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EFFECT OF LACIDIPINE ON ENDOTHELIAL FUNCTION IN HYPERTENSIVE PATIENTS.

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Essential hypertensive patients (EH) are characterized by impaired endothelium (END)-dependent vasodilation (VD). This study was designed to test whether the antihypertensive treatment with the Ca channel blocker lacidipine (LAC) can improve END-dependent VD in HT. In 12 EH (46.1± 5.4 yrs, BP: 152.2±11.2/100.6±6.2 mmHg) we tested the effect of acute (intraarterial infusion at 0.03 ng/100 ml /min for 20 min) and prolonged (2 monthes oral treatment 6 mg/die p.o.) LAC on forearm blood flow (FBF, strain-gauge plethysmography) modifications induced by the intrabrachial infusion of acetylcholine (ACH. 0.15, 0.45,1 5,4.5,15 μg/100 ml/min) and bradykinin (BDK: 5,15,50 ng/100 ml/min), two endothelium-dependent vasodilators, acting through different receptors and signal transduction pathways, and sodium nitroprusside (SNP:1,2,4 μg/100 ml/min), an endothelium independent vasodilator. As compared to normotensive controls (n=10, NT, age 45.8±4.6 yrs, BP 119±7.6/78.3±4.9 mmHg), EH showed a significantly ($p<0.01$) blunted response to BDK (%FBF increase above basal;x±SEM; NT: 215±28,332±32,543±49; EH:95±16,197±24, 278±41%) and to ACH (%FBF: NT.15±4,52±8,264±32,473±59, 611±58%, EH:7±2, 38±12,109±16,211±27,296±37%) while the response to SNP was similar in the two groups (%FBF: NT: 183±19, 267±35,370±40; EH: 175±20,246±30,349±38). Acute LAC infusion failed to increase VD to Ach (% FBF: 12±5,52±15,125±19,224±32, 328±41), or to BDK (% FBF: 99±11,186±19,271±34) and to SNP (141±22,219±25,300±36). In contrast two month LAC treatment significantly ($p< 0.001$) decreased BP (140.1±11.2/89.3±6.4 mmHg) and increased (*$p<.05$, #$p<.01$) VD to the highest dose of ACH (%FBF:9±3,44±11,137±15,288±33,407±54*) and to BDK (%FBF: 135±22#,267±35*,345±45#), while it did not alter the response to SNP (135±17,267±34,345±38). In EH prolonged (two monthes) oral treatment with LAC increases endothelium-dependent vasodilation to ACh and BDK, suggesting that this drug can improve endothelial function in EH.

Key Words: endothelium, vasodilation, lacidipine

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Acute and long-term adaptation of central hemodynamics and renal physiology in hypertensive patients on Logimax, a metoprolol/felodipine fixed dose combination .

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After a 4-w placebo period,central hemodynamics and renal function was monitored during baseline and during four hours following the first dose of a metoprolol/ felodipine fixed dose combination in 11 hypertensive patients (WHO II) BP was measured i a and cardiac output by dye-dilution and in the same setting GFR by Cr-EDTA, and renal blood flow by PAH-clearence These measurements were then repeated after 12 weeks of chronic therapy(24 hours post-dose=chronic trough and then 4 hours post-dose=chronic peak)

Results(conf int)	Baseline	Chronic through	Chronic peak
MAP (mmHg)	129	110 (-25, -13)	105 (-29,-19)
CO (l/min)	6 5	6 2(-0,96,0.39)	5.7(-1 55,-0 04)
TPR (units)	21	18 (-4.7,-0 3)	19 (-4.2,0 7)
HR (b/min)	70	63(-12,7,-2 3)	59(-15 6,-6 0)
GFR (ml/min)	376	420(-41,131)	453(-17,173)
RBF (ml/min)	97	94(-22,16)	98(-13,14)
FF (%)	26	22(-8,-1)	22(-8,1)

MAP=mean arterial pressure,CO=cardiac output,TPR=total peripheral resistance,HR=heart rate,GFR=glomerular filtration rate, RBF=renal blood flow,FF=filtration fraction

Conclusion.Chronic treatment with Logimax effectively lowers BP mainly by vasodilation but also a beta-adrenoceptor inhibitory effect is evident since heart-rate was significantly reduced as was cardiac output at peak-effect during chronic treatment No significant change in renal blood flow or filtration was noticed while filtration fraction tended to normalize The through/peak ratio for the change in MAP was 79 % (conf int 58 2,99 0)

Hemodynamics,renal function,calcium antagonist,felodipin, metoprolol,logimax

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INDUCTION OF NOCTURNAL BLOOD PRESSURE (BP) FALL BY ISRADIPINE (ISRAD) RX IN HYPERTENSION (HTN) AFTER LIVER TRANSPLANTATION (LTx).

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HTN develops soon after LTx using cyclosporine plus steroid-based immunosuppression. The normal nocturnal BP fall is lost, although restored partially over years. We examined the day-night BP variations during monotherapy with a short-acting dihydropyridine calcium channel blocker, isradipine (ISRAD average daily dose 4.1 mg b.i.d.) for 3 months in 16 LTx recipients early after Tx. ABPM recordings (SpaceLabs) were divided into awake and nocturnal 5-hour time blocks, excluding a 2-hour sleep transition. BP rose from Pre-Tx (110±2/64±2 to 151±4/ 90±3 mmHg one month after LTx $P<.01$). Pre-Rx CSA dose was 662±59 mg/d and Prednisone dose was 33± mg/d.

Pre-ISRAD:	Awake 5-hr	Nocturnal 5-hr	
SBP (mmHg)	147±4	143±5	NS
DBP (mmHg)	94±2	91±2	NS
HR (bpm)	86±3	75±3	
ISRAD Rx:			
SBP (mmHg)	129±3	120±3	†*
DBP (mmHg)	83±2	75±3	†*
HR (mmHg)	86±3	73±3	*

Mean±SEM, *$p<.05$ vs awake, †$p<.05$ vs Pre-Rx

During ISRAD Rx the fraction having a nocturnal fall ≥10% rose from 0% to 68% ($p<.01$). Analysis of ABPM records demonstrated a transient rise in HR and fall in BP after the nocturnal ISRAD dose, suggesting a pharmacologic effect on BP. These data demonstrate restoration of nocturnal BP fall during Rx with a short-acting CCB, which was not observed in previous studies with extended release nifedipine. Our results indicate that post-Tx nocturnal BP patterns can be altered favorably, potentially avoiding the adverse target effects of nocturnal HTN.

Key Words: ABPM, cyclosporine, transplantation, steroids, circadian rhythm, hypertension

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PERSISTENT ANTIHYPERTENSIVE EFFECT OF AMLODIPINE 3 DAYS AFTER DISCONTINUATION OF THERAPY: A PROSPECTIVE DOUBLE BLIND RANDOMISED STUDY

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To assess the residual antihypertensive effect of amlodipine (A) 3 days after discontinuation of therapy, a multicenter double-blind study was performed in 33 patients with mild to moderate primary hypertension After one month wash-out (V1), all patients received A 5 mg o d for 8 weeks (V2) After this, patients were given double-blind either placebo (14 patients) or A (19 patients) for 3 more days (V3) Office (OBP) and the 24-h ambulatory blood pressure (ABPM) were measured at V1 V2, V3 Because of technical difficulties, high quality ABPM was available only in 9 patients receiving placebo and 15 patients receiving A Results (mmHg ± S D.) are given in the table

	BP	V1	V2	V3
AM L	OBP(mmHg)	168 ± 19/ 101 ± 7	148 ± 11/ 88 ± 5	152 ± 14/ 90 ± 8
	daytime BP (mmHg)	156 ± 19/ 95 ± 12	145 ± 10/ 88 ± 9	144 ± 11/ 88 ± 10
	nightime BP(mmHg)	137 ± 17/ 80 ± 11	129 ± 11/ 76 ±10	128 ± 11/ 74 ± 11
	24-hour BP(mmHg)	148 ± 19/ 88 ± 11	139 ± 9 / 83 ± 9	138 ± 11/ 82 ± 10
PL	OBP(mmHg)	172 ± 14/ 101 ± 5	144 ± 12/ 85 ± 6	146 ± 14/ 85 ± 9
	daytime BP (mmHg)	152 ± 15/ 94 ± 8	143 ± 13/ 88 ± 8	144 ± 13/ 89 ± 8
	nightime BP(mmHg)	129 ± 24/ 76 ± 14	121 ± 16/ 71 ± 12	121 ± 18/ 72 ± 13
	24-hour BP(mmHg)	145 ± 17/ 87 ± 8	136 ± 4/ 81 ± 8	137 ± 14/ 84 ± 8

The 2 groups were comparable for their main demographic data as well as their BP values at baseline (V1) and after 6 weeks of A (V2), $p> 0.05$ Replacement of A by placebo did not cause any increase of BP even at 3 days after cessation of administration

Thus, the antihypertensive effect of A is well maintained far beyond the 24-hour span when administered in a 5 mg once daily dosage. This property could improve patient's therapeutic coverage (in partly compliant patients). and incidentally, would open possibilities for low frequency dosage form.

Key Words: AMLODIPINE, AMBULATORY BLOOD PRESSURE MEASUREMENTS, CONTINUOUS