THE EFFICACY AND SAFETY OF SOTALOL IN DIGITALIZED PATIENTS WITH CHRONIC ATRIAL FIBRILLATION

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The effects of Sotalol (S) (doses 80-320mg daily) in 34 digitalized (digoxin ≤0.5mg/day) Pts with atrial fibrillation (AF) were evaluated by a randomized, double-blind, placebo-controlled study. After one week of S or placebo (P), Pts not in normal sinus rhythm received electrical cardioversion (EC). Six (2 P, 4 EC) out of 10 P Pts and 12 (2 S, 10 EC) out 20 S Pts achieved normal sinus rhythm (4 Pts on S refused EC). All 6 P Pts reverted to AF within a month; 5 of 12 S Pts remained in normal sinus rhythm for the entire 6 month period ($p<0.05$). S significantly reduced resting heart rate (94 to 83 bpm), exercise increases in heart rate (171 to 154 bpm) and systolic blood pressure (164 to 151mmHg) compared to baseline, whereas placebo had no such effects. S did not increase serum digoxin levels. Three Pts discontinued S therapy due to side effects. No proarrhythmia was observed during S therapy. Thus, S prevents recurrence of AF and blunts exercise increases in heart rate and systolic blood pressure in digitalized Pts.

STATISTICAL EVALUATION OF LONG TERM ELECTROCARDIOGRAMS IN ORDER TO CLASSIFY ANTIARRHYTHMIC AND ARRHYTHMOGENIC EFFECTS OF ANTIARRHYTHMIC DRUGS.

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Only empirical approaches have been used to define individual antiarrhythmic and arrhythmogenic effects of antiarrhythmic drugs in individual patients. A new method for assessment of these effects has been developed based upon comparisons of statistical distributions of ectopic beats recorded on long term electrocardiograms (ECG). The method comprises 4 steps: (A) a standard analysis system is used to obtain a precise timing of each ectopic beat and arrhythmia episode; (B) random sampling of the record generates a population of independent observations of the arrhythmia; (C) the independent samples are used to construct empirical distribution curves; (D) the Smirnov test is employed to compare the empirical distribution curves. In order to obtain a true independent observations in the step (B), the random sampling can consider only a small portion of the complete record which may not be representative. Therefore, the steps B - D are repeated many times and the individual results of Smirnov test are subsequently summarised using the binomial test.

The method has been tested in a pilot study involving 7 patients who suffered from a variety of ventricular arrhythmia. In each of these patients, one base-line Holter recording and one recording on each of three different drugs (flecainide, sotalol, and verapamil) were made. The results showed that (a) the type of distribution of ectopic beats is highly individual which makes the methods based merely on their counting inappropriate, (b) treatment with an antiarrhythmic preparation may cause a significant change in the character of arrhythmia which cannot be classified as antiarrhythmic or arrhythmogenic, (c) the definition of arrhythmogenesis can be addressed in a precise mathematical way. In the pilot population of 7 patients, a significant aggravation of arrhythmia on flecainide was found in 1 case, on sotalol in 3 cases, and on verapamil in 1 case. In 2 cases on sotalol and in 2 cases on verapamil, significant change in the character of arrhythmia was found which had neither antiarrhythmic nor arrhythmogenic quality.

DOES ADJUNCT BETA-BLOCKADE ENHANCE THE EFFICACY OF MEMBRANE DRUGS IN PATIENTS WITH INDUCIBLE VENTRICULAR TACHYCARDIA?

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Inducible ventricular tachycardia (VT) frequently persists despite solitary membrane stabilizing drug (MSD) therapy. Therefore, combination antiarrhythmic drug therapy is often considered. To determine the role of beta-adrenergic blocking drugs (BB) as additive therapy to MSD, we evaluated 22 patients with persistently inducible VT despite therapy with MSD. Of 53 patients who underwent serial drug testing guided by programmed stimulation, 16 were noninducible with MSD alone. Of 37 patients who were persistently inducible, 22 were tested with the combination of MSD plus BB. Twelve Pts became noninducible on combination therapy (Group I), while 10 Pts remained inducible (Group II). The groups did not differ with regard to the clinical characteristics of sex, age, ejection fraction or presence of coronary disease. BB increased sinus cycle length from 770 to 971 msec ($p < 0.001$). MSD prolonged the ventricular effective refractory period compared to baseline (240 to 258 msec, $p < 0.05$) and this was further increased by BB (286 msec, $p < 0.05$). In group II Pts, BB did not have any effect on VT cycle length or ease of induction. We conclude adjunct BB renders a significant number of Pts noninducible when added to MSD.

THE INTRAVENOUS AMIODARONE MULTI-CENTER STUDY GROUP: PRELIMINARY REPORT

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To determine the efficacy and optimal dose of intravenous amiodarone in the treatment of hemodynamically destabilizing ventricular tachyarrhythmias (VT/VF) refractory to lidocaine, procainamide, and bretylium, 120 patients were treated with 525 mg, 1050 mg or 2100 mg (double-blind) of amiodarone given over 24 hours. Supplemental 150 mg boluses of amiodarone were permitted for breakthrough VT/VF in the first 6 hours. Success was defined as no episode of VT/VF after the first 6 hours.

Results: 1) Administration of amiodarone was associated with a 47% success rate in suppressing VT/VF in these refractory patients. 2) No dose-related trend in mortality, use of supplemental boluses, or overall success were observed.

	LOW	MOD	HIGH
N	41	40	39
TOTAL DOSE (MG±SD, 24 HOURS)	739±529	1179±533	2023±618
SUCCESS, TOTAL, N (%)	18 (44)	21 (53)	17 (44)
SUCCESS, NO BOLUS, N (%)	14 (34)	14 (35)	14 (36)
BOLUSES (# OF PTS,HOURS 0-6)	18	16	12
BOLUS DOSE (MG±SD,HOURS 0-6)	305±229	291±222	263±158
MORTALITY, 24 HOUR, N (%)	9 (22)	6 (15)	7 (18)
HYPOTENSION, N (%)	4 (10)	6 (15)	9 (23)

Deaths in the first 24 hrs were due to refractory VT/VF in 6/9 patients in the low, 2/6 in the moderate, and 2/7 in the high group. Hypotension, when reported by an investigator as an adverse event, showed a dose-related increase.

Conclusion: 1) Intravenous amiodarone may be effective in a significant proportion of patients with refractory VT/VF. 2) As little as 500 mg/24 hrs of amiodarone may be as effective as the higher doses often administered and may be associated with less hypotension.