LONGTERM EFFICACY OF NICARDIPINE ALONE AND IN COMBINATION WITH BETA-BLOCKERS IN STABLE ANGINA

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The antianginal efficacy of Nicardipine (NIC) was evaluated in 171 stable angina patients by treadmill (modified Bruce) exercise testing, anginal attack (AA) rate and nitroglycerine use. Two parallel groups were enrolled: GrA (n=96) without beta-blockers (BB); GrB (n=75) patients symptomatic on BB therapy which was continued during the study. After 2 wks of placebo (PLA), NIC was titrated in all patients to an optimal dosage of 20, 30, or 40 mg tid. Of the 171 pts, 64% were successfully treated for 1 year with adequate symptom control. The mean values for total Ex time (TT) and time to angina (TA) during treadmill, and median AA at baseline and during NIC therapy are shown:

	TT(min)		TA(min)		Median AA	
	Gr-A	Gr-B	Gr-A	Gr-B	Gr-A	Gr-B
Baseline	10.6	9.7	9.1	7.6	5	4
Nicardipine	12.9*	11.5*	11.4*	9.6*	0	0

(*=p <0.05 compared to baseline using 2-way ANOVA)

At the end of 1 yr, 76% of Gr-A and 68% of Gr-B patients were free of angina. During a final 3 wk double blind phase, about half in each group received PLA in lieu of NIC. At both 1 and 3 wks, exercise duration significantly (p<.02) deteriorated in patients assigned to PLA compared to those continuing on NIC. Headache and edema were common side effects in both groups. Conclusion: NIC given alone and in combination with BB is a safe and effective antianginal agent for longterm therapy in stable angina.

INDICES TO ASSESS AUTONOMIC AROUSAL IN MENTAL STRESS: IMPLICATIONS FOR CLINICAL TRIALS

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To assess the effects of cardiac drugs on the sympathetically-mediated changes from mental stress (MS), the degree of arousal from MS must be reproducible in serial studies. Blood pressure (BP) and heart rate (HR) cannot be used to reflect arousal since they are altered by cardiac drugs while skin conductance level (SCL), a cholinergically-mediated index of sympathetic arousal, is not. To determine reproducibility of indices to different MS stimuli and reproducibility of responses in serial testing, SCL, HR, and BP were examined once weekly for 3 weeks in 11 healthy subjects with mental arithmetic (MA), the Stroop test (ST), and a stress interview (SI). During each session, SCL significantly increased in response to MA, ST, and SI (each $p<0.005$); HR significantly increased in response to MA and ST ($p<0.05$), but not SI; BP increased in response to MA ($p<0.05$), but not ST or SI. Comparing the responses between the 3 sessions, the increases in both SCL and HR from MS were similar, but the increases in BP varied significantly ($p<0.01$). We conclude that SCL is a more sensitive and stable index of arousal than BP and HR in response to serial MS testing with the paradigm typically used in behavioral-cardiology studies.

ANTIISCHEMIC AND ANTIANGINAL EFFECTIVENESS OF AMLODIPINE, A ONCE - DAILY CALCIUM ANTAGONIST, IN THE TREATMENT OF STABLE ANGINA PECTORIS

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Amlodipine (A) 10 mg, a new long-acting dihydropyridine calcium antagonist, was evaluated for antiischemic and antianginal efficacy in 12 patients (pts) with doc. CAD, stable angina pectoris (AP) and > 2 mm of exercise - induced ST - segment depression (ST↓). For 2 days pts received A at 8 a.m.. According to a randomized, placebo - controlled, crossover and db protocol, pts were then assigned to A or placebo (P) to be taken once a day at 8 a.m. for 3 weeks each with 2 intercurrent weeks for washout. During both treatment phases, diaries were kept for anginal attacks. Exercise tests and blood sampling for plasma levels of A were performed before (= 24h) and 8 hours after dosing on the following day after acute testing as well as on day 18 of each of the 3 weeks. Effects (percent changes) on ST↓ at comparable workload, exercise capacity (EC, in W x min) without AP (EC - AP), EC without ischemia (EC - ST↓) during acute and chronic treatment, AP - attacks during chronic treatment and corresponding plasma levels (PL, in ng/ ml) were:

	8 h (acute)	24 h	8 h (chronic)	24 h
ST ↓	-33%***	-10%*	-30%***	-31%***
EC - AP	+82%***	+32%*	+10%	+. 5%
EC - ST ↓	+191%***	+64%*	+74%***	+108%**
PL	4. 88	4. 23	23. 90	12. 07
AP - attacks			-45%*	

* p < . 05; ** p < . 01; *** p < . 005 as compared to control/ P

Thus, A 10 mg is an effective antiischemic and antianginal agent. It warrants therapeutic coverage for at least 24 hours with the advantage of dosing once daily. During chronic treatment, antiischemic effects increased at 24 hours which was considered due to higher plasma levels after repeated administration.

HDL CHOLESTEROL PROMOTES NORMAL ENDOTHELIAL FUNCTION AND CORONARY ARTERY VASOREACTIVITY

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Recent data suggests that HDL cholesterol has vasoactive properties which may contribute to its beneficial effects on coronary artery disease (CAD). We investigated the relationship between serum lipoproteins and response of angiographically normal (N=19) and diseased (N=16) coronary segments to the endothelium-dependent vasodilator, acetylcholine (ACH, 2.0×10^{-4}M i.c.), in 20 patients with mild to moderate CAD. ACH produced significant vasoconstriction of smooth (10±3%, $p<0.05$) and diseased (26±5%, $p<0.05$) segments. An inverse correlation was observed between HDL and ACH-induced vasoreactivity in both smooth ($r=.61$, $p<0.006$) and diseased ($r=.70$, $p<0.004$) segments. Similar relationships were observed between HDL fractions (HDL2, HDL3) and vasoreactivity; however, these were not superior to that of total HDL. No significant relationship was observed between total cholesterol (TC), LDL, or TC/HDL ratio and the response of smooth or diseased segments to ACH. These findings suggest that HDL cholesterol promotes normal endothelial cell function in patients with mild to moderate CAD. Thus, in addition to anti-atherogenic properties, the beneficial effects of HDL on CAD events may be related to its effect on endothelial cell function and coronary vasoreactivity.