To clarify the effects of long-term treatments with weight reduction (WR), ACE inhibitor (ACEI; enalapril) and angiotensin II antagonist (AIIA; candesartan) in obese hypertensives on BP reduction, especially focusing on sympathetic activity, renin angiotensin system (RAS), plasma insulin (INS) and leptin (LEP). Five groups with 20 obese hypertensives (HT) each were treated with WR alone, ACEI alone, AIIA alone, ACEI+WR, AIIA+WR over 12 months. WR was defined as 10% or more reduction in BMI for the first 6 months. The doses of ACEI and AIIA were chosen as less than 140/90 mmHg. At entry, month 6 & 12, BMI, BP, pulse rate (PR), plasma norepinephrine (NE), PRA, AII, INS and LEP were measured after overnight fast. WR program was performed in low caloric diet (1000 kcal, NaCl 7g/day) and exercise. At month 6, WR was succeeded in 65% of WR alone, 60% of ACEI+WR, and 50% of AIIA+WR. BP and NE were suppressed in 5 groups at month 6. PRA and AII increased in AIIA alone group, although those decreased in the other 4 groups. At month 6 & 12, BP was lower in order of ACEI+WR < AIIA+WR < ACEI alone < AIIA alone < WR. Plasma NE and PR were lower in order of ACEI+WR < ACEI alone < AIIA+WR < AIIA alone < WR. All was lower in order of ACEI+WR < ACEI alone < AIIA+WR < AIIA alone. Plasma INS and LEP were lower in AIIA+WR < AIIA+WR < AIIA alone < ACEI alone. In a whole cohort, at month 6 and 12 the reduction in plasma AII (ΔAII) correlated with ΔNE (P<0.01 at month 6, P<0.05 at month 12) and Δleptin (P<0.05 at month 6, P<0.05 at month 12). In addition, Δinsulin correlated with Δleptin (P<0.05 at month 6, P<0.01 at month 12). These results demonstrate that both pharmacological therapies with ACEI & AIIA with WR suppressed sympathetic hyperactivity and activated RAS in obesity hypertension. Despite the fact that BP reduction with WR alone is less than achieved by drugs, weight reduction should be regarded as an essential component of treatment program for obesity hypertension, because of the favorable metabolic responses. Plasma leptin level appears to be regulated by plasma insulin and AII without bradykinin or angiotensin converting enzyme pathways.

Key Words: Angiotensin II antagonist; ACE inhibitor; weight reduction; obesity; sympathetic activity