DISCONTINUATION, SWITCHING AND ADDING AMONG ANTIHYPERTENSIVE DRUG CLASSES
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Medical and pharmacy claims from a database containing 2.5 million covered members were used to estimate discontinuation, switching, and adding rates for calcium channel blockers (CCB), angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and beta-blockers (BB).

Continuously enrolled members (1/1/97 to 8/30/99) with at least one ICD-9 diagnosis code for hypertension, no claims for antihypertensive drug in 1997, and at least one claim for a CCB, ACEI, ARB and BB initially filled in 1998 were followed until end of study period (8/30/99). For all drug groups, discontinuation rates were estimated using non-parametric survival analysis. Switching patterns were assessed for patients who discontinued therapy and addition patterns were assessed for patients who did not discontinued therapy.

Patients identified in each drug classes were as follows: CCB 7,315; ACEI 6,882; ARB 2,018 and BB 5,829. Mean age of patients was similar between the drug classes (range 57-61). Most patients were females (range 52-55%) except for beta-blocker patients where 48% were females. The percentages of patients discontinuing therapy in each drug class were 51% (CCB), 50% (BB), 49% (ACEI), and 46% (ARB). Non-parametric survival estimates of time to discontinuation indicated slightly higher persistency at one year for ARB (44%) compared to ACEI and BB (42%) and CCB (40%). Almost 7% of patients who discontinued CCB switched to other antihypertensives (10.7% ACEI, 12.7% ARB and 7.7% BB). Among patients who did not discontinue initial therapy, 25.2% of BB; 22% of CCB patients; 20.3% of ACEI patients; and 7.7% of ARB patients added another antihypertensive medication. Diuretics were the most commonly added medication for all drug groups (CCB 9.5%, ACEI 8.3%, ARB 7.3%, and BB 10.5%). In addition, ACEI therapy was added to 5.7% of CCB patients. For ACEI, ARB, and BB patients, 5-6% added CCB therapy.

In review of the drug classes, this analysis suggests that patients initiating ARB therapy have the highest persistency. Additionally, ARB has the lowest and BB has the highest rates of antihypertensive drug added to the regimen.

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Key Words: Discontinuation, Drug use patterns, Antihypertensives

A POPULATION-BASED STUDY OF COMPLIANCE AND PERSISTENCY WITH CARDIOVASCULAR AGENTS USED IN HYPTERTENSION MANAGEMENT
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Purpose: To conduct a head to head comparison of persistency and compliance associated with representative agents used in the pharmacologic management of hypertension including lisinopril (Zestril), valsartan (Diovan), amlodipine (Norvasc) in a usual care setting.

Methods: This retrospective database study utilized patients continuously benefit-eligible from the Merck-Medco pharmacy claims database from 8/1997 through 7/2000 (N = 142,945). Patients who received an initial (no prescription filled within class during prior 12 months) prescription for lisinopril, valsartan, or amlodipine between 8/1998 through 7/1999 (N = 142,945) were included and followed for 12 months. Compliance was assessed using the medication possession ratio (MPR), or the percentage of time a patient had drug available over a 1-year time period. Persistency was defined as having drug on hand at least one day in the month. To control for differences in overall baseline chronic disease burden, a Chronic Disease Score (CDS), which uses drug markers to identify chronic conditions, was used to classify the cohort as mild, moderate, or severe.

Results: Mean age of the study cohort was 63.1 years and 53% were female. Over half (51%) of the cohort used amlodipine as initial therapy, 21% valsartan, and 28% lisinopril. More valsartan patients remained persistent on therapy at 12-months post-therapy initiation (66%) compared to amlodipine (57%) and lisinopril (55%) (P < .0001, both comparisons). Mean duration of therapy was 266 days for valsartan patients versus 246 days for amlodipine and 240 days for lisinopril (P < .0001, both comparisons). Compliance was also greatest for valsartan patients, reflecting a mean MPR of 76% vs. 67% for amlodipine, 65% for lisinopril (P < .0001, both comparisons). While a slightly greater proportion of valsartan patients had a lower CDS (31% classified as severe, versus 35% for both lisinopril and amlodipine), compliance and duration of therapy remained greater for valsartan patients across all CDS strata. Valsartan patients classified as severe via CDS had a mean duration of therapy of 266 days, compared to 245 for amlodipine and 237 for lisinopril (P < .0001, both comparisons). These patients also had a mean MPR of 75% as compared to 67% and 64% for amlodipine and lisinopril patients, respectively (P < .0001, both comparisons).

Conclusions: These preliminary results suggest that patients receiving valsartan in a typical managed care setting for the treatment of hypertension may be more adherent to therapy. These differences appear to be independent of baseline CDS.

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Key Words: Hypertension, Compliance, Chronic Disease Score

COST-EFFECTIVENESS EVALUATION OF FIXED-DOSE COMBINATION OF ANGIOTENSIN-II RECEPTOR BLOCKERS WITH AND WITHOUT HYDROCHLOROTHIAZIDE
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The purpose of this study is to compare the cost-effectiveness of the 3 commercially available fixed-dose combinations (FDC) of angiotensin-II receptor blockers (ARBs) with hydrochlorothiazide (H). Published randomized controlled trials with FDC of losartan (L), telmisartan (T), and valsartan (V) with H were identified by MEDLINE search. Pooled estimates of systolic (sBP) and diastolic blood pressure (DBP) lowering and response rates were calculated using the meta-analytic technique of Cochran and DerSimonian with sample size and variance adjustments. Average reductions in sBP and DBP and average response rates were used to calculate cost-effectiveness ratios expressed as $ per mmHg reduction and $ per successfully treated patient.

A total of 3883 patients were included in 14 trials with 1371 receiving L (8 cohorts), 1309 receiving T (2 cohorts), and 1203 receiving V (4 cohorts). Pooled estimates of sBP and DBP lowering and response rates and cost-effectiveness ratios are shown in the table. All doses of FDC of ARB plus H are more cost-effective than ARB alone, except L100/H25. L100/H25 is more cost-effective than L100, but not L50. T80/H12.5 is the most cost-effective ARB/H FDC.
INTOLERANCE

PSYCHIATRIC ASPECTS OF MULTIPLE DRUG

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PSYCHIATRIC ASPECTS OF MULTIPLE DRUG INTOLERANCE
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Poor adherence to antihypertensive drugs is common and increases risk of cardiovascular morbidity. Drug side effects may contribute to poor adherence, but some patients who repeatedly discontinue medication may misinterpret non-specific symptoms as drug side effects, possibly due to psychiatric problems. In hypertensive patients attending hospital we examined the relation between drug intolerance and the presence of panic disorder, panic attacks, anxiety and depression. From standardised records of a hypertension clinic we identified all patients recorded as having had 2 or more episodes of intolerance to antihypertensive drugs, and a sample of patients of similar age and sex who had no record of drug intolerance. Intolerance was defined as reduction in dose or stopping an antihypertensive drug due to putative adverse effects. All episodes of intolerance were verified by case note scrutiny, then evaluated independently by 2 raters who were blind to patient characteristics, and categorised for subjectivity (symptomatic or asymptomatic) and when symptomatic, for specificity of the side effect to the drug. Patients were classified by the number of a) symptomatic non specific intolerances, b) symptomatic specific intolerances and c) total intolerances. All patients were mailed questionnaires, for self-completion, on panic disorder and panic attacks, a Hospital Anxiety and Depression Scale and the trait anxiety section of Spielberger’s Inventory. Analyzable questionnaires were returned by 233 of 276 (85%) patients, who had experienced 576 episodes of intolerance. Of these, 532 (92%) were symptomatic (284 (53%) drug specific and 248 (47%) non-specific). There was no relation of drug intolerances to age, sex or number of antihypertensive drugs prescribed. Number of symptomatic non-specific intolerances was associated with significantly higher DBP (p=0.012, e.g. 0 v >4 episodes; 160/89mmHg v 172/99mmHg). Total episodes of intolerance were associated significantly with panic attacks (p=0.008), anxiety (actual HAD score p=0.027, HAD Score>7 p=0.024, trait anxiety p=0.042) and depression (actual HAD score p=0.011, HAD Score>7 p=0.018). Symptom specific non drug intolerances, were related significantly to panic attacks (p=0.008), anxiety (actual HAD score p=0.043) and depression (actual HAD score p=0.005, HAD score>7 p=0.008). Specific intolerances showed no significant associations with psychiatric morbidity. These data suggest recurrent intolerance to antihypertensive drugs is associated with psychiatric problems. This association is with non-specific rather than specific side effects. Physicians treating hypertensive patients need to recognise and manage the psychiatric aspects of multiple drug intolerance.

Key Words: Antihypertensive drugs, Drug intolerance, Psychiatric aspects

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EFFECTS OF CANDESARTAN, METFORMIN AND PRAVASTATIN COMBINATION ON CARDIOVASCULAR RISK FACTORS IN A POOR CONTROLED HYPERTENSIVE POPULATION WITH CHRONIC METABOLIC SYNDROME
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Hypertension as a part of the chronic metabolic syndrome has a multiplicative and devastating cardiovascular risk effect that advises an aggressive intervention over all the risk factors in order to preserve the amount and quality of life in this high-risk population. 23 patients with hypertension, type 2 diabetes, dislipemia and central obesity (Chronic Metabolic Syndrome) had macrovascular affection as consequence of a poor control over their diseases (see below table) secondary to lack of treatment adherence and sub-optimal selection of the available therapeutic options following the JNC-VI, WHO/ISH; ADA recommendations. None of them where receiving ARA-II, biguanides or statins. Medium age was 62.4 years (+/- 9.3), hypertension was known for 9.9 years (+/- 2.36) and diabetes for 8.1 years (+/- 3.2). All received educative interventions by the nurses plus candesartan 16 mgr per day, metformin 850 mgr twice a day and pravastatin 20 mg per day. The high prevalence of non-compliance with diet, exercise and other healthy non-pharmacological interventions supports the intensive drug therapy in this high-risk patient’s subpopulation. Associating candesartan as the second or third antihypertensive drug permits to control the blood pressure fulfilling the ADA, WHO and JNC-VI criteria. The pravastatin and butformin association significantly improves the lipids profile, atherogenic index and