Candesartan Cilexetil-HCT in Primary Hypertension Insufficiently Controlled on Monotherapy—A Comparison with Losartan-HCT

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The purpose was to evaluate the antihypertensive effect, safety and tolerability of a candesartan cilexetil/hydrochlorothiazide (16/12.5 mg) combination tablet (Candes-HCT) in patients with mild to moderate primary hypertension insufficiently controlled on previous monotherapy, in comparison with that of a losartan/hydrochlorothiazide (50/12.5 mg) combination tablet (Los-HCT).

Men and women, aged 20–80 years, with a sitting blood pressure (BP) ≤200/≥90 and ≤110 mmHg during treatment with any kind of antihypertensive monotherapy for at least 4 weeks were randomised to treatment with Candes-HCT or Los-HCT once daily for 12 weeks. Efficacy analysis was performed according to intention to treat and last value carried forward. Mean and SD or CI are given. A total of 340 patients were enrolled, out of which 299 patients (144 women and 155 men, mean age 59.5 (10.5) yrs) were randomised to Candes-HCT (n = 151) or Los-HCT (n = 148). BP’s at randomisation were 159.5 (15.4)/98.4 (5.8) and 160.5 (16.1)/98.5 (5.4) mmHg, respectively. There was a greater reduction of BP with Candes-HCT than with Los-HCT; diastolic BP –10.4 (–11.8; –8.9) vs. –7.8 (–9.3; –6.3), diff. –2.6 (–4.7; –0.5) mmHg (p = 0.016); systolic BP –19.4 (–22.1; –16.7) vs. –13.7 (–16.5; –10.9), diff. –5.7 (–9.6; –1.8) mmHg (p = 0.004). The proportion of patients achieving DBP <90 mmHg was greater in the Candes HCT group; 60.9 (53.1; 68.7) vs 49.3 (41.3; 57.4) % (p = 0.044). There were 12 drop-outs in the Candes-HCT group of which 8 were due to adverse events, and 17 and 12, respectively, in the Los-HCT group. The reduction in BP was independent of previous antihypertensive agent, gender and age of the patient. We conclude that the combination Candes-HCT reduced blood pressure effectively and was well tolerated. BP was normalised in 61% of these patients who had insufficient response to previous monotherapy. The reduction in blood pressure and proportion of patients with normalised BP was greater with Candes-HCT 16/12.5 mg than with Los-HCT 50/12.5 mg.

Key Words: Primary hypertension; AT1-receptor blocker; candesartan; efficacy; tolerability

Increased Frequency of Acid Suppressive Drug Use in Hypertensive Patients Receiving Calcium Channel Antagonists

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In addition to their cardiovascular effects, calcium channel antagonists (CCA) have also been shown to decrease lower esophageal sphincter pressure and reduce esophageal motility, which may precipitate or aggravate gastroesophageal reflux disease. Thus, we hypothesized that patients who receive CCA’s would have a greater frequency of acid suppressive drug use. We reviewed the pharmacy records of 16,384 hypertensive patients identified by ICD-9 401.9 from the 12 months period 7/1/98 to 6/30/99. Patients were categorized according to which class of antihypertensive agent they received (CCA, diuretic, beta-blocker or other agents). The frequency of acid suppressive drug use, H2 antagonists (H2A) or proton pump inhibitors (PPI), among the different classes of antihypertensive agents was determined and analyzed using Chi-square. Of the patients receiving antihypertensive drug therapy, the mean (±SD) age was 66 (±14) years old, 43% were males and 58% were ≥ 65 years old. Thirty-seven percent of patients were treated with a CCA alone or in combination. The frequency of H2/PPI use was significantly greater in patients receiving a CCA than in patients not receiving a CCA, 24% vs 17%, respectively, p < 0.0001. Of those not receiving a CCA the frequency of H2/PPI use was 18%, 16%, and 19%, in patients receiving diuretics, beta-blockers and other antihypertensives, respectively.

Conclusion: The use of CCA’s in hypertensive patients was associated with an increased use of acid suppressive agents. The potential morbidity and financial burden of these findings warrant further investigation.

Key Words: Calcium channel antagonist; diuretics; beta-blockers; adverse effects

Effects of Lercanidipine on Forearm and Calf Vascular Structural Changes in Hypertension

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It is still undetermined whether pharmacological regression of vascular structural changes associated with hypertension depends on the drug-induced blood pressure reduction “per se” or rather on the antihypertensive effects of the drug coupled with its additional properties (e.g., antioxidative effects, vascular selectivity, etc.). To clarify this aspect in 24 mild to moderate untreated essential hypertensives (age: 47.3 ± 0.8 years; mean arterial pressure, MAP: 115.4 ± 3.6 mmHg, mean ± SEM), with no other major cardiovascular or non-cardiovascular diseases, we measured beat-to-beat MAP (Finapres), heart rate (HR, EKG), forearm and calf blood flows (FBF, CBF, venous occlusion plethysmography) and calculated forearm and calf vascular resistance (FVR:MAP/FBF, CVR:MAP/CBF respectively). We also evaluated forearm and calf minimal vascular resistance (FVRmin and CVRmin) following 12 min of local ischaemia associated with 2 min of isometric exercise. The entire protocol was performed in the no drug condition and...
repeated following a 6 month treatment with lercanidipine (L, 10 mg/day per os, n = 12) of hydrochlorothiazide (H, 25 mg/day per os, n = 12) accordingly to a double blind design.

L caused a significant (p < 0.01) reduction in MAP (−12.9 ± 1.1 mmHg), FVR (−12.6 ± 1.6 U) and CVR (−15.1 ± 1.7 U) without affecting HR values. These effects were coupled with a significant reduction in FVRmin (from 3.1 ± 0.3 to 2.0 ± 0.2 U, p < 0.01) and in CVRmin (from 4.6 ± 0.3 to 3.5 ± 0.3 U, p < 0.05). In contrast, for similar MAP reduction (−10.8 ± 1.4 mmHg, p < 0.01), H caused a slight decrease in FVR and CVR (−6.5 ± 1.3, −7.6 ± 1.5 U respectively) without significantly affecting FVRmin and CVRmin.

These data provide evidence that for similar blood pressure reductions only drugs, such as L with additional vasoprotective properties, are capable of favouring a regression of the vascular structural changes associated with hypertension. This implies that the blood pressure reduction “per se” may be not sufficient to cause regression of vascular hypertrophy.

Key Words: Vascular hypertrophy; calcium antagonists; diuretics; hypertension; drug treatment

A072
A COMPARISON OF 24 HOUR BLOOD PRESSURE IN HYPERTENSIVE PATIENTS SWITCHED FROM AMLODIPINE TO NISOLDIPINE
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Blood pressure control and medication costs are two important parts in antihypertensive drug product selection. Within a therapeutic drug class, acquisition costs many times take precedence over efficacy. The purpose of this study was to evaluate 24 hour blood pressure control and adverse effects in patients with essential hypertension when switched from Amlodipine (A) to Nisoldipine (N). Hypertensive patients stabilized on A5 mg or 10 mg were monitored over 24 hours with an ambulatory blood pressure monitor (AMBP). The following day the patients were switched to (N) 10 mg (≥65 yrs old) or 20 mg (<65 yrs old). (N) dose was adjusted to maintain BP equivalent to (A) dose or <140/90, whichever was lower. After 8–16 weeks patients were again monitored with the 24 hour blood pressure monitor. Mean 24 hour, daytime and nighttime blood pressures, diurnal variation, number of dose titrations, significant adverse reactions and cost differences were measured. This study is currently in progress with 48% (11/23) of patients completed. Results thus far have shown no significant difference between (A) and (N) with regards to mean 24 hr AMBP (+1.8 mm Hg/+2.4 mm Hg), daytime (+1.3/+2.5) and nighttime (+2.6/+2.0) blood pressures and diurnal variation (10.1%/11.3% vs. 9.1%/11.6%, Sys/Dia (A) vs. (N)). Three dose titrations were observed, and no significant adverse events were reported. AWP for low dose (A) is $1.29/day vs. $0.93 of (N). High dose AWP is $2.50 vs. $0.93 for (A) and (N), respectively. Based on the data obtained thus far, patients taking (A) can be safely and effectively switched to (N).

Key Words: Amlodipine; nisoldipine; ambulatory blood pressure

A073
EFFICACY AND SAFETY OF QUINAPRIL 40 mg IN UNCONTROLLED HYPERTENSION. VICTORIA STUDY
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Last Joint National Committee (JNC) recommendations are stricter, especially with hypertensive patients with associated risk factors. Our objective is to determine if the convenience in dosage range in monotherapy could improve hypertensive control.

Victoria Study was designed in order to evaluate the efficacy and safety of Quinapril 40 mg in 22,000 patients treated during 8 weeks.

The study began in March 1999. In November 1999 we obtained the information of 2012 patients, 54% males, 15% diabetics and 10% with cardiovascular disease. Most of them (71%) were previously treated with anti-hypertensive treatment. 1% had controlled systolic blood pressure (SBP) (<140 mmHg or <135 mmHg, depending on the risk factors) and 6% had controlled diastolic blood pressure (DBP) (<90 mmHg or <85 mm Hg depending on the risk factors) with mean values of SBP 165 ± 16 and DBP 98 ± 9 (mmHg ± SD). After 2 months of treatment with Quinapril 40 mg, the percentage of controlled blood pressure values (<140/90 mmHg or 130/85 mmHg) increased up to 28% in SBP and 65% in DBP. Quinapril 40 mg was well tolerated and no relevant adverse events were detected.

We conclude that Quinapril 40 is able to control blood pressure in hypertensive population previously treated and uncontrolled. The number of patients controlled were 65% for DBP and 28% for SBP, in patients previously treated with other anti-hypertensive medication but without reaching the minimum JNC recommendations (<140/90 mmHg).

Key Words: Hypertension; quinapril; efficacy

A074
EFFICACY AND SAFETY OF OMAPATRILAT WITH HYDROCHLOROTHIAZIDE FOR THE TREATMENT OF HYPERTENSION IN SUBJECTS NONRESPONSIVE TO HYDROCHLOROTHIAZIDE ALONE

This multicenter, double-blind study evaluated the efficacy and safety of omapatrilat (OMA), a vasopeptidase inhibitor (VPI), when given in conjunction with hydrochlorothiazide (HCTZ) to subjects unresponsive to HCTZ alone. The study randomized 274 subjects with mild to severe hypertension (seated diastolic blood pressure [SeDBP] 95–120 mm Hg). After a 2-week placebo lead-in period and 4-week HCTZ filter period, subjects with SeDBP 93–100 mm Hg were randomized to receive OMA (10 mg or 20 mg, titrated to 20 mg or 40 mg respectively at week 4 if SeDBP was ≥90 mm Hg) or matching placebo, both in addition to HCTZ 25 mg as