10:45

ATENOLOL IS MORE EFFECTIVE THAN NIFEDIPINE IN SUPPRESSION OF SPONTANEOUS SILENT ISCHEMIC EVENTS DURING DAILY LIFE

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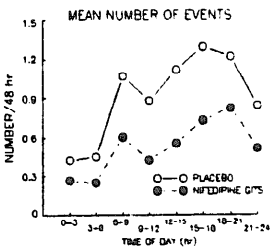
The anti-ischemic effects of Atenolol (A, 100 mg/day) and Nifedipine (N, 90 mg/day) on transient ischemic events (TIE) during ambulatory ECG monitoring (AEM) were evaluated in a double blind, placebo-controlled, randomized, crossover trial in 20 patients (mean age 63) with stable CAD and TIE's during AEM. All patients had a positive exercise test and ≥5 min of silent ischemia on AEM. Treatment phases consisted of 2 placebo (1 wk) and 2 active therapy (3 wk) periods during which 48 hr AEM's were performed using frequency modulated recorders. The data were analyzed in a blinded manner utilizing the 1x1x1 rule. Results: Both A and N significantly reduced the mean (±SE) number of TIEs from 16±4 events during placebo to 3±1 and 6±1 respectively (p<.005). The average duration of ischemia/24 hrs decreased from 4103±1071 sec on placebo to 634±55 and 1296±276 sec respectively during A and N (p<.05). Fifty percent of patients were free of ischemia during A compared to only 25% with N. Atenolol was better than N in reducing the frequency (p<.05) and duration (p<.01) of silent ischemia during AEM. Atenolol was more (p<.05) effective than N in reducing TIE between 6 AM and NOON. There were more side effects during N (26% dizziness and 21% edema). Summary: Atenolol is more effective and better tolerated than nifedipine for the treatment of silent ischemia during daily life.

11:00

NIFEDIPINE GITS REDUCES ANGINA AND AMBULATORY ISCHEMIA OVER 24 HOURS: RESULTS OF THE NIFEDIPINE CIRCADIAN ANTI-ISCHEMIC PROGRAM (N-CAP) MULTICENTER TRIAL.

William Parmley, UC San Francisco, For the N-CAP Study Group

We studied the effects of once daily nifedipine (N-GITS) in 207 stable angina pts (92 on monotherapy and 115 on B-blocker) with ≥2 angina attacks/wk and ≥2 ischemic episodes (IE), on ambulatory ECG monitoring (AECG) and angina in a single-blind trial. 48 hr digital AECG was performed after 1 week placebo run-in (P), 9 wks N-GITS (30-180mg), and 2 wks placebo washout (PW). IE on AECG were significantly reduced (P 7.3/48 hr, N-GITS 4.0, p=0.0001; mean reduction 45%) and significantly increased during PW (5.2, p=0.011 vs N-GITS). This was paralleled by significant reductions in weekly angina (P 5.7, N-GITS 1.8, PW 3.9, p=0.0001 for both comparisons) and NTG use (P 4.1, N-GITS 1.6, PW 3.3; p=.0001 for both comparisons). Reductions in IE on AECG, angina, and NTG use were found with N-GITS when used alone or when added to B-blockers. A circadian variation of AECG events was present at baseline and N-GITS significantly reduced the number of events at each time interval over 24 hours (Figure).



Thus, once daily N-GITS markedly reduced subjective and objective evidence of ischemia over the whole day, both as monotherapy and in combination with B-blockers.

11:15

MYOCARDIAL RELEASE OF ENDOGENOUS OPIOIDS IN THE HUMAN HEART AND THE EFFECTS OF EPIDURAL SPINAL ELECTRICAL STIMULATION (ESES) IN PACING-INDUCED ANGINA PECTORIS

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In order to investigate if there is a local myocardial release in the human heart of endogenous opioids and to study the short-term effects of ESES in angina pectoris, 7 patients with severe CAD underwent a right-sided catheterization with atrial pacing via a catheter in the coronary sinus. Blood samples were simultaneously drawn from a peripheral artery and the coronary sinus in the heart for later assay of lactate and endogenous opioid concentration. The heart was paced to anginal symptoms during a control session and during treatment with ESES. An epidural stimulator had previously been implanted for antianginal treatment.

Results: There was a net release from the myocardium in all patients of beta-endorphins (BE), leu-enkephalin (L-enk), met-enkephalin (M-enk) and dynorphin (Dyn). Treatment with ESES increased tolerance to pacing (129±18 compared to 151±17 beats/minute; p<0.05) and improved lactate metabolism (lactate production during control, -7%±23%, turned to extraction, 9±16%; p<0.05). At maximal pacing rate where all patients experienced anginal pain, myocardial lactate extraction turned to production (9±16% compared to -5±23%; p<0.05).

Conclusions:

1)The human heart is capable of releasing the opioid peptide BE, L-enk, M-enk and Dyn. Enkephalins are thought to stimulate presynaptic delta-receptors on adrenergic nerve terminals in the myocardium, which inhibit the release of NE and the effector response following sympathetic stimulation.

2) Treatment with ESES seemed to have an antianginal effect as a result of antiischemic influence. There was also a tendency to an increased myocardial release of BE and L-enk during ESES in all 5 patients studied.

11:30

PROGNOSIS OF PATIENTS MEDICALLY CONVERTED FROM SYMPTOMATIC ANGINA TO SILENT ISCHEMIA

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The prognositc significance of silent ischemia (SI) was studied in 50 patients with stable angina pectoris (AP) who had been medically treated to an end point of absence of chest pain. Each patient had coronary artery disease documented by angiography, exercise testing, previous myocardial infarction, or classic AP. All patients had AP that was controlled with medical therapy; nitrates 64%, calcium blockers 64%, beta-blockers 28%, aspirin 78%. Ambulatory Holter monitoring was performed for 36±12 hours. Ischemia was defined as ST segment depression of >1mm for ≥60 seconds. Seventeen patients (34%) had ischemia; 16 (32%) had SI, 1 (2%) had AP, and 1 (2%) had mixed angina. Ischemic episodes ranged from 1-14 per patient (median 5) with a mean total ischemic time of 143 min/patient. Sixteen cardiac events (unstable angina 10, need for revascularization 4, sudden death 2) occurred during a mean follow-up of 10 months (range 1-31 months). The event free survival at 10 months was 77% in the non-SI group and 39% in the SI group; the difference was significant at p<0.02. The persistence of SI after the control of AP identifies a high risk subset.