

## **Effect of combination therapy with the angiotensin receptor blocker Losartan plus Hydrochlorothiazide on brain perfusion in patients with both hypertension and cerebral hemodynamic impairment due to symptomatic chronic major cerebral artery steno-occlusive disease : a SPECT study**

H. Saura<sup>1</sup>, K. Ogasawara<sup>1</sup>, H. Saito<sup>1</sup>, K. Yoshida<sup>1</sup>,  
K. Terasaki<sup>2</sup>, M. Kobayashi<sup>1</sup>, K. Yoshida<sup>1</sup> and A. Ogawa<sup>1</sup>

<sup>1</sup>Department of Neurosurgery, Iwate Medical University  
19-1 Uchimaru, Morioka, Iwate 020-8505, Japan

<sup>2</sup> Department of Cyclotron Research Center, Iwate Medical University  
348-58 Tomegamori, Takizawa, Iwate 020-0173, Japan

### **Abstract**

**Background:** While the combination of an angiotensin receptor blocker with thiazide diuretics produces a clinically beneficial reduction in blood pressure in patients who otherwise only partially respond to monotherapy with an angiotensin receptor blocker, blood pressure-lowering therapy with combination antihypertensive drug regimens in patients with cerebral hemodynamic impairment may adversely affect cerebral hemodynamics. The purpose of the present exploratory study was to determine whether blood pressure-lowering therapy with the combination of the angiotensin receptor blocker losartan plus hydrochlorothiazide (LPH) worsens brain perfusion in patients with both hypertension and cerebral hemodynamic impairment due to symptomatic chronic major cerebral artery steno-occlusive disease.

**Methods:** Patients with losartan-resistant hypertension and reduced cerebrovascular reactivity (CVR) to acetazolamide due to symptomatic chronic internal carotid artery (ICA) or middle cerebral artery (MCA) steno-occlusive disease were prospectively entered into the present study and received 50 mg/day of losartan plus 12.5 mg/day of hydrochlorothiazide at 14 weeks after the last ischemic event. Cerebral blood flow (CBF) and CVR were measured before and 12 weeks after initiating LPH using N-isopropyl-p-[(123) I]-iodoamphetamine single-photon emission computed tomography (SPECT). A region of interest (ROI) was automatically placed in the MCA territory on each SPECT image using a three-dimensional stereotactic ROI template.

**Results:** None of the 18 patients who participated in the study experienced any new neurological symptoms or adverse effects related to antihypertensive drugs. Systolic ( $p < 0.001$ ) and diastolic ( $p < 0.001$ ) blood pressures were significantly reduced after the administration of LPH, with average reductions of 11 mm Hg in systolic blood pressure and 10 mm Hg in diastolic blood pressure. While in the affected hemisphere CBF did not differ between measurements taken before and after the administration of LPH, CVR was significantly higher after the administration of LPH than before ( $p = 0.007$ ) and was significantly improved in 5 of 18 patients. In the contralateral hemisphere, CBF and CVR did not differ between measurements taken before and after the administration of LPH. There were no patients who experienced a significant deterioration in CBF or CVR in the affected or contralateral hemisphere after the administration of LPH.

**Conclusions:** Although the present study was exploratory and its results were preliminary due to the small sample size, the current data suggest that blood pressure-lowering therapy with LPH apparently does not result in worsening of cerebral hemodynamics in patients with both hypertension and cerebral hemodynamic impairment due to symptomatic chronic ICA or MCA steno-occlusive disease.