EFFECTS OF VALSARTAN MONOTHERAPY ON THE CIRCADIAN BLOOD PRESSURE PROFILE OF PATIENTS WITH GRADE 1–2 ESSENTIAL HYPERTENSION

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Angiotensin II receptor blockers (ARBs) are a relatively new class of antihypertensive medications that selectively and specifically antagonize the action of angiotensin II, a potent vasoconstrictor impacting blood pressure (BP) regulation. Valsartan is an orally active, specific, and selective ARB. After a single oral dose, the onset of its BP lowering action is within 2 hours, with peak effect occurring within 4–6 hours. We investigated the effects of valsartan on the 24-hour BP profile of hypertensive patients. We studied 187 patients with grade 1–2 essential hypertension (63 men), 50.4 ± 13.3 (mean ± SD) years of age, assigned to receive valsartan monotherapy (160 mg/day). BP was measured by ambulatory monitoring at 20-min intervals from 07:00 to 23:00 hours and at 30-min intervals at night for 48 consecutive hours before and after 3 months of therapeutic intervention. Physical activity was also monitored every minute by wrist actigraphy, and the information used to determine diurnal and nocturnal means of BP for each patient according to individual resting time. There was a highly significant BP reduction after 3 months of valsartan (P<0.001), similar for both treatment times (14.1 and 7.7 mm Hg reduction in the 24-hour mean of systolic and diastolic BP after valsartan on awakening; 14.7 and 8.2 mm Hg when valsartan was administered before bedtime). The day/night ratio measured as the nocturnal decline of BP relative to the diurnal mean was unchanged after valsartan on awakening (~2.1 and 0.6 for systolic and diastolic BP; P>0.184). This ratio was highly significantly increased (6.1 and 6.3 for systolic and diastolic BP, P<0.001) when valsartan was administered before bedtime. The reduction of nocturnal mean was, therefore, significantly larger after valsartan before bedtime (P<0.032). Results indicate that, at either the time of administration, 160 mg/day valsartan efficiently reduce BP for the whole 24 hours. In elderly hypertensive patients, characterized by a diminished nocturnal decline in BP, dosing time with valsartan might be chosen at bedtime, for improved efficacy during the nocturnal resting hours, and the potential reduction in cardiovascular risk associated to the normalized day/night ratio.

Key Words: Valsartan, Elderly, Chronopharmacology

ADMINISTRATION TIME-DEPENDENT EFFECTS ON AMBULATORY BLOOD PRESSURE OF AMLODIPINE AS ADDED THERAPY IN UNCONTROLLED HYPERTENSIVE PATIENTS

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Amlodipine has been shown to be effective in reducing blood pressure (BP) throughout the day and night when given once daily. However, the potential chronopharmacologic differing effects on BP of amlodipine have only been addressed occasionally. We investigated the administration time-dependent antihypertensive efficacy of amlodipine given as added therapy in hypertensive patients. We studied 87 patients with uncontrolled grade 1–2 essential hypertension (45 men), 54.4 ± 12.2 years of age, who were already taken an average of 1.8 drugs (mainly an ARB or ACE inhibitor combined with a diuretic). Patients were randomly assigned to receive a single daily dose of amlodipine (5 mg/day) either on awakening or before bedtime. BP was monitored at 20-min intervals from 07:00 to 23:00 hours and at 30-min intervals at night for 48 consecutive hours at baseline and after 3 months of therapeutic intervention. Physical activity was simultaneously monitored every minute by wrist actigraphy, and the information used to determine diurnal and nocturnal means of BP for each patient according to individual resting time. After amlodipine on awakening, the reduction in BP was highly statistically significant (8.6 and 5.6 mm Hg reduction in the 24-hour mean of systolic and diastolic BP, respectively; P<0.001). The BP reduction was equivalent after amlodipine before bedtime (9.4 and 5.9 mm Hg reduction in systolic and diastolic BP, respectively; P<0.001). This BP reduction was similar during both daytime activity and nighttime resting hours, independently of dosing time, indicating a 24-hour therapeutic coverage of amlodipine administered either on awakening or before bedtime. The day/night BP ratio was slightly reduced after morning treatment (~0.6 and ~1.2 for systolic and diastolic BP), but increased after evening treatment (1.4 and 1.3, respectively), although differences between treatment-times were not significant (P<0.137). Results from this trial on uncontrolled hypertensive patients demonstrate that, independently of the time of administration with respect to the rest-activity cycle of each individual patient, a single daily dose of amlodipine efficiently reduces BP for the whole 24 hours of the day. The similar BP reduction observed for the diurnal and nocturnal means indicates that amlodipine does not modify the circadian pattern of BP variability.

Key Words: Amlodipine, Chronopharmacology, Circadian