SUCCESSFUL CONTROL OF THE CHRONIC FORM OF SUPRAVENTRICULAR TACHYCARDIA WITH ORAL VERAPAMIL HYDROCHLORIDE

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Chronic supraventricular tachycardia (SVT), in contrast to the paroxysmal form of SVT, is characterized by its almost incessancy interposed by short periods of sinus rhythm. Verapamil hydrochloride (V) was used to treat 12 patients(pts) with the chronic form of SVT at rates ranging from 140 to 180 beats per minute. Three pts had sinus nodal reentrant tachycardia, 4 pts atrioventricular (A-V) nodal reentrant tachycardia and 5 pts A-V reciprocating tachycardia involving concealed retrograde conducting bypass tracts. All 12 pts were symptomatic and were resistant or intolerant to digitalis, propranolol, quinidine, procainamide and disopyramide used alone or in various combinations. V was given orally at dosages ranging from 320 to 800 mg per day and all pts were followed at bimonthly intervals at our arrhythmia control clinic. With a follow-up period of 5-23 (mean 14.6) months, all 12 pts had symptomatic improvement. Repeated holter monitoring during V therapy demonstrated that 8/12 pts manifested only atrial echo phenomenon and 4/12 pts slow, short-lived SVT at rates of less than 100 beats per minute. The therapeutic plasma V concentrations measured 112 to 572.6 (mean 232 ± 127) ng/ml. One pt developed headache, 1 pt constipation and 2 pts peripheral edema presumably due to venous relaxation effect of V. Each of these side effects was mild and clinically manageable. We conclude that oral V therapy is safe and effective for pts with the chronic form of SVT. In addition, this study suggests that V therapy may be tried before contemplating pacemaker therapy or surgical intervention in these pts.

ORAL FLECAINIDE ACETATE FOR ELIMINATION OF VENTRICULAR ARRHYTHMIAS IN MAN

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In order to determine the antiarrhythmic efficacy and safety of oral flecainide acetate (FA) in man, a placebo controlled dose-ranging and short-term oral maintenance study was undertaken in 13 patients (pts) with chronic, ventricular ectopy (VE) of frequency >600 VE/12 hrs. During a 2 day placebo control period, 11/13 maintained stable VE frequency (mean 11,254/12 hr,range 653-35,551) and entered dose-ranging. Dosage was increased in increments at 3 day intervals from 100-300 mg/12 hr until 95% VE suppression, limiting side effects, or dosage maximum was attained. Ten pts completed dose-ranging, and pt 11 experienced a transient ischemic attack and was excluded. Of the 10 pts, 9(90%) were complete responders (CR)(mean suppression 98.7%, range 96.1-100%), and one responded partially (68% suppression). Repetitive VE was totally eliminated in all 10 pts. Pt 11 showed 77% VE suppression on 100 mg/12 hr before exclusion. Of CR, 2 pts ended dose-ranging successfully at 100 mg, 5 at 200 mg, and 2 at 250mg/12 hr. Average dose calculated to achieve 95% suppression was 169 mg/12 hrs. A 3 day placebo-controlled drug washout period was accompanied by a significant return in VE in each of the 9 CR. VE first recurred at 21.9 hrs (range 7-40), and by 3 days VE averaged149.6% of control frequency. During the subsequent outpt trial, FA remained highly effective with total and average VE suppression of 98.0% and 94.6%, respectively. ECG response included prolongation ($p<0.01$) of PR(16.5%) and QRS (10.6%). Echocardiographic CI was unchanged. FA was well tolerated except for headache in 2 pts. Thus FA appears to be a highly effective antiarrhythmic in man.

ROLE OF SERUM T4 AND REVERSED T3 IN MONITORING ANTIARRHYTHMIC EFFICACY AND TOXICITY OF AMIODARONE IN RESISTANT ARRHYTHMIAS

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Amiodarone (Am), a potent iodinated antiarrhythmic drug, increases serum T4 and reversed T3 (rT3) without producing clinical hyper or hypo-thyroidism. Thus, T4 and rT3 and QTc were measured serially in 15 euthyroid pts with resistant (to other agents) cardiac arrhythmias (7 ventricular, 8 atrial) before, during and after withdrawal of Am (600-1000 mg/day) therapy and correlated with drug toxicity and antiarrhythmic efficacy (AE), documented by serial 24 hr Holter analysis. Results (mean±S.D.; *$p<0.001$):

	T4 µg/dl	rT3 ng/dl	Q-Tc
Predrug	7.8±2.2	37±7	0.44±0.03
3 week	12.1±2.8	67±22	0.48±0.02
Peak (2-5 wk)	15.9±3.2*	84±21*	0.49±0.04*
6 wk after drug stopped	9.5±1.9	55±5.5	0.46±0.04

Amiodarone increased T4 and rT3 in all patients; a linear correlation was found between an increase in rT3, AE and Q-Tc. AE was invariably associated with rT3 level >55 ng/dl and drug side effects with >100 ng/dl. The correlation with T4 was less striking. On drug withdrawal, side effects disappeared when rT3 fell <100 ng/dl and arrhythmias returned at levels <55 ng/dl.
Conclusions: 1) Serum rT3 provides a sensitive index to monitor efficacy (55-100 ng/dl) and toxicity (>100 ng/dl) of Amiodarone and 2) the data provides evidence for the drug producing a selective inhibition of T3 action on the heart as a potential basis for its antiarrhythmic effect.

FLECAINIDE ACETATE, A NEW ANTIARRHYTHMIC AGENT: DOSE-RANGING AND EFFICACY STUDY

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Flecainide acetate (R-818) is a new antiarrhythmic agent with Class I properties. Potential advantages include a long plasma half-life (ave: 14 hr); effectiveness by both oral and IV routes; efficacy at relatively small doses; and few serious side effects noted to date. We evaluated flecainide with a single-blind dose-ranging and efficacy study in 9 patients with frequent ventricular ectopic depolarizations (VEDs). Patients were hospitalized and the ECG was monitored continuously by tape recordings which were analyzed quantitatively in a blinded fashion. Two days of placebo BID were followed by three increasing oral doses of flecainide (100, 200 and 300 mgm BID for 3 days each) until complete suppression or the 300 mgm BID dose was reached; 3 days of placebo BID were then observed to assure return of baseline rhythm and to evaluate plasma pharmacokinetics. During the 2-day control period, the patients averaged 15.2 VEDs/min (range 1.3-50.0), and all patients were observed to have complex ventricular arrhythmias (> Lown Class II). At the most effective dose (200 mgm BID in 6 pts, 300 mgm BID in 3 pts), average VED suppression was 96.0% (range 77.9%-100%), with 6 of the 9 achieving 100% suppression. During placebo washout, VED return averaged 146% of control. Outpatient treatment resulted in average suppressions of 99.6% and 99.5% at 1 and 2 wks, respectively. There were no significant changes in blood pressure or heart rate, but the PR, QRS and QTc intervals increased by 29%, 24% and 7% respectively ($p < .05$ for all). Observed side effects were an occasional sense of unsteadiness (4 pts), transient blurring of vision (1 pt), and a sense of warmth (1 pt). No side effect was serious enough to require discontinuation of drug. We conclude that oral flecainide, 200 or 300 mgm BID, is highly effective at suppressing VEDs and complex ventricular arrhythmias. Side effects in these 9 pts were minimal.