4) Effect of the Long-term Antihypertensive Treatment on Cerebral Ischemia induced by BLCL in SHRSR

—Effect of Nicardipine Hydrochloride—

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Our previous report demonstrated that a long-term antihypertensive treatment of SHRSR by the combination of captopril and hydroflumethiazide administration effectively reduced the ischemic brain damage induced by bilateral common carotid artery ligation (BLCL). In this study, nicardipine hydrochloride which is the calcium antagonist was similarly administered, and its effect on the brain metabolism and the degree of brain edema were investigated. The ameliorating effect were compared and discussed with untreated SHRSR, and the histopathological study of brain vessels by electronmicroscopy was also employed on this model.

Materials and Methods

The male SHRSR, aged 8 weeks, were randomly divided to two groups. One group started its antihypertensive treatment (T-SHR group) and the other group was left untreated (U-SHR group). The antihypertensive treatment was to administer nicardipine hydrochloride (80 mg/kg/day) orally by mixing it to the drinking water and to the chow diet. The treatment lasted for 8-10 weeks. The cerebral ischemia was induced by BLCL. The brain energy metabolites (ATP, lactate, c-AMP) and water content of these groups were measured on frontal and occipital regions 4 hrs after BLCL. The histopathological changes of the brain vessels were observed 3 hrs after BLCL by scanning electronmicroscopy.

Results

The mean blood pressure of T-SHR before initiation of the antihypertensive treatment was 185 ± 10 mmHg, and after 8-10 weeks of treatment, the blood pressure decline to 154 ± 8 mmHg which is statistically significant to the blood pressure before the treatment. On the other hand, the blood pressure of U-SHR were 185 ± 8 mmHg at the beginning, and 206 ± 12 mmHg after 8-10 weeks. ATP and c-AMP levels 4 hrs after BLCL in T-SHR were significantly higher than those of U-SHR, and lactate levels were significantly lower in T-SHR in the both frontal and occipital regions. The brain water content 4 hrs after BLCL in T-SHR were significantly lower than those of U-SHR in the both regions. (Table) From the observation by scanning electronmicroscopy in the brain vessels, the T-SHR showed a lesser propagation of microvillies on the endothelial surface than U-SHR after 3 hrs of BLCL. The vasoconstrictions were markedly observed in U-SHR compared with T-SHR, and the marginal folds were observed to remain in T-SHR.

Conclusions and Discussion

There was a significant amelioration of the brain energy metabolites and brain edema 4 hrs after BLCL in T-SHR by administration of nicardipine hydrochloride compared with U-SHR. In the morphological study, the vascular endothelial ischemic changes of the brain were less in T-SHR.

These results were similar to our previous report, in which different antihypertensive agents (captopril and hydroflumethiazide) were employed. The results indicated that a long-term antihypertensive treatment is the most responsible for this ameliorating effect to ischemic damage, including the influence of their pharmacological consequence.

Table

Brain Metabolites and Brain Water Content 4hr after BLCL in treated and untreated SHRSR

Group	ATP	lactate	c-AMP	W.C.
T-SHR F	$0.67 \pm 0.25^*$ N=10	$12.64 \pm 9.93^*$ N=10	$1.04 \pm 0.17^{**}$ N=10	$78.03 \pm 0.62^{***}$ N=14
O	$0.68 \pm 0.17^{***}$ N=10	$9.99 \pm 9.35^*$ N=10	$0.90 \pm 0.08^{**}$ N=10	$77.28 \pm 0.53^{***}$ N=14
U-SHR F	0.25 ± 0.08 N=10	36.75 ± 7.87 N=10	0.50 ± 0.59 N=10	78.95 ± 0.69 N=14
O	0.34 ± 0.24 N=10	30.04 ± 6.15 N=10	0.51 ± 0.43 N=10	78.34 ± 0.92 N=14

N: number of quarter hemispheres

F: frontal region O: occipital region

Values are mean $\pm$ S.D. ATP, lactate and c-AMP concentrations were indicated by nmol/mg wet wt, n mol/mg wet wt and pmol/mg wet wt. Water content were indicated by %. Statistical difference from the corresponding value of U-SHR: P* < 0.01, P** < 0.02, P*** < 0.01