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CLINICAL USEFULLNESS OF POLYGRAPHIC TRACINGS WITH SPECIAL REFERENCES TO EVALUATION OF ANTIARRHYTHMIC AGENTS

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Abstract

Antiarrhythmic agents have recently become increasingly frequent in use and the untoward symptoms related to their side effects may be unavoidable at times. Effect of 2 drugs, Procainamide and Ajmalin, on cardiovascular system, therefore, was evaluted by non-invasively derived parameters.

Forty patients with ischemic heart disease and/or myocardial disease (NYHA II in all) and 20 normal subjects were selected, and polygraphic recordings with phonocardiogram, carotid arteriogram, femoral arteriogram, electrocardiogram and Minnesota impedance cardiogram were simultaneously taken before and after 500 mgs of Procainamide and 50 mgs of Ajamlin give intravenously.

Pre-ejection period, isometric icontraction time and ejection time/pre-ejection period were significantly ($P<0.01$) deteriorated in Procainamide and in Ajmalin. Total mechanical systole, election time, electromechnical interval, systemic blood pressure, heart rate, stroke volume, cardiac output and peripheral resistance were variably changed. Since QRS duration and PR interval became prolonged, atrioventricular and intraventricular conduction delays may partly be related to the above-mentioned left ventricular dysfunctions. Ajmalin more derpessed mechanical as well as electrical disorder than Procainamide, which might be atributable to higher incidence of the side effects in Ajimalin. Some patients even developed left ventricular conduction delay (left bundle branch block) with reversed splitting of the second heart sound during Ajmalin infusion. No statistically significant difference in deviation of the parameters was found between patients and normal subjects.

With increase in varieties and use of antiarrhythmic drugs there arises an important problem of side effects of these drugs on the cariovascular system[1,2].

MATERIALS AND METHODS

Forty patients (in age ranging 34-69 years with average of 52.4) with ischemic heart disease and with myocardial disease were selected for the studied group. All showed a normal sinus rhythm and a class II by New York Heart Association. Those who had hypertension, valvular disease, and were treated with specific medications such as digitalis or β-blocking agents were excluded. Twenty healthy hospital workers (in age ranging 26-49 years with average of 30.5) were chosen as the control group. All had no history or findings of cardiovascular disease.

The carotid artery pulse, phonocardiogram, electrocardiogram, and femoral artery pulse or Minnesota impedance cardiogram were siumltaneously taken in each subject. The recordings were made before and immediately, 5, 10, 15 and 20 minutes after administration of the two drugs. Procainamide in the dose equivalent to 500 mg and Ajmalin to 50 mg were given intravenously in 5 minutes for each injection.

The parameters obtained by these methods consist of the heart rate (HR), the left ventricular systolic time intervals (LVSTI), i. e. Q-II (total electromechamical systole) index, ET (ejection time) index, PEP (pre-ejection period) index, ET/PEP ratio, ICT (isometric contraction time)[3], as well as stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR) by Minnesota impedance method[4] or Wetzler-Boeger's method[5]. In addition, they included the amplitude of the first sound (S_1) and Q-1st sound interval (Q-I) on the phonocardiogram, the width of QRS and PQ intervals on the electrocardiogram as well as the systolic and diastolic blood pressures (BPs, BPd) by a cuff method.

These 15 measured values were averaged over 5 cardiac cycles at each period to obtain the respective average values and the standard error within the 99% confidence limit.

RESULTS

Table 1 shows the percent changes in the maximal deviations from the control values of the 15 items including 5 LVSTI-parameters after each drug administration, and the standard error and the 99% confidence limit in the studied and the control groups. Figs. 1 and 2 illustrate similarly the effects of the two drugs on the two groups. Table 2 gives the intergrated results (all statistically significant) according to the drugs and the groups at the time when the drug effects showed the maximal changes.

Among the different items, there could be observed an increase of

TABLE 1.

The percent changes in the maximal deviations from the control values of the 15 parameters in each group and drug

	Procainamide		Ajmalin	
	normal group	diseased group	normal group	diseased group
Q-IIi	+ 2.2± 3.8	+ 3.1± 3.9	+ 3.2± 2.1	+ 5.4± 3.5
ETi	− 1.5± 3.4	+ 2.1± 2.9	− 3.1± 3.1	+ 0.5± 3.6
PEPi	+ 7.6± 3.2	+12.0± 2.3	+19.9± 5.9	+20.3± 6.7
ET/PEP	− 9.7± 6.5	−11.0± 4.1	−21.2± 5.9	−19.1± 7.0
HR	+11.1± 9.9	+20.1± 7.2	+16.5± 8.2	+23.8±10.1
BPs	− 8.9± 9.6	− 4.0± 8.6	− 3.9± 5.8	− 0.6± 7.3
BPd	− 5.1± 6.8	− 4.2± 5.7	− 1.5± 6.1	+ 4.5±11.5
ICT	+18.1±10.6	+21.2±16.2	+35.9±11.0	+41.0± 9.3
Q-I	+ 4.8± 6.0	− 1.9± 6.9	− 0.4± 6.8	+ 1.5± 6.3
S_1	−26.0±18.1	−58.5±22.7	−71.2± 8.9	−80.3± 9.4
QRS	+14.9±11.0	+13.8± 9.8	+47.8±14.2	+40.1± 9.1
PQ	+ 5.0± 4.5	−11.4± 4.6	+23.6± 5.1	+29.0± 8.2
SV	− 7.4± 7.2	− 7.8±18.2	− 8.8±10.7	− 4.5± 7.7
CO	− 5.6± 7.9	− 4.0± 6.1	− 3.1± 7.2	− 3.4± 8.5
TPR	+ 5.1± 8.4	+ 2.2± 7.6	+ 1.4± 8.6	+ 0.7± 6.8

Note: ±=99 % confidence limit, abbreviations refer to the text

TABLE 2.

Effects of 2 drugs on main items in 2 groups of subjects

	Procain amide		Ajmalin	
	Nl	HD	Nl	HD
PEPi	↑↑	↑↑	↑↑	↑↑
ET/PEP	↓↓	↓↓	↓↓	↓↓
ICT	↑	↑	↑↑	↑↑
HR	↑↑	↑	↑↑	↑↑
S_1	↓↓	↓	↓↓	↓↓
QRS	NS	↑	↑↑	↑↑
PQ	↑	NS	↑↑	↑↑

Note: ↑↑=$p < 0.01$, ↑=$0.01 < p < 0.05$ NS=nonsignificant,
Nl=normal group, HD=heart disease group

PEP index, a decrease of ET/PEP ratio, an increase of ICT, an increase of HR, a decrease of 1st sound amplitude, each being significant.

On comparing the effect of the two drugs, Ajmalin gave more marked effect than Procainamide. All the items obtained by Ajmalin showed statistically significant changes ($P < 0.01$). Moreover, despite age differ-

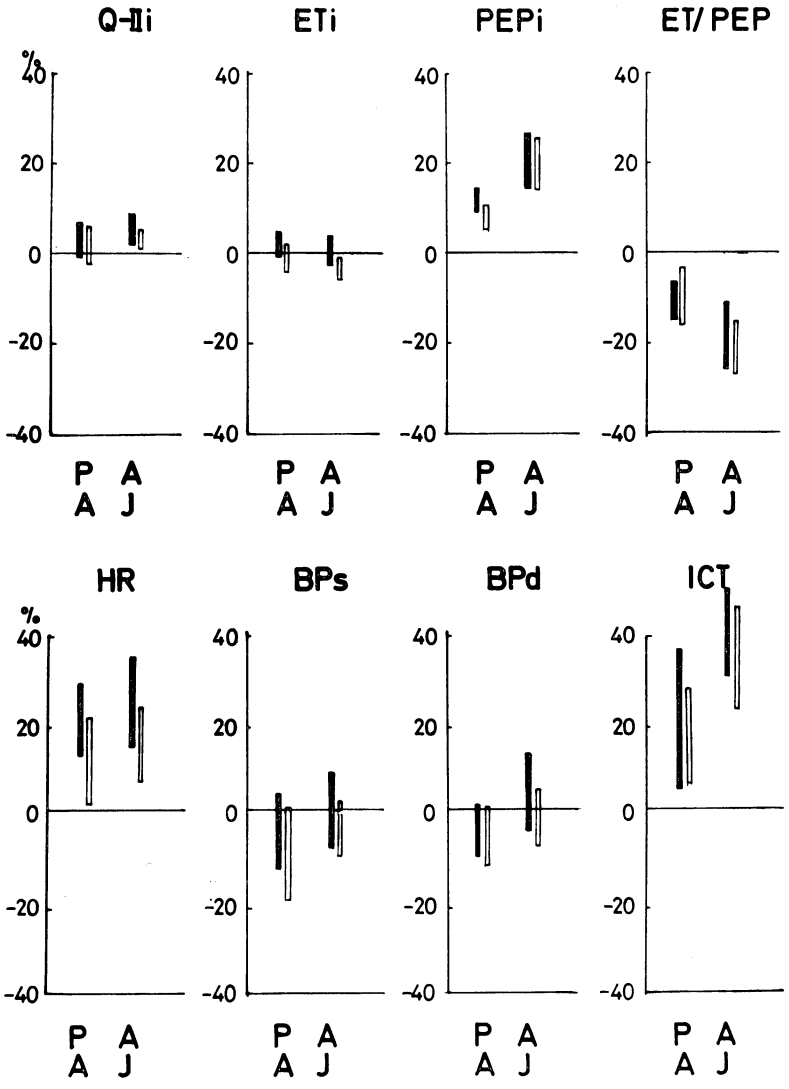

Fig. 1. The percent changes with 99% confidence limits in the maximal deviations from the centrol values of the 8 parameters in each group and drug. PA=Procainamide, AJ=Ajmalin, black column=diseased group, white column=normal group

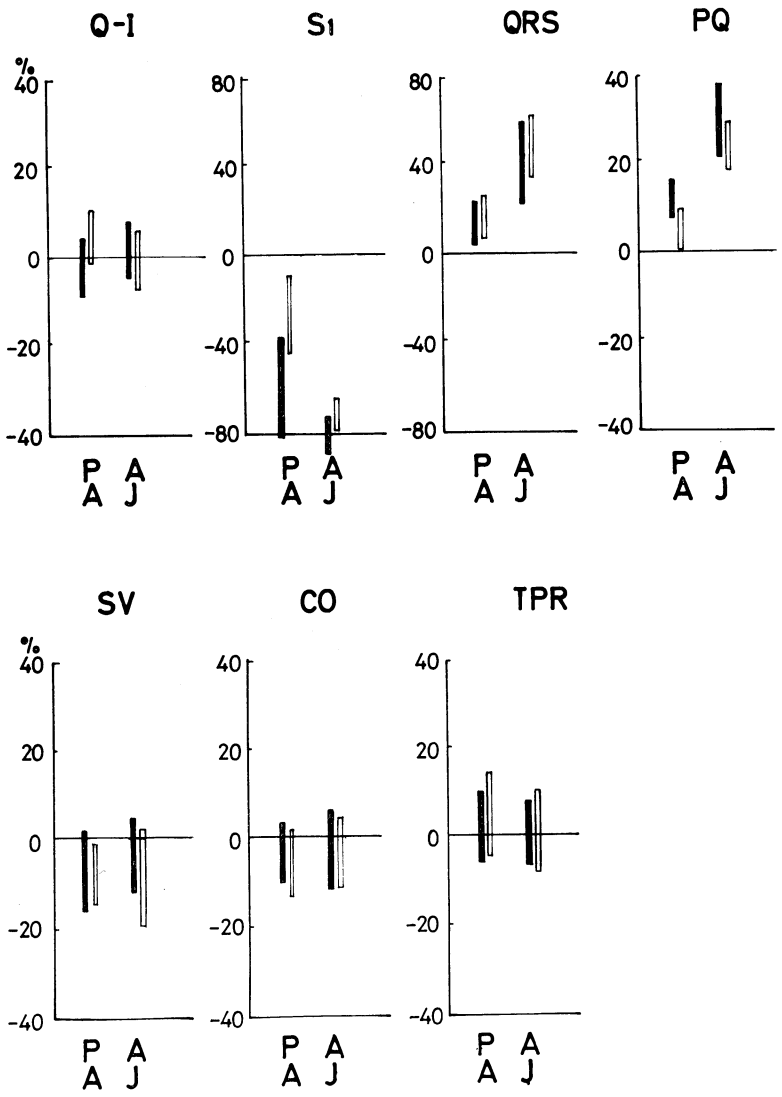

Fig. 2. The percent changes with 99% confidence limits in the maximal deviation from the centrol values of the 7 parameters in each group and drug (abbreviation see the Fig. 1)

ence among the subjects between patients and normal individuals studied, almost uniform changes could be seen.

Fig. 3 shows a polygraphic tracing from a 72-year-old male, where

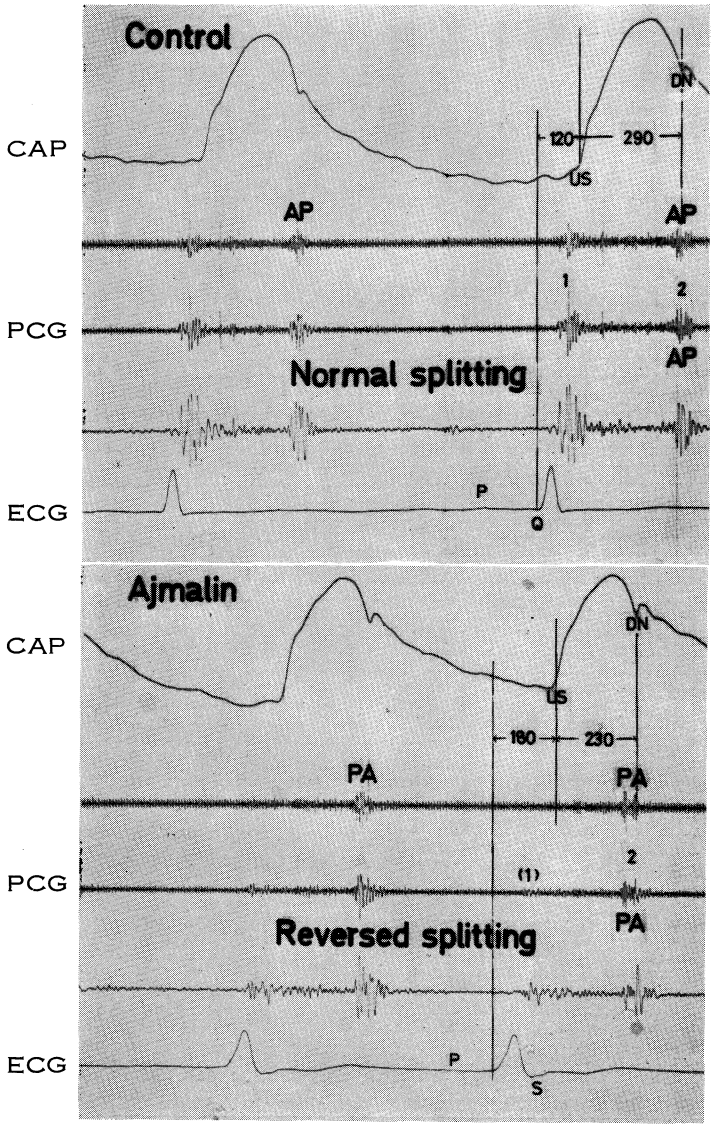

Fig. 3. Polygraphic tracings from a 72-year-old male with myocardial disease before (upper panel) and 5 minutes after (lower panel) Ajmalin, showing reversed splitting of the second heart sound (P and A in this order) associated with wide QRS, faint S_1 and abnormal LVSTI values after Ajmalin. CAP=carotid artery pulse, PCG=phonocardiogram, ECG=electrocardiogram

the upper part illustrates the control tracing and the lower the tracing taken 5 minutes after injection of Ajmalin. Considering the increase of HR, there appeared to be an increase of Q-II index, which was mainly due to the prolongation of QRS width. For this reason it was clear that there occurred a reversed splitting of the second heart sound as seen in the Figure. In addition, ET and PEP changed in a reversed direction from each other. Furthermore, on comparing fluctuations of various item brought about by the drugs, there could be seen no significant difference between the two groups.

DISCUSSION

For the purpose to defibrillate the atrial fibrillation we previously studied cardiac functions after administration of Procainamide[6]. We found that in the cases unable to defibrillate the polygraphic parameters were depressed only by this drug. In this study for the sake of comparison, we observed the effect of this drug as well as Ajmalin in patients with cardic diseases and normal subjects by using various non-invasive parameters.

As a result it was demonstrated that PEP index, ET/PEP ratio, and ICT all showed abnormal changes after administration of both drugs. This fact can be interpreted that the electrical depression caused the mechamical depression of the left ventricle on account of insignificant decrease in both stroke volume and cardiac output, and insignificant increase in TPR and marked delay in the atrioventricular and the intraventicular conduction as well as significant fall in the 1st sound amplitude.

The fact that Ajmalin, generally considered[7] to have little hemodynamic effect on the cardiovascular system, induced more marked electric and mechanical depression than Procainamide did, needs a caution on its use when taking into account that it produced frequent subjective symptoms such as hot sensation and uncomfortable feeling. Furthermore, the finding that Ajmalin induced a reversed splitting of the second sound being accompanied by the left ventricular conduction abnormality in some cases is another phenomenon to be taken into careful consideration. No such a change could be observed with Procainamide, but a different phenomenon is mentioned in an article[8] which described diminution of critical heart rate when this drug was administered to a patient with heart rate-dependent intermittent left bundle branch block. The fact that the drug-induced changes in various parameters was not more striking in the patients than in the normal subjects (despite mostly

composed of persons at relatively younger age) may partly be attributable to our selection of patients with class II by New York Heart Association.

According to McClendon et al.[9] it is said that on the intravenous use of Procainamide the heart rate and the blood pressure were decreased markedly in the patients with cardiac diseases, but in the subjects without heart disease such changes were not so prominent. Pascale et al.[10] state that in the cases with cardiac disease already having a hypotension this drug induced further fall of the blood pressure, and such a change was also dose-related.[11,12]

Interesting findings in addition to it are our observations that even in normal young individuals, while the cardiac output was not very much decreased by these drugs, there occured abnormality in the electrical and mechanical systolic sequences which was visualized on the non-invasively designed parameters such as the left ventricular systolic time intervals.

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