



The Impact of Fixed-dose Combinations on Blood Pressure Control, Persistence, and Comorbid Disease

Fixed-dose combinations are superior in achieving goal and earlier blood pressure control to

regimens not containing a fixed-dose combination, reported Frank Perrone, DO, of Pennel Medical Practice in Levittown, Pennsylvania.

Dr Perrone and colleagues conducted a retrospective chart review of 243 patients diagnosed with hypertension from a primary care database (ASH 2006. Abstract P216). The blood pressure goal was defined as $\leq 140/90$ mm Hg or $\leq 130/80$ mm Hg in those with diabetes. Time to blood pressure goal attainment was assessed in 149 patients whose most recent addition was a fixed-dose combination compared with 94

patients whose most recent addition did not include a fixed-dose combination. Patients in the latter group could be receiving the same drugs as in a fixed-dose combination, but as separate agents.

Sixty-six percent of patients in the fixed-dose combination group achieved blood pressure control compared with only 48% of those not taking a fixed-dose combination ($P = .01$). The probability of blood pressure control was 53% greater after 12 months among those receiving a fixed-dose combination ($P = .05$). The median time to blood pressure control was 49 days in those receiving a fixed-dose combination versus 69 days in those taking single or separate agents.

Although the pill burden, or number of dosage units received, was comparable in both groups, those taking a fixed-dose combination were prescribed an average of 2.7 antihypertensive drugs, whereas patients not taking a fixed-dose combination took an average of only 1.9 antihypertensive medications ($P < .01$).

Initiating antihypertensive therapy with the fixed-dose combination of amlodipine besylate/benazepril hydrochloride may offer superior

cardiovascular and renal protection compared with amlodipine monotherapy, reported Thomas E. Delea, MSIA, senior research consultant, Policy Analysis Inc, Brookline, Massachusetts.

Investigators evaluated medical and pharmacy claims data from 56 432 patients who initiated therapy with either amlodipine, ramipril, or the fixed-dose combinations amlodipine/benazepril or lisinopril/hydrochlorothiazide (ASH 2006. Abstract P215). To be eligible for inclusion, patients had at least 2 prescriptions within 120 days for the study drugs.

After adjusting for differences in baseline characteristics, patients who initiated therapy with amlodipine/benazepril were 20% less likely to experience a cardiovascular or renal event over a mean follow-up of 15 months compared with patients started on amlodipine monotherapy ($P = .0123$). In addition, incident heart failure was 30% less likely in patients treated with amlodipine/benazepril compared with lisinopril/hydrochlorothiazide.

Gilbert C. Ngan, PharmD, from the University of Texas at Austin College of Pharmacy, reported that medication adherence and persistence

Table. Unadjusted Antihypertensive Persistence and Compliance

Outcome measures	Diuretics	ARB + diuretic	ACE inhibitor + diuretic	Beta blocker + diuretic
Persistence (%)	29.9	52.6	51.4	51.9
Adherence (%)	24.2	39.2	38.8	43.9
MOR ("days covered") ± SD	32.5 ± 46.8	53.7 ± 49.9	50.9 ± 50.0	51.3 ± 50.0
Compliance ± SD	75.4 ± 27.4	79.8 ± 23.4	82.9 ± 22.3	84.2 ± 21.2
MPR ± SD	44.5 ± 34.5	60.5 ± 32.7	58.3 ± 34.2	62.1 ± 34.1
Days to therapy discontinuation ± SD	164.5 ± 141.8	240.1 ± 140.3	235.9 ± 140.8	238.2 ± 140.9

Users of diuretics as monotherapy consistently experienced the least persistence and adherence compared with fixed-product combinations with diuretics. Overall, users of ARBs with diuretics are the most persistent (as measured by percent persistent, MOR ["days covered"], and mean days to therapy discontinuation), and users of beta blockers with diuretics are the most adherent (as measured by MPR, compliance, and adherence measurements).

ARB indicates angiotensin receptor blocker; ACE, angiotensin-converting enzyme; MOR, medication ownership ratio; SD, standard deviation; MPR, medication possession ratio.

within a staff-model managed care organization was superior with use of fixed-dose amlodipine/benazepril compared with the component-based dual therapy (ASH 2006. Abstract P23).

Medical and pharmacy claims data were used to assess adherence by calculating the medication possession ratio (MPR) among 436 patients taking fixed-dose amlodipine/benazepril and 739 patients taking both agents separately. MPR determines the continuity of medication usage, and is determined by the total number of days of medication supplied divided by the number of days between the first and last refill in addition to the day's supply of the last refill. An MPR ratio of <1 occurs if there are lapses in refilling. This ratio was significantly higher in the group receiving fixed-dose amlodipine/benazepril than in the group receiving separate components (0.79 vs 0.59, respectively; $P < .001$). Furthermore, significantly more patients receiving fixed-dose amlodipine/benazepril remained on therapy compared with patients taking dual agents (48% vs 24%, respectively; $P < .0001$). Patients on fixed-dose amlodipine/benazepril were half as likely to switch or discontinue their medication as patients taking dual agents.

A study led by Bimal V. Patel, MD, at Health Outcomes Research in San Diego, California,

showed that, compared with fixed-dose combinations, antihypertensive diuretic monotherapy resulted in inferior persistence. The investigators used the MedImpact database to identify 48 212 patients with at least 1 prescription claim for either a diuretic or a fixed-dose combination of diuretic/angiotensin receptor blocker (ARB), diuretic/angiotensin-converting enzyme (ACE) inhibitor, or diuretic/ beta blocker (ASH 2006. Abstract P218). Most (72.5%) of the study group used diuretic monotherapy. Persistence was measured over 12 months. Key findings include:

- Diuretic users were 63% less likely to be persistent compared with users of a fixed diuretic/ARB, 62% less likely than users of a fixed diuretic/ACE inhibitor, and 61% less likely than users of a fixed diuretic/beta blocker.
- Persistence at 12 months was 52.6% with a diuretic/ARB fixed combination, 51.9% with a fixed diuretic/beta blocker, 51.4% with a diuretic/ACE inhibitor fixed combination, and 29.9% with diuretic monotherapy.
- Users of diuretics were almost twice as likely to discontinue their medication as users of the fixed-product combination therapies with diuretics.

The unadjusted rates for antihypertensive persistence and compliance for the study drugs appear in the **Table**.