groups. The primary end point was the change from baseline in mean trough SeDBP at Week 8.

There were no significant differences in baseline vitals signs among the 12 treatment groups; mean SeDBP and mean seated systolic BP (SeSBP) ranged from 102.6 to 104.4 mm Hg and 151.9 to 156.6 mm Hg, respectively. At Week 8, olmesartan medoxomil/HCTZ combination therapy demonstrated greater reductions in SeSBP/SeDBP than did monotherapy with either component. All olmesartan medoxomil/HCTZ combinations significantly reduced SeSBP/SeDBP compared with placebo. Changes from baseline in SeSBP/SeDBP for the starting 20 mg/d dose of olmesartan medoxomil, alone and in combination with HCTZ 12.5 or 25 mg/d, were 15.5/13.8, 20.1/16.4, and 27.1/20.0 mm Hg, respectively. Corresponding SeSBP/SeDBP reductions at the 40 mg/d maximum dose of olmesartan medoxomil, alone and in combination with HCTZ 12.5 or 25 mg/d, were 16.0/14.6, 20.6/17.3, and 26.8/21.9 mm Hg, respectively. Reductions in SeSBP/SeDBP with placebo were 3.3/8.2 mm Hg. The overall incidence of AEs in all treatment groups was similar to that of placebo.

The combination of olmesartan medoxomil/HCTZ is an effective and well tolerated therapeutic option. The combination produces dose-dependent reductions in SeSBP/SeDBP of up to 27/22 mm Hg, with an overall incidence of AEs similar to that of placebo. This combination should prove useful in a wide variety of hypertensive patients.

Key Words: Olmesartan medoxomil, combination therapy, hydrochlorothiazide

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EFFECT OF NEBIVOLOL OR LERCANIDIPINE ON AMBULATORY BLOOD PRESSURE VARIABILITY IN PATIENTS WITH MILD-TO-MODERATE ESSENTIAL HYPERTENSION

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Blood pressure (BP) variability over the 24-hour period has been considered a valid prognostic indicator since it correlates independently with target-organ damage due to hypertension.

Ambulatory blood pressure monitoring (ABPM) provides useful and precise information on BP variability through the standard deviation (SD) of BP means (24-hours, daytime and nighttime) and their coefficient of variability (CV = SD/BP mean).

In this double-blind study, the effects on ambulatory BP variability of a beta-adrenergic blocker (nebivolol 5 mg, once daily) and a calcium-cannel blocker (lercanidipine 10 mg, once daily) have been evaluated in 2 comparable groups of patients, each constitued of 12 subjects (age ≤ 65 years), affected with mild-to-moderate essential hypertension.

ABPM was performed at the end of a 15-day wash-out and repeated after 3 months of active treatment. Both drugs caused a significant and similar decrease in systolic and diastolic blood pressure but nebivolol significantly reduced systolic and diastolic, 24-h and daytime BP variability, while lercanidipine did not.

	24-h CV	Daytime CV	Night. CV
Nebivolol b. (systolic)	18.3 ± 3.9	17.3 ± 3.0	13.1 ± 3.8
Nebivolol a. (systolic)	12.1 ± 1.9**	11.9 ± 2.0**	10.8 ± 3.0
Nebivolol b. (diastolic)	19.1 ± 3.6	17.6 ± 4.4	14.9 ± 4.1
Nebivolol a. (diastolic)	14.3 ± 2.6**	13.0 ± 2.9*	14.1 ± 3.7
Lercanidipine b. (systolic)	18.7 ± 4.7	16.9 ± 4.4	13.1 ± 4.1
Lercanidipine a. (systolic)	16.9 ± 3.6	15.7 ± 3.2	12.3 ± 3.0
Lercanidipine b. (diastolic)	18.7 ± 3.1	17.3 ± 4.3	13.7 ± 2.7
Lercanidipine a. (diastolic)	19.4 ± 3.6	14.2 ± 2.5	12.9 ± 4.0

*CV = coefficient of blood pressure variability; SD = standard deviation of the means; * = $p<0.05$; * * = $p<0.025$ (Student's t test for paired data); contrasts between CV values calculated before (b.) and after (a.) treatment.*

After 3 months of active treatment, systolic and diastolic BP variability resulted significantly decreased, during daytime, in patients treated with nebivolol, both with respect to pre-treatment values and to lercanidipine post-treatment values ($p<0.05$). On the contrary, lercanidipine did not significantly change BP variability.

Our data confirm the observation that some beta-adrenergic blocking agents may buffer BP variability and support the importance of simpathetic activity on this prognostically important ABPM-derived variable.

Key Words: Nebivolol, Lercanidipine, blood pressure variability

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EFFECTS OF TELMISARTAN, RAMIPRIL AND AMLODIPINE ON CIRCADIAN BLOOD PRESSURE, HEART RATE AND NOREPINEPHRINE CYCLES IN ESSENTIAL HYPERTENSIVE PATIENTS

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The objective of this trial was to study the effect of chronic treatments with telmisartan (TELMI), ramipril (RAM) and amlodipine (AMLO) on the circadian rhythm of blood pressure (BP), heart rate (HR) and circulating norepinephrine (NE) levels in mild to moderate essential hypertension.

Fifty-seven essential hypertensive patients were incorporated in a randomized parallel design study after a 2 to 4 week placebo run-in period. Patients with diastolic BP greater or equal to 95 mmHg and less or equal to110 mmHg were randomized in a double blind fashion to either TELMI 80 mg qd for 8 weeks, or AMLO (5 mg for 4 weeks followed by 10 mg for 4 weeks) or RAM 2.5 mg for 1 week, 5.0 mg for 3 weeks and 10 mg for the following 4 weeks. Patients were hospitalized for the last 24 hours of placebo treatment and for the last 24 hours of active treatment to have their BP, HR and NE levels measured every 4 hours and hourly for the last 4 hours (from 4:00 to 8:00 A.M.) in the supine position followed by a study in the standing position for 10 min. NE levels were measured with HPLC technique and BP and HR were measured respectively with ambulatory BP or HR monitoring devices.

Circadian cycles were found for all 3 parameters. Systolic and diastolic BP were highest around 8:00 A.M. whereas HR tended to be highest around 8:00 P.M. and NE levels around noon, under placebo treatment. Both AMLO and TELMI reduced significantly systolic and diastolic BP but the fall in BP was highest with AMLO. No changes were observed in NE levels with TELMI or RAM but a 50% increase in NE levels was found in AMLO treated patients. The various treatments did not altered the pattern of the circadian rhythm but both RAM and TELMI tended to attenuate the variations in NE levels. The NE responses to standing increased in AMLO treated patients.

Chronic therapies with AMLO and TELMI both lowered significantly BP for 24 hours, but not RAM. TELMI did not activate the sympathetic system, despite a significant reduction in blood pressure, whereas AMLO did increase supine NE levels all through the day and potentiated the NE response to standing.

Key Words: Antihypertensive agents, autonomic nervous system, clinical study