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COMPARISON OF THE PHARMACODYNAMIC PROFILES OF TWO DIFFERENT LONG-ACTING DILTIAZEM DELIVERY SYSTEMS. DHG Smith*, JM Neutel*. Orange County Heart Institute and Research Center, Orange, CA, and Clinical Investigation Analysis, Orange, CA.

In an attempt to achieve effective 24 hour blood pressure (BP) control, various sophisticated extended drug release systems have been developed. In the case of Tiazac (T) (single micro-bead diltiazem population) and Cardizem-CD (C-CD) (two micro-bead diltiazem populations) the pharmacokinetic (PK) profiles have been shown to be notably different. To determine if there are corresponding pharmacodynamic (PD) differences when administering 240mg of diltiazem using the two different release systems, we evaluated the PD profile of T and C-CD in 40 mild-to-moderate hypertensive patients. The study design was randomized, double-blind, cross-over, with an initial 4 week single blind placebo period, followed by two 4-week treatment periods. All patients were dosed at 8 ± 30 min a.m. Ambulatory blood pressure monitoring (ABPM) was performed at the end of the placebo period and at the end of each of the treatment periods.

During the 10-16 hours post dose time period, T resulted in a statistically significantly greater ($p<0.04$) reduction in systolic BP (-9.0 ± 11.6 mmHg) than C-CD (-5.4 ± 3.1 mmHg). Similarly, T resulted in a greater reduction in diastolic BP (-7.4 ± 9.3 mmHg) than C-CD (-5.0 ± 9.0 mmHg; $p<0.09$). For the period 8-9pm, when the PK profiles were projected to maximally different, T resulted in a significantly greater reduction than C-CD in systolic BP (-10.2 ± 16.0 and -5.1 ± 15.3 mmHg, respectively; $p<0.03$) and diastolic BP (-8.9 ± 9.6 and -4.4 ± 11.0 mmHg, respectively; $p<0.01$). When compared to C-CD, T resulted in slightly greater reductions in average 24 hour systolic BP (T: -7.2 ± 8.1 and C-CD: -5.3 ± 9.1 mmHg; $p=0.12$) and diastolic BP (T: -6.2 ± 5.6 and C-CD: -4.8 ± 6.2 mmHg; $p=0.14$). These PD differences were not associated with any episodes of hypotension, differences in adverse effects, or heart rate profiles.

This data demonstrates that administering the same dose of diltiazem with different release systems and PK profiles may result in corresponding clinically important PD differences. Thus, the release system using Tiazac produces a smoother, greater, and more consistent 24 hour reduction in BP than that which occurs with Cardizem-CD.

Key Words:

Diltiazem delivery systems; Pharmacodynamic profiles; Therapeutics

EFFICACY AND SAFETY OF THE QUINAPRIL-HYDROCHLOROTHIAZIDE COMBINATION ON AMBULATORY BLOOD PRESSURE PROFILES.

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We evaluated the efficacy and safety of the ACE inhibitor Quinapril combined with Hydrochlorothiazide in 50 patients (42 men and 8 women),with mild to moderate hypertension.
After 2 weeks of pharmacological wash-out, the circadian behaviour of blood pressure values was studied in all patients by 24-hour,non invasive,automatic,intermittent monitoring. After 12 weeks treatment, blood pressure monitoring showed a significant reduction both of systolic and diastolic mean values,expressed as total, day-time and night-time values.
Besides we noticed a significant reduction both of systolic and diastolic blood pressure variability,assessed by the 24 hour standard deviation (-13.2% and -8.7% respectively). No patient had to withdraw from the study and no noticeable side effect was observed during treatment.

Key Words: Blood pressure monitoring,ACE inhibition.

THE EFFECT OF ANGIOTENSIN CONVERTING ENZYME INHIBITOR ON TOTAL VASCULAR TONE AND LEFT VENTRICULAR HYPERTROPHY IN ESSENTIAL HYPERTENSION.

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We studied the effect of Angiotensin converting enzyme inhibitor (imidapril 10 mg once a day) on the total vascular tone (TVT) index (calculated as total vascular resistance) and left ventricular hypertrophy (LVH). The subjects were 13 patients with essential hypertension (EH) according to WHO's classification and 15 healthy individuals used as a control group. Non-invasive ambulatory blood pressure (BP) monitors and noninvasive continuous cardiac output (CO) monitors were simultaneously attached over 24-hour period. LVH was determined by echographic criteria using left ventricular mass (LVM) index. BP, heart rate, CO, TVT index and LVM index were measured immediately prior to, and 12 months following the administration of the agent. TVT was calculated asfollows :(mean BP/cardiac index)× 1, 332 dyne/sec/cm^{-5}. TVT index was measured based on the value at 2:00 a.m. as follows:[(each hourly value—value at 2:00 a.m.)/ value at 2:00 a.m.]× 100. The TVT index and LVM index after administration of the agent were significantly larger than those of before of the administration of the agent. There was a significant correlation coefficient between the TVT index and the LVM index in both before and after administration of the agent. It suggests that Angiotensin converting enzyme inhibitor reduce the TVT index and LVM index in patients with EH.

Key Words: total vascular tone, left ventricular mass, Angiotensin converting enzyme inhibitor

THE IMIDAZOLINE I-1 RECEPTOR AGONISTS IN THE TREATMENT OF HYPERTENSION.

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Stimulation of imidazoline receptors results in reduction of catecholamine levels.
Moxonidine is a highly selective imidazoline I-1 receptor agonist with minimal effect at central a-2-receptors.
The purpose of the study was to examine the effect of moxonidine on cardiohaemodynamic and side effect profile in 20 hypertensive patients.
The studies have indicated that moxonidine results in falls of the order of 21 mmHg systolic (from 179 to 158) and 13 mmHg diastolic (from 97 to 84) blood pressure.
Reduction of left ventricular hypertrophy has been indicated over a 6 month period of treatment with moxonidine.
Moxonidine behaved at least neutrally with regard to lipid and glucose metabolism as well as in patients with concominant diseaseses such as bronchial asthma.
Heart rate and ejection fraction were unchanged
No side effects other than headache, dry mouth and fatigue were reported.
Therefore based on the trials moxonidine is an attractive and safe alternative for successful treatment of hypertension.

Key Words: moxonidine, imidazoline receptors