Hypertension

ORIGINAL ARTICLE

Spironolactone Versus Clonidine as a Fourth-Drug Therapy for Resistant Hypertension

The ReHOT Randomized Study (Resistant Hypertension Optimal Treatment)

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Abstract

The aim of this study is to compare spironolactone versus clonidine as the fourth drug in patients with resistant hypertension in a multicenter, randomized trial. Medical therapy adherence was checked by pill counting. Patients with resistant hypertension (no office and ambulatory blood pressure [BP] monitoring control, despite treatment with 3 drugs, including a diuretic, for 12 weeks) were randomized to an additional 12-week treatment with spironolactone (12.5–50 mg QD) or clonidine (0.1–0.3 mg BID). The primary end point was BP control during office (<140/90 mm Hg) and 24-h ambulatory (<130/80 mm Hg) BP monitoring. Secondary end points included BP control from each method and absolute BP reduction. From 1597 patients recruited, 11.7% (187 patients) fulfilled the resistant hypertension criteria. Compared with the spironolactone group (n=95), the clonidine group (n=92) presented similar rates of achieving the primary end point (20.5% versus 20.8%, respectively; relative risk, 1.01 [0.55–1.88]; *P*=1.00). Secondary end point analysis showed similar office BP (33.3% versus 29.3%) and ambulatory BP monitoring (44% versus 46.2%) control for spironolactone and clonidine, respectively. However, spironolactone promoted greater decrease in 24-h systolic and diastolic BP and diastolic daytime ambulatory BP than clonidine. Per-protocol analysis (limited to patients with ≥80% adherence to spironolactone/clonidine treatment) showed similar results regarding the primary end point. In conclusion, clonidine was not superior to spironolactone in true resistant hypertensive patients, but the overall BP control was low (≈21%). Considering easier posology and greater decrease in secondary end points, spironolactone is preferable for the fourth-drug therapy.

Clinical Trial Registration—URL: **http://www.clinicaltrials.gov**. Unique identifier: **NCT01643434**.

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