a general rule. However, such investigations cannot exclude the possibility that some patients may have an area within the brain with a marginal blood supply and with lost autoregulation. If so, a reduction in blood pressure may be critical.

For daily clinical use determination of regional cerebral blood flow in all hypertensive patients is too complicated a procedure and even angiography of the arteries in the neck and brain may not often otherwise be indicated. But clinical observation with EEG monitoring during acute controlled hypotension remains a possibility for obtaining a screening procedure. It was the purpose of the present study to determine whether in this way a non-traumatic and easily performed method could be established by which those hypertensive patients might be identified who because of increased cerebrovascular resistance or stenosis of extracranial major arteries could be recognized as non-tolerant to any reduction of their blood pressure, and in other cases to determine the level of the critical blood pressure and whether in these individuals the reduction of blood pressure through hypotensive therapy therefore might or might not involve any risk of global or focal cerebral ischaemia.

METHODS

Forty-seven patients were investigated with the acute hypotension test. They were divided by their resting blood pressure and hypotensive therapy into four groups. We defined hypertension as the blood pressure being above 170 mm Hg systolic and above 110 mm Hg diastolic. Group I comprised hypertensive cases having had no hypotensive medication at the time of the investigation, group II comprised hypertensive cases receiving hypotensive therapy at the time of investigation, group III and IV normo- and hypotensive cases respectively, and group V two cases of cerebral tumour, included here because a focal loss of cerebrovascular autoregulation is usual in these patients and EEG changes were therefore likely to occur during hypotension (Pálvölgyi, 1969). In group I the first 11 cases were patients with untreated essential hypertension consecutively admitted to the medical department C and the neurological department N of Bispebjerg Hospital during an 11 month period. Four of these had cerebrovascular disease at the time of the investigation. Apart from general physical and neurological examination with routine laboratory examinations which were carried out on all patients in all groups, these 11 had intravenous urography and ophthalmological examinations performed. The remaining seven cases in group I were patients with unspecified hypertension likewise receiving no hypotensive medication at the time of the investigation. All of these showed focal symptoms of cerebrovascular disease.

The acute hypotension test as a rule was performed immediately after the routine EEG recording. The patient was lying in the supine position on a tilt-table, the EEG electrodes remaining in routine positions and the common reference electrode lead being used during the test. Resting blood pressure was recorded, and the hypotension was induced by intravenous injection of pentholonium (Ansolysen®) 2·5 mg and head-up tilt to 25-78° for two to 20 minutes. In some cases further injections of pentholonium (2·5 mg) and/or chlorpromazine 5 mg were needed in order to achieve any noticeable blood pressure reduction. The blood pressure was recorded on the right arm with a mercury sphygmomanometer at close intervals (30 seconds during blood pressure changes) and recorded on the EEG curve. Mean resting blood pressure and mean minimum blood pressure were calculated as one-third of the difference between systolic and diastolic pressure added to the diastolic pressure. The minimum blood pressure was corrected for the vertical hydrostatic pressure difference during the tilt

between the brachium and the internal carotid levels. During the test the patient was closely observed clinically by assessment of speech, eye movements, power of facial movement, grip and elbow flexion, tendon reflexes of biceps and patella, and appreciation of any subjective symptoms. As soon as signs of general cerebral ischaemia developed in the form of dizziness, nausea, yawning, involuntary body movements, or fainting, the table was tilted back to horizontal and the corresponding rise in blood pressure confirmed. In two cases metaraminol (Aramine®) had to be given to secure sufficient return of blood pressure to the original level. After the test the patient was kept in a horizontal position for four to six hours after which time the effect of pentholonium should be negligible. There were no ill effects of the procedure. The performance of the test usually took 30 to 45 minutes. The EEG curves included a part obtained during rest immediately before the test itself and parts obtained during the hypotension at various degrees of tilt. They were studied for any appearance of slow wave, high voltage activity at hypotension which was not present in the resting curve.

In a few instances the test was enlarged to include inhalation of 6% carbon dioxide in atmospheric air for three minutes with clinical observation and EEG monitoring in order to assess any appearance of change in either due to the change in cerebral blood flow induced by the carbon dioxide. By changing the degree of the tilt the rise in blood pressure with carbon dioxide inhalation could be compensated and the pressure kept near the level of the resting state. Carotid or vertebral angiography were performed in a number of the cases.

RESULTS

Table 1 summarizes the cases and the results of

TABLE 1

HYPERTENSIVE CASES WITHOUT HYPOTENSIVE THERAPY

Case no.	*Age (yr)*	*Sex*	*Neurol. deficit*	*Routine EEG*	*Resting BP mean (mm Hg)*	*Minimum BP mean (mm Hg)*	*BP reduction (%)*	*At hypotension:*	
								Change in focal neurol. symptoms	*EEG change*
14	68	F	None	Diffuse abnormality	190	100	47	No	No
18	55	F	None	Normal	147	57	61	No	No
29	65	F	None	Normal	160	57	64	No	No
26	66	M	None	Normal	143	93	35	No	No
36	68	M	None	R side abnormality	147	57	61	No	
46	49	F	None	Normal	180	58	68	No	No
17	71	F	None	Diffuse abnormality	137	50	63	No	No
			Arithmetical	mean	158	67	57		
9	55	M	Slight R hemiparesis	Normal	150	57	62	No	No
15	44	F	R hemiparesis	L side abnormality	135	63	53	No	No
19	54	M	R hemiparesis	Normal	143	70	51	No	No
41	71	M	L hemiparesis	Normal	133	36	73	No	No
			Arithmetical	mean	140	57	60		
7	78	F	L hemiparesis	R side abnormality	170	78	54	No	No
16	75	F	L hemiparesis	R side abnormality	167	57	66	No	No
20	66	M	Transient L hemiparesis	Normal	140	77	45	No	No
22	71	M	Transient L hemiparesis	L side abnormality	135	57	58	No	No
40	66	F	L hemiparesis	R side abnormality	140	50	64	No	Slight diffuse slowing
47	52	M	R hemiparesis	L side abnormality	133	83	38	No	No
			Arithmetical	mean	148	65	54		
			Arithmetical all 3 subgroups	mean	149	63	57		
44	84	M	Transient R hemiparesis	L side abnormality	143	140	16	No	No

acute hypotension in group I (hypertensive cases not receiving hypotensive therapy). None of these showed signs of focal neurological changes or aggravation of preexisting focal deficits at hypotension, and in only one a diffuse, slight slowing of EEG activity appeared symmetrically, the change amounting to approximately 1 Hz with no change in amplitude. Cases 9, 7, 16, 22, and 44 had carotid angiography performed, showing general arteriosclerosis intracranially on the relevant side. Cases 15 and 19 had normal findings at carotid angiography, and cases 40 and 47 had an occlusion of the middle cerebral artery shown at angiography. Cases 9, 15, 20, 22, and 44 had transitory ischaemic attacks before hospital admission. No such attacks could be provoked through the acute hypotension test. In case 44 no pentholonium was administered but instead the tilt was performed as quickly as possible in order to provoke symptoms or EEG changes by this method only. The tilt could be changed from 0 to 78° in 25 seconds. No symptoms or EEG changes were noted, and the blood pressure reduction obtained was small.

The results of acute hypotension in group II (hypertensive cases receiving hypotensive therapy) are shown in Table 2. The blood pressure reduction obtained was of the same order of magnitude as in the previous group. No changes in clinical neurological focal symptoms could be noted and only in two cases did changes in the EEG appear. These were, however, slight and did not occur over the relevant hemisphere. In 10 of the patients transient ischaemic attacks had occurred either as sole symptom or accompanying the permanent neurological deficit (cases 2, 3, 5, 8, 10, 11, 12, 13, 23, and 43) and again no symptoms similar to the previous ischaemic attacks could be provoked at the hypotension test. Carotid angiography in case 12

TABLE 2

HYPERTENSIVE CASES WITH HYPOTENSIVE THERAPY

Case no.	*Age (yr)*	*Sex*	*Neurol. deficit*	*Routine EEG*	*Resting BP mean (mm Hg)*	*Minimum BP mean (mm Hg)*	*BP reduction (%)*	*At hypotension:*	
								Change in focal neurol. symptoms	*EEG change*
2	72	F	R hemiparesis	L side abnormality	102	52	49	No	No
3	68	F	Transient aphasia	Normal	127	37	71	No	No
5	61	M	Brain-stem symptoms	Diffuse abnormality	113	71	38	No	No
6	56	F	Brain-stem symptoms	Normal	157	77	51	No	No
8	67	F	R hemiparesis	L side abnormality	153	70	54	No	No
10	55	M	R hemiparesis	R side abnormality	183	126	31	No	No
11	57	F	R hemiparesis	L side abnormality	127	50	61	No	Slight slowing R side
12	52	F	L hemiparesis	R side abnormality	143	57	60	No	Slight slowing L side
13	57	M	R hemiparesis	Diffuse abnormality	147	76	48	No	No
21	62	F	Brain-stem symptoms	Normal	153	117	23	No	No
23	59	M	Transient brain-stem symptoms	L side abnormality	113	57	50	No	No
30	54	M	R hemiparesis	Normal	147	88	40	No	No
32	50	F	R + L hemiparesis	Diffuse abnormality	163	53	67	No	No
35	72	F	R hemiparesis	L side abnormality	167	83	50	No	No
38	63	F	L hemiparesis	R side abnormality	120	53	56	No	No
42	77	F	L hemiparesis	R side abnormality	140	70	50	No	No
43	55	M	Transient R hemiparesis	Normal	147	90	39	No	No
50	46	M	L hemiparesis	Diffuse abnormality	167	66	60	No	No
			Arithmetical	mean	143	66	50		

was normal on both sides, whereas in case 13 both internal carotid arteries showed subtotal stenosis. (This patient had six years previously had radiotherapy for cancer of the larynx.) Case 30 with a grave hypertension had two years previously, at institution of hypotensive therapy, developed a right-sided hemiparesis which disappeared completely when hypotensive treatment was stopped. Later a gradual reinstitution of hypotensive treatment had no ill effects, and at the hypotension test no symptoms could be provoked. Case 32 showed a rapid fall in blood pressure after pentholonium without any tilting. It was necessary to give metaraminol (Aramine®) and at the subsequent rise in blood pressure to above the resting state level there were no changes in clinical symptoms or in the EEG. Case 3 was admitted to hospital because of syncopal attacks of which one had been accompanied by aphasia for three to four hours. At the hypotension test no neurological deficits were present, and at the minimum blood pressure of 70/50 mm Hg at 68 degrees of tilt still no neurological deficits occurred. The patient became dizzy but regained full consciousness as soon as the tilting was returned to horizontal and blood pressure was restored to the previous level.

Table 3 gives the results of group III, comprising normotensive cases with cerebrovascular disease. Three of these cases (4, 34, and 37) had had transient ischaemic attacks but similar symptoms did not occur at acute hypotension here. Only case 44 showed in the EEG a very slight slowing of the activity on both sides with no increase in amplitude. Angiography in case 4 showed normal conditions in both internal carotid arteries but the right vertebral artery seemed absent. In case 31 angiography revealed an occlusion of the middle cerebral artery on the left side during his first hospital admission and at the second visit even the right middle cerebral artery was occluded. Case 33 had an occlusion of the left internal carotid artery and case 34 occlusion of the right internal carotid artery. Case 31 (a, b) had no clinical change in neurological symptoms at hypotension, but in the EEG a definite slowing in activity with slightly increased amplitude appeared (Figure), this however did not occur on the relevant side as expected and at a repeat test the following day the same result was obtained. The patient was readmitted a few months later with a new cerebrovascular attack, this time from the opposite side (a left hemiparesis) (case 49). The hypotension test performed on the second admission still showed no change in clinical symptoms and in the EEG there was again a similar change of slowing focally on the same side (right side) as previously. In cases 33, 34, 37, 39, and 49 carbon dioxide 6% inhalation was administered, the blood pressure being kept near normal for the patient. No changes occurred in clinical symptoms or in the EEG except for case 37 where a very slight diffuse slowing of activity was noted. In case 39 blood pressure did not rise sufficiently towards the original level after returning the tilt position to horizontal and Aramine® was consequently given. During the subsequent rise in blood pressure no changes were noted in the clinical state or in the EEG. On the whole, it seemed that

TABLE 3

NORMOTENSIVE CASES

Case no.	*Age (yr)*	*Sex*	*Neurol. deficit*	*Routine EEG*	*Resting BP mean (mm Hg)*	*Minimum BP mean (mm Hg)*	*BP reduction (%)*	*At hypotension:*	
								Change in focal neurol. symptoms	*EEG change*
4	48	M	Brain-stem symptoms	Normal	103	50	51	No	No
31a	67	M	R hemiparesis	R side abnormality	47	40	59	No	Focal slowing *right* side
31b	67	M	R hemiparesis	R side abnormality	102	38	63	No	Focal slowing *right* side
33	60	M	R hemiparesis	L side abnormality	117	61	48	No	No
34	58	M	L hemiparesis	R side abnormality	122	50	59	No	No
37	67	F	L hemiparesis	R side abnormality	120	30	75	No	Diffuse slight slowing
39	76	M	R hemiparesis	L side abnormality	110	40	66	No	No
49	67	M	L + R hemiparesis	Diffuse abnormality	93	30	68	No	Focal slowing *right* side
51	70	M	R hemiparesis	Diffuse abnormality	107	45	58	No	No
			Arithmetical	mean	108	43	61		

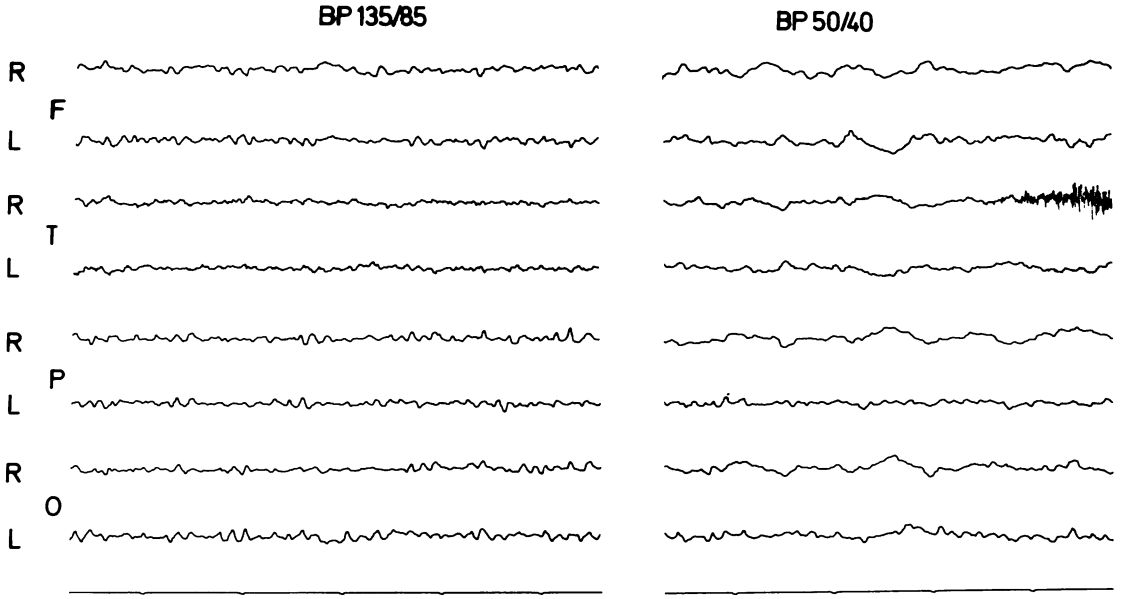

FIGURE. *Illustration of positive EEG response at acute hypotension test in case no. 31 where the most pronounced change of EEG towards slow wave, high voltage activity in the whole series was observed. Note that the change unexpectedly occurred over the hemisphere ipsilateral to the side of hemiparesis. Time scale — seconds.*

patients with recent cerebrovascular attacks were more prone to drop in blood pressure with the standard pentholonium dose than patients with attacks occurring a week or more before.

In Table 4 are presented the two cases considered hypotensive. Both had suffered transitory ischaemic attacks and these were the only symptoms in case 24. Even here no symptoms or EEG changes were noted at acute hypotension.

Table 5 gives the results of the hypotension test in two patients with cerebral tumour (a meningeoma and a glioma respectively). The test here gave no changes in clinical picture or in the EEG and therefore gave no indication of any change in functional activity in the tissue areas around the tumours, where it is known that regional cerebral blood flow and its regulation are disturbed (Pálvölgyi, 1969).

DISCUSSION

It is evident from the results that in this series we have not been able by application of the acute controlled hypotension test to identify subjects who might not tolerate a blood pressure reduction of the order required for routine hypotensive therapy. This is in spite of the fact that the blood pressure was in nearly all cases reduced to the critical level where general cerebral ischaemia developed.

That patients with hypertension and/or cerebrovascular disease do tolerate a blood pressure reduction to or below normal levels without this

TABLE 4

HYPOTENSIVE CASES

Case no.	*Age (yr)*	*Sex*	*Neurol. deficit*	*Routine EEG*	*Resting BP mean (mm Hg)*	*Minimum BP mean (mm Hg)*	*BP reduction (%)*	*At hypotension:*	
								Change in focal neurol. symptoms	*EEG change*
24	87	F	Transient R hemiparesis	Diffuse abnormality	87	61	30	No	No
25	75	M	Brain-stem symptoms	Normal	97	51	47	No	No
			Arithmetical	mean	92	56	39		

TABLE 5

CASES OF CEREBRAL TUMOUR

Case no.	Age (yr)	Sex	Neurol. deficit	Routine EEG	Resting BP mean (mm Hg)	Minimum BP mean (mm Hg)	BP reduction (%)	At hypotension:	
								Change in focal neurol. symptoms	EEG change
45	63	M	L hemiparesis	R side abnormality	123	56	54	No	No
48	30	M	L hemiparesis	R side abnormality	88	62	30	No	No
			Arithmetical	mean	106	59	42		

manifesting itself in clinical focal or EEG ischaemic symptoms appears at first sight surprising. It is, however, in good agreement with the clinical study of Kendell and Marshall (1963) and consistent with the studies by Skinhøj *et al.* (1970) of the cerebral regional blood flow during controlled hypotension. But it is in contrast with the findings of Meyer *et al.* (1956) of changes in EEG in a great proportion of patients with cerebrovascular disease with acute blood pressure reduction through tilting. An explanation of this discrepancy may be the abruptness with which the hypotension was induced. The autoregulation of the cerebral blood flow with changes in systemic blood pressure is effected with a certain delay even if it is short, as is known from clinical experience, for instance in cases of orthostatic vertigo. This has also been shown experimentally by Rapela and Green (1964). By tilting the patient abruptly it is therefore possible that transitory EEG changes and transitory clinical symptoms may appear, but of fundamental importance in this connection seems to be that transitory phenomena of such short duration do not involve any risk of cerebral infarction with persistent neurological deficits. We therefore think it possible to conclude that the majority of hypertensive patients with or without previous stroke do tolerate a normalization of their blood pressure. We also feel that controlled hypotension with tilting is a simple and valuable test for excluding those few subjects who might not tolerate a blood pressure reduction. A frequency-analysis by computer of the electroencephalograph records might have sophisticated and increased the value of the method, but this was not performed in the present study. The reason for this is implicit in one of the principal aims, which was the search for a simple clinical way of evaluating in which hypertensive subjects the cerebral circulation would permit a blood pressure reduction and how far the blood pressure could be reduced without any risk in the individual patient.

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