

## Letter to the Editor

## Compliance and Fixed-Dose Combination Therapy in a Sample of Greek Hypertensive Patients

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**H**ypertension is a major risk factor for cardiovascular mortality.<sup>1-3</sup> However, only 34% of hypertensive patients are under control.<sup>2</sup> Polypharmacy is one of the risk factors for medication non-compliance.<sup>4</sup> In Greece the existing data regarding polypharmacy and patient compliance are limited. Therefore, we aimed to evaluate the impact of fixed-dose combination antihypertensive treatments on patient compliance.

A total of 4641 hypertensive patients (56.5% males, mean age  $\pm$  standard deviation (SD) 64.1  $\pm$  10.2 years, duration of treatment  $\pm$  SD 8.2  $\pm$  5.8 years) were recruited by 3 cardiology departments and 185 private pathology/cardiology clinics between August and December 2010. Study subjects had received component-based free-combination therapy in the past and were on fixed-dose combination therapy for at least 6 months prior to the study visit (Table 1). Compliance with treatment, treatment effectiveness, and quality of life were evaluated. The above three parameters were defined as described in detail elsewhere.<sup>5</sup>

Of the study participants, 93.8% showed high compliance and 93.4% better qual-

ity of life with the fixed-dose versus component-based free-combination therapy; 91.7% of participants reported better effectiveness, 92.7% more easy use, and 84.9% fewer adverse effects of the fixed-dose compared to component-based free-combination therapy. The cost of fixed-dose combination therapy compared to component-based free-combination therapy was reported by 51.0% of participants to be an important factor in their compliance with treatment. However, 88.4% of participants reported that fixed-dose combination therapy had good effectiveness regardless of the cost.

The fixed-dose combination therapy included a calcium channel blocker (CCB) and an angiotensin II receptor blocker (ARB) in 57.4% of participants, while 28.6% were taking fixed-dose combination therapy with a diuretic and an ARB.

The majority of Greek hypertensive patients showed high compliance and fewer adverse effects with fixed-dose versus component-based free-combination therapy. A study has shown that initiating treatment with a combination of two drugs is associated with lower risk of treatment discontinuation.<sup>6</sup> A recent meta-analysis

**Table 1.** Component-based free-combination and fixed-dose combination therapy of the study participants.

Component-based free-combination therapy:	n (%)
Diuretics	2889 (62.3)
Calcium channel blocker	2375 (51.2)
Angiotensin converting-enzyme inhibitor	1967 (42.4)
Angiotensin II receptor blocker	1701 (36.7)
Beta-adrenergic blocking agent	1516 (32.7)
Other	329 (7.1)
Fixed-dose combination therapy:	
Calcium channel blocker / angiotensin II receptor blocker	2661 (57.4)
Diuretic / angiotensin II receptor blocker	1314 (28.6)
Diuretic / beta-adrenergic blocking agent	345 (7.4)
Diuretic / calcium channel blocker / angiotensin II receptor blocker	340 (7.3)
Diuretic / angiotensin converting-enzyme inhibitor	229 (5.0)
Other	607 (13.1)

of studies in hypertension showed that fixed-dose combinations decreased the risk of non adherence by 24% compared with free-drug combinations.<sup>7</sup>

Studies have shown that adherence to treatment increases with fixed-dose combinations.<sup>8,9</sup> Adherence to fixed-dose combination therapy of CCB with angiotensin-converting enzyme (ACE) inhibitor was significantly greater than for free combination therapy.<sup>8</sup> Patients receiving a once-daily, single-capsule, fixed-dose combination of ACE and CCB demonstrated better medication adherence than subjects receiving ACE and CCB as separate components.<sup>9</sup> Initiating fixed-dose combination therapy with diuretic and ACE, ARB, or beta-adrenergic blocking agent was associated with better adherence as compared to diuretic monotherapy.<sup>5</sup>

The reduction in adverse events associated with the use of fixed-dose combination therapy reported in our study is consistent with previous studies.<sup>10-12</sup> A meta-analysis showed that the use of fixed-dose combination therapy had a better safety profile than single agents.<sup>11</sup> In another meta-analysis, the adverse effects associated with the use of combinations of 2 drugs were reported to be fewer than those associated with the additive effects of the 2 drugs given independently.<sup>12</sup>

In conclusion, the use of fixed-dose therapy in hypertension leads to increased compliance and adherence with a positive impact on quality of life.

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