

CONCEPTS IN HYPERTENSION

A Journal Article-Based Approach to Understanding the Clinical Aspects of Hypertension

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Low dose combination therapy - Same punch, less side effects

Article of Interest

Law, M et al. Value of low dose combination treatment with BP lowering drugs: analysis of 354 randomized trials. British Medical Journal. 2003. ([Click to Access](#))

Context and Study Objective

A common approach to treating hypertension involves initiating mono-therapy, up-titrating to full dose, and then adding a second agent. This article explores whether low dose combination therapy achieves similar blood pressure (BP) reductions but with a lower prevalence of adverse effects.

Design, Setting, and Participants

A literature search of double-blind randomized controlled trials involving fixed doses of anti-hypertensive agents, either as mono- or dual therapy, was undertaken. Trials involving subjects with cardiovascular disease were excluded. The degree of BP reduction and side effect rates were extracted from each publication and then subtracted from placebo.

Results

-350 trials comprising 55,000 participants were included. Mean patient age was 53. No additional characteristics were provided.

-Table: Half standard dosing of an individual agent achieved 80% of the BP lowering effect of full dose therapy (N.B. BP reductions depicted as active therapy minus placebo).

-Among those treated with combination therapy, mean BP reduction was 14.6/8.6 mm Hg when each agent was administered at full dose and 13.3/7.3 mm Hg when each agent was administered at half dose.

-Figure: Among thiazides, CCBs, and β -blockers, side effects were dose dependent. ACEi/ARB related adverse effects (principally cough) were dose independent.

Mean Systolic Reduction (mm Hg)		
	Half Dose	Full Dose
ACEi/ARBs	7.4	9.4
β -blockers	7.4	9.2
CCBs	5.9	8.8
Thiazides	7.4	8.8

Clinical Perspective

-The preferential use of combination tablets is one of my best kept secrets. As this meta-analysis illustrates, by prescribing a medium-strength dose one captures 80% of the anti-hypertensive effect (of a full dose) yet with only a fraction of the side effect burden.

-Since many 2-in-1 formulations are available, the patient continues to take a single pill. Azor (amlodipine-olmesartan) and Aldactazide (spironolactone-hctz) are particularly invaluable. When administered together, these 2 pills have allowed me to successfully control the BP of individuals on 6-8 medications.

-As a rule, I initiate low dose combination therapy in treatment-naïve patients. This minimizes symptoms at therapy onset and allows for up-titration once required.

-Disclosures: I have no conflicts to declare.

