

NEW PAPERS

Antihypertensive treatment improves target organ damage in patients with masked hypertension

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Masked hypertension is a special subtype of hypertension characterized by a normal office blood pressure (BP) but elevated out-of-office BP. Its prevalence varies from around 10-15% in the general populations up to 30-40% in patients with diabetes mellitus or chronic kidney diseases.¹ Plenty of studies have demonstrated that masked hypertension, irrespective of its subtype, was associated with target organ damage and increased risk of cardiovascular mortality and morbidity.^{2,3} Therefore, current hypertension guidelines recommend an active strategy of intervention in masked hypertension. For untreated patients with masked hypertension, early and active improvement of lifestyle and the initiation of antihypertensive drug treatment are proposed. For treated patients with masked uncontrolled hypertension, antihypertensive treatment should be intensified. However, all these recommendations largely rely on previously-published observational studies and expert wisdom without direct evidence from clinical trials.

The antihypertensive treatment for target organ protection in patients with masked hypertension (ANTI-MASK trial, NCT02893358) is a multicentre, double-blind, placebo-controlled trial.⁴ Untreated outpatients aged 30-70 years with an office BP of <140/<90 mm Hg and 24-hour, daytime or nighttime ambulatory BP of $\geq 130/\geq 80$, $\geq 135/\geq 85$, or $\geq 120/\geq 70$ mm Hg, respectively, were enrolled in 15 Chinese hospitals from February, 2017 to October, 2020. Patients had at least 1 sign

of target organ damage (TOD), including electrocardiographic left ventricular hypertrophy (LVH), arterial stiffness defined as an elevated brachial-ankle pulse wave velocity (baPWV) ≥ 1400 cm/s, or microalbuminuria defined as a urinary albumin-to-creatinine ratio (ACR) ≥ 3.5 mg/mmol in women and ≥ 2.5 mg/mmol in men. After stratification for centre, sex and the presence of nighttime hypertension, eligible patients were randomly assigned (1:1) to active antihypertensive treatment or placebo. The active antihypertensive treatment started with allisartan 80 mg daily, titrated to allisartan 160 mg daily at month 2, and combined with amlodipine 2.5 mg per day at month 4, if ambulatory BP had not been controlled. Matching placebos were used likewise in the control group. The primary outcome was the improvement of TOD, defined as the normalisation of baPWV, urinary ACR or LVH below the thresholds or a $\geq 20\%$ reduction in baPWV or urinary ACR over the 1-year follow-up.

Among the 320 randomized patients (43% women; mean age 54 years) in the ANTI-MASK trial, 7.8%, 12.5% and 97.5% had LVH, microalbuminuria or arterial stiffness at baseline, respectively. The office, 24-hour, daytime, and nighttime BPs averaged 130/81, 136/84, 140/87, and 126/78 mm Hg, respectively. In the intention-to-treat analysis, the TOD improvement was observed in more ($P < 0.0001$) patients on active antihypertensive treatment (79 patients [51.6%, 95% CI 43.7% to 59.5%]) than those on placebo (49 [29.3%, 95% CI 22.1% to 36.5%]). The office, 24-hour, daytime and

nighttime BPs decreased on average by 8.8/4.2, 10.1/6.4, 10.2/6.4, and 9.4/6.1 mm Hg, respectively, in 153 patients on active treatment and by 0.3/1.2, 1.3/1.0, 1.4/1.2, and 0.9/0.9 mm Hg, respectively, in 167 patients on placebo. Per-protocol and subgroup analyses produced confirmatory results. Adverse events were generally mild and occurred in a similar incidence rate between the two groups. In conclusion, antihypertensive treatment improved TOD and reduced office and ambulatory blood pressure in patients with masked hypertension. Our study provided supportive evidence to the guidelines in the active antihypertensive treatment of masked hypertension, albeit long-term benefit of treatment in the prevention of cardiovascular complications still needs to be established.

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