

A Prospective Clinical and Field Study Evaluating the Role of Salt Sensitivity Phenotyping in Guiding Antihypertensive Drug Selection and Reducing the Psychological Burden of Trial-and-Error Therapy

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The objective of the prospective study was to investigate the significance of phenotypic characterization of salt sensitivity in the selection of initial antihypertensive therapy and its effect on blood pressure control among patients with stage 1 hypertension. Another aim was to assess whether a phenotype-driven strategy could reduce the psychological burden associated with trial-and-error prescribing. The field study was carried out as a cluster-randomized trial in three primary care centers in Tashkent and the Fergana Valley region of Uzbekistan from May to November 2025. A total of 210 patients with recently detected stage 1 hypertension were included in the study and allocated into two groups: phenotype-directed therapy ($n = 112$) and conventional management ($n = 98$). In the phenotype group, all participants were screened for salt sensitivity through oral salt tolerance testing before any interventions; baseline readings and readings after administration of 200 mL of solution containing 2 g of sodium chloride were measured at 120 min, with salt sensitivity indicated by a 10 mm Hg rise in systolic blood pressure. Salt-sensitive patients were prescribed hydrochlorothiazide (25 mg/day), whereas salt-resistant patients were administered amlodipine (5 mg/day). If the goal had not been met by Week 4, telmisartan 40 mg was added. In the standard care group, one of the following monotherapies could be administered by the treating physician based on national guidelines: an ACE inhibitor, angiotensin receptor blocker, calcium channel blocker, or thiazide diuretic. The primary objective of the study was the percentage of patients attaining their blood pressure target ($<140/90$ mm Hg) after Week 12. In the phenotyping group, 53.6% of patients were found to have a salt-sensitive phenotype. After 12 weeks, the proportion of patients who attained target blood pressure was significantly higher in the phenotyping group, 78.6% versus 62.2% in the standard care group ($p = .009$). There was a significant difference in the mean systolic blood pressure decrease between the two groups (18.9 vs. 14.7 mm Hg; $p = .001$). Moreover, there was a reduced requirement for a second medication in the phenotyping group (36.4% vs. 51.6%; $p = .03$) and no statistically significant difference in adverse events between the groups. The results indicate that a simple salt sensitivity phenotyping strategy can help identify patients for drug therapy and significantly increase treatment efficacy. Because this method reduces the amount of experimentation necessary to change medications, it may also help reduce the psychological stress that patients experience when first dealing with hypertension.

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