INVESTIGATION OF THE POSSIBILITIES OF CARDIAC DEFIBRILLATION BY ULTRASOUND

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SUMMARY

In 15 experiments on dogs ultrasound with a frequency of 500 kHz and and intensity of 10 W/cm^2, exerted a defibrillatory and antiarrhythmic effect and stopped ventricular fibrillation in 28% of the animals. Electrophysiological studies on isolated right ventricles of rabbits in oxygenated chambers demonstrated that the antiarrhythmic action of the ultrasound acted by prolonging the refractory period of the myocardial cells. Ultrasound with an intensity of 4 W/cm^2 and 30 s duration increased the refractory period up to 37%. Any further increase of intensity and duration of the ultrasound action resulted in a shortening of the refractory period and inhibition of the electrical activity of the myocardial cells. Investigations of the harmful effects of ultrasound with a frequency of 500 kHz and an intensity of 10 W/cm^2 showed that ultrasound for up to 2 min did not cause evident histological changes.

INTRODUCTION

The high voltage electrical impulses used in defibrillators have not only a defibrillating property, but also exert several adverse influences on the cardiovascular system (Castellanos, Lamberg and Fonseca, 1965; Kuznetsova and Solovjova, 1968; Sirkin, Ivanitskaya and Nedostup, 1968; Dulevičius and Gasiunas, 1970; Resnekov, 1978; Tacker, Davis, Lie, Titus and Geddes, 1978; Jones, Proscounter, Pauli, Lepeschkin and Jones, 1980). Therefore it is advisable to search for new and better kinds of impulses, new designs of defibrillators and their electrodes and new types of energy, which have antiarrhythmic properties and less adverse effects.

The therapeutic properties of ultrasound have been known for a long time and the sphere of its use becomes greater every year. It has been found that ultrasound has a favourable influence on the outcome of myocardial infarction by reducing the possibility of complications (Yamanaka, Wagai, Okada and Kitamura, 1971). The intensity of ultrasound used in medicine at present does not exceed 3 W/cm^2, and the therapeutic effect is reached

within 10 min (Bayer and Demer, 1958; Speransky and Rokityansky, 1970). It is possible that by increasing the ultrasound intensity a therapeutic effect may be achieved in a shorter time and this is necessary when the heart is defibrillating. In addition, the rigidity of the cells determines the ultrasound frequency oscillations. At present the devices that are in use generate ultrasounds at a frequency of from 800 to 1000 kHz. It can be assumed that ultrasound of a much lower frequency would show a more pronounced influence on the cells, that is to say, have a more marked mechanical effect, since this increases with the reduction of the frequency (Elpiner, 1963; Gorshkov, Gorbunov and Antropov, 1965).

For this reason, we investigated whether ultrasound with a frequency of 500 kHz, besides its known therapeutic properties, would possess an antiarrhythmic action.

MATERIALS AND METHODS

The possibility of defibrillation of the heart by means of ultrasound was studied on 15 mongrel dogs, weighing 7—11 kg, under morphine-thiopental anaesthesia. The heart was exposed by a left-side thoracotomy or a middle sternotomy. The source of the ultrasound was applied to the front surface of the heart. Fibrillation of the ventricles was brought on by frequently stimulating the heart with square wave impulses of up to 5 V amplitude. During the experiments with automatic recorder the second lead of the electrocardiogram and the arterial blood pressure in the descending aorta were recorded. During the passage of ultrasound the recorder was turned off because the strong electric field which was the source of the ultrasound distorted the recording. Restoration of the heart activities was controlled visually by an electromanometer, when the arterial blood pressure reappeared.

In order to affect the heart with ultrasound a generator was used which produced ultrasound with a frequency of 500 kHz and an intensity of up to 15 W/cm^2. The source of ultrasound was a quartz crystal held in a special head which was placed on the heart during the experiment. Two or three control tests were performed with the aim of establishing the spontaneous cessation of ventricular fibrillation which is sometimes seen especially in young dogs. To do this, ventricular fibrillation was provoked and within 1.5—2 min, if spontaneous defibrillation did not appear, electrical defibrillation was performed.

During the experiments, after causing fibrillation, the source of ultrasound was placed on the heart and left there for 1.5—2 min until the fibrillation stopped. If defibrillation from the effect of ultrasound did not occur spontaneously, then electric current for treatment was used.

We performed 16 experiments to study the mechanism of the defibrillatory effect of ultrasound, measuring the refractory period of the myocardial cells of the isolated right ventricle of rabbits. The preparations were per-

formed in a perfusion chamber with oxygenated Tyrode's solution at 37°C and pH 7.4. The preparation was stimulated with a frequency of 60 impulses/min by monopolar silver chloride electrodes producing square waves of five times threshold amplitude and for 3 ms duration. The ultrasound source was placed directly on the wall of the chamber. The refractory period was measured before and after the effect of ultrasound by putting in a test stimulus after every tenth conditioned one. The electrical activity was recorded by two electrodes placed in the perfusion chamber. The electrocardiogram was recorded on the automatic recorder and was photographed simultaneously from the oscilloscope screen.

RESULTS

When ultrasound of a frequency of 500 kHz and an intensity of 10 W/cm^2 was used, the ventricular fibrillation was observed to stop in seven dogs (Table I). At the beginning of the experiment there was a spontaneous defibrillation in three dogs so the experiments were stopped. In the other five cases, in spite of the identical conditions and methods, the ultrasound did not stop the ventricular fibrillation.

In Table I 72 attempts at defibrillation, performed on 7 dogs, were found to have been successful. The ultrasound was usually started during the first seconds of cardiac fibrillation and the effect of defibrillation was seen in 20 (28%) of the cases. The duration of the ultrasound was from 30 to 100 s. In a number of cases ultrasound was begun within 20—90 s after fibrillation. Sometimes cessation of ventricular fibrillation occurred in such cases (Fig. 1). This is evidence that the fibrillation did not stop by itself but as a result of the ultrasound.

TABLE I

RESULTS OF CARDIAC DEFIBRILLATION

Experiment no.	No. of induced fibrillations	Defibrillation					
		By ultrasound		By electric impulses		Spontaneous as a result of former ultrasound effect	
		number	%	number	%	number	%
4	8	3	37.5	—	—	5	62.5
5	14	2	14.3	8	57.2	4	28.5
7	25	6	24	2	8	17	68
8	2	1	50	—	—	1	50
10	9	3	33.3	1	11.1	5	55.6
11	6	1	16.6	5	83.4	—	—
12	8	4	50	—	—	4	50

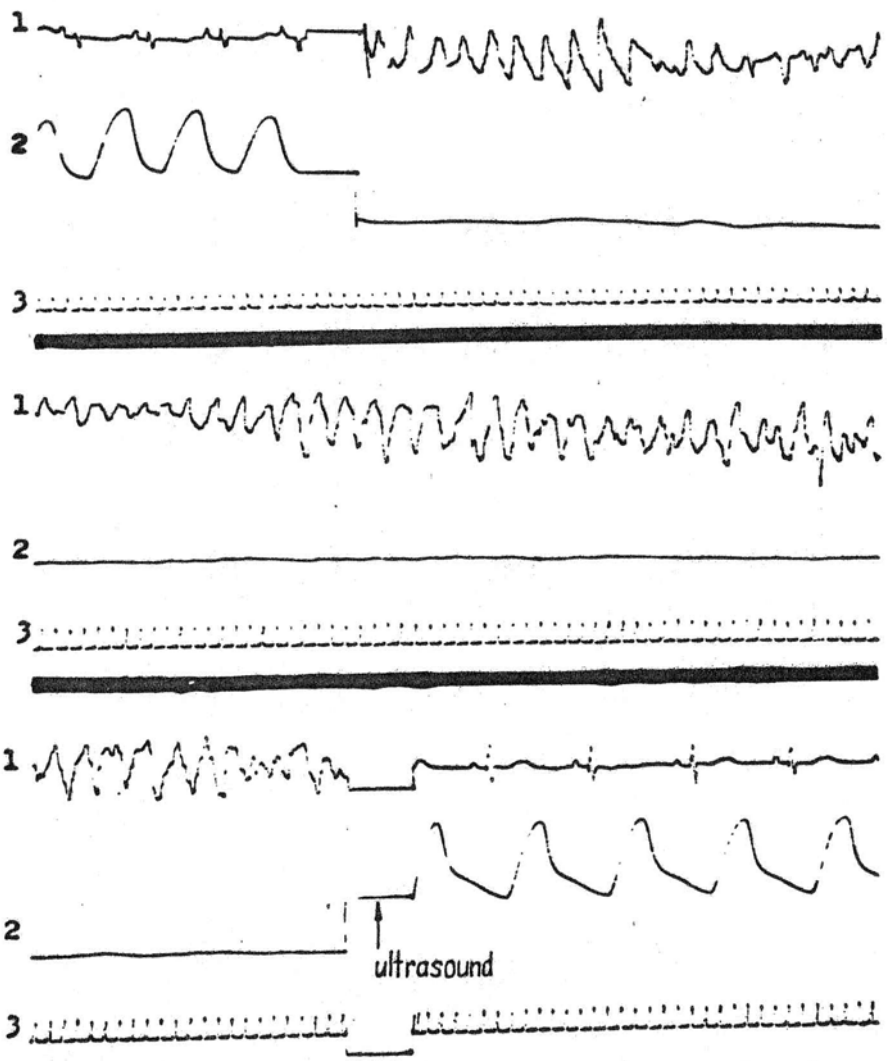

Fig. 1. Restoration of cardiac activity by ultrasound. The ultrasound was begun after 25 s of fibrillation. Its duration was 40 s. (1) Electrocardiogram II; (2) arterial blood pressure; (3) 0.1 s.

In almost all the experiments, in which ultrasound had a defibrillatory effect, spontaneous cessation of fibrillation was seen after 2—4 episodes of defibrillation from ultrasound, even although this was not observed during the control tests (Fig. 2). These findings show that ultrasound exerts an antiarrhythmic effect. However, it is not known what frequency has most significant antiarrhythmic effect and also what is the maximum intensity that can be used without damage to the heart.

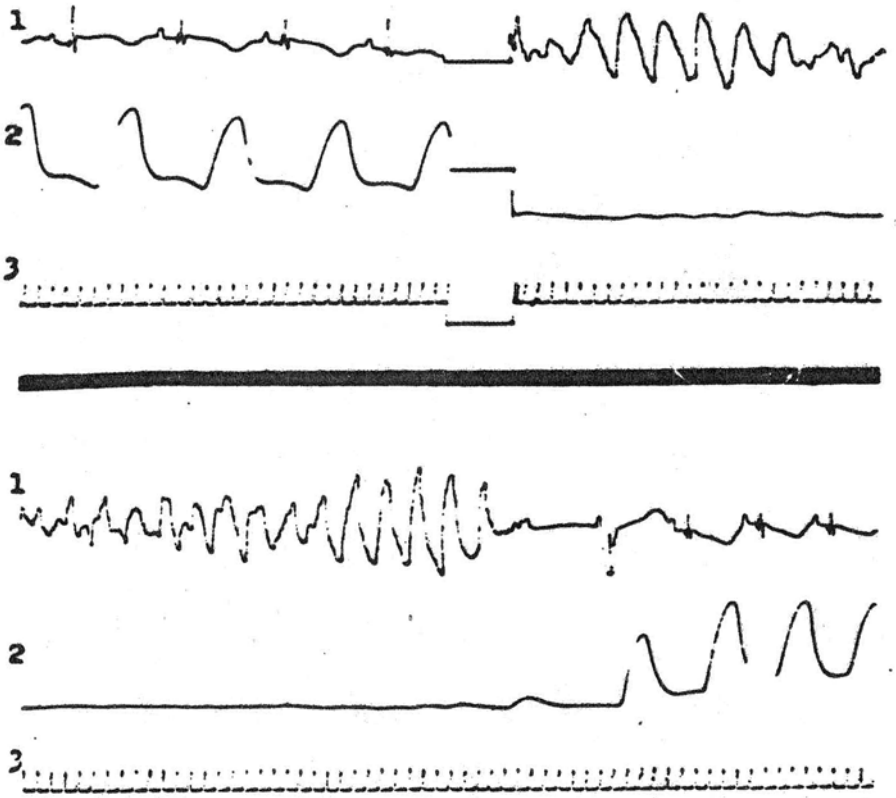

Fig. 2. Spontaneous restoration of cardiac activity as a result of earlier effect of ultrasound. (1) Electrocardiogram II; (2) arterial blood pressure; (3) 0.1 s.

We also performed electrophysiological investigations of the effect of ulrasound on myocardial cells. It is known that the majority of antiarrhythmic drugs prolong the refractory period of the myocardial cells (Oram and Davies, 1963; Davis and Temte, 1969). Therefore, we first investigated the effect of different intensities and durations of ultrasound on the refractivity of the myocardial cells. It was found that ultrasound of a frequency of 500 kHz and an intensity of 4 W/cm^2 lasting up to 30 s increased the refractory period by up to 37% (Fig. 3).

Increased duration of the ultrasound decreased the refractory period, and a duration of 2 min decreased the effect of ultrasound to 20% less than the control values. An ultrasound intensity of 8 W/cm^2 shortened the refractory period by up to 37% of the control level. The stimulation threshold increased and extrasystoles appeared. A further increase of the intensity inhibited the electrical activity of the myocardial cells.

The electrical activity of an isolated right ventricle during paired stimulation is shown in Fig. 4. The period between electrical stimulus corresponds

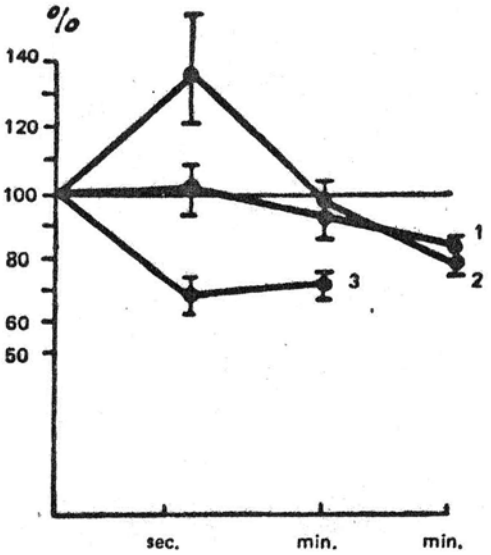

Fig. 3. Changes in the refractory period due to ultrasound, and the effect of its duration and intensity. The abscissa is the duration of ultrasound. The ordinate is the axis of the refractory period; (1) 4 W/cm²; (2) 6 W/cm²; (3) 8 W/cm².

to the shortest interval during which excitation appears with both stimuli (Fig. 4A). After ultrasound of 6 W/cm² intensity for 55 s the response of the myocardium disappeared as a result of an increase of the refractory period and consequently the second impulse began to fall in the refractory period of the first stimulus (Fig. 4B).

Figure 5 shows the electrical activity that was recorded when an electrical impulse produced ventricular tachysystole (Fig. 5A). After 8 s of ultrasound

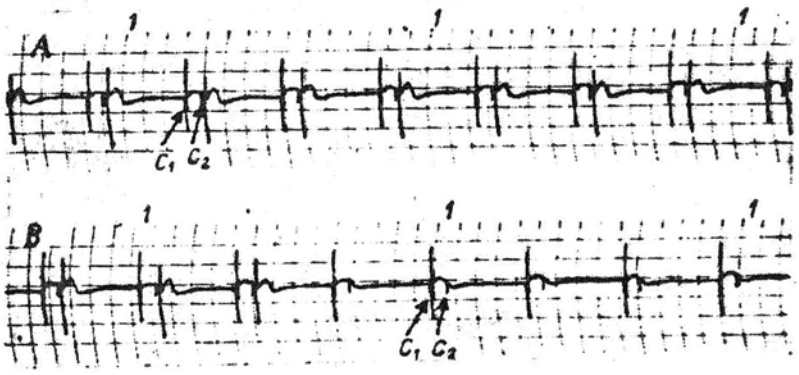

Fig. 4. Electrical activity of an isolated right ventricle of a rabbit. (A) During paired stimulation; (B) after 55 s of 6 W/cm² ultrasound. C_1, C_2; electrical impulses.

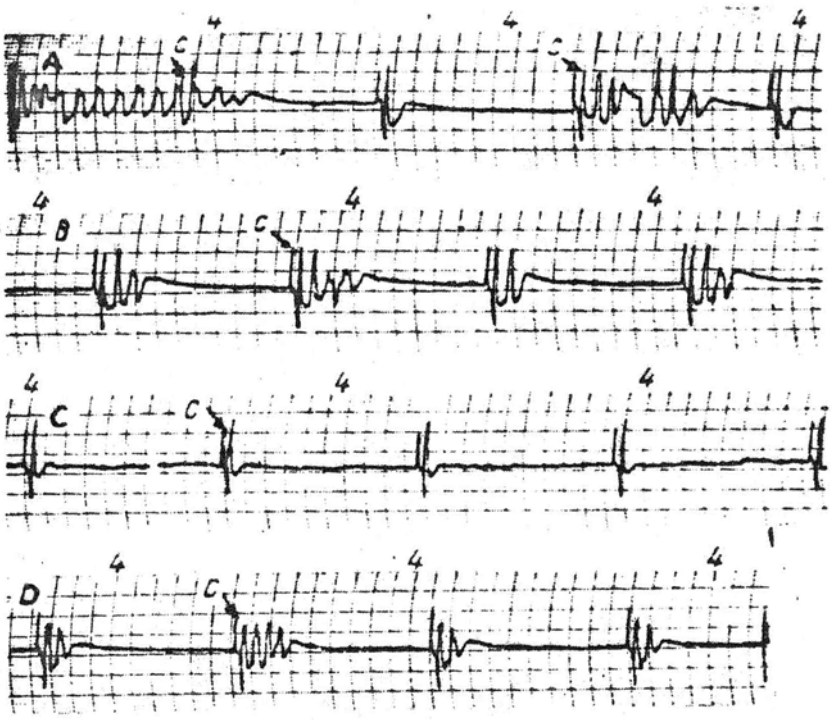

Fig. 5. Electrical activity of an isolated right ventricle of rabbit. (A) Episode of short ventricular tachysystole; (B) after 8 s of 5 W/cm² ultrasound; (C) after a 30 s ultrasound; (D) within 3 min after; (c) electrical impulse.

of 5 W/cm² intensity the duration of ventricular tachysystole shortened (Fig. 5B), disappeared within 30 s (Fig. 5C), and reappeared within 3 min after the cessation of the ultrasound (Fig. 5D). This example shows that ultrasound broke the excitation circuit due to the increase of the refractory period of the myocardial cells.

The histological changes in the skin of rabbits from ultrasound of 10 W/cm² have mainly a dystrophic character; they include parakeratosis, paranecrosis, vacuolation and granular degeneration of axis cylinders. The apparent morphological changes of various skin elements were intensified with increasing duration of the ultrasound. Visual changes were not found when the ultrasound lasted less than 2 min.

Examination of large chest muscles and the myocardium by polarising microscopy, showed the drawing together of the A lines, multiple contractures of sarcomeres and intensification of anisotropy of A lines. Capillary dilatation was seen as venous hyperaemia. The above changes appeared after only 2 min of ultrasound prolonged and they were more evident in skeletal muscles than in myocardium since a large part of the ultrasound energy is absorbed by the skin.

Fig. 6. Contraction bands in the myocardial cells. Polarisation microscopy × 600.

Examination of the large chest muscles and the myocardium on the 2—6th day after ultrasound showed that the above mentioned changes had a recurrent character. On the 6th day skin changes remained apparent and in several cases they were progressive.

When the ultrasound source was applied directly to the heart of dogs the histological changes in the myocardium had a more pronounced dystrophic character. The myofibrils were lysed and they were regions of intensified anisotrophy of A discs with lengthening of the sarcomeres (Fig. 6). The capillaries were dilated and they showed stasis. It should be emphasized that the pieces of myocardium for histological examination were taken out after 7—12 periods of ultrasound each of up to 2 min.

Thus, our investigations of the harmful effects of ultrasound with a frequency of 500 kHz and an intensity of 10 W/cm^2 showed that the ultrasound influence up to 2 min does not cause any noticeable changes in the tissues.

DISCUSSION

Thus the investigations showed that the antiarrhythmic action of ultrasound, just like the known antiarrhythmic medicines, manifests itself by lengthening of the refractory period. It is most likely that there exist other mechanisms and ways of antiarrhythmic influence of ultrasound and their elucidation can be brought out by further electrophysiological investigations.

However, attention should be paid to the fact that the antiarrhythmic effect of ultrasound on the ventricular myocardial strip manifests itself under the influence of a lesser intensity than on the heart as a whole. The reason for the observed differences seen under different intensities can possibly be explained by the fact that a large portion of ultrasound is lost when it is absorbed by the large mass of myocardium and also the dispersion of the ultrasound when it comes in contact with the myocardium. For a more exact differentiation it is necessary to have an intensity that is aimed at achieving an antiarrhythmic effect and the intensity should be measured directly in the myocardium. This was not done at the present stage of work for technical reasons. We were interested mainly in the presence of an antiarrhythmic effect and the possibility of its mechanisms and also the dependency of the ultrasound intensity on the duration of the influence.

A serious problem remains in the possibility of using ultrasound on the heart through the chest because a large portion of ultrasound waves are absorbed by the chest tissue or else stopped by the air in the alveoli of the lungs. The necessary ultrasound intensity in the heart area can be achieved by increasing the radiation intensity. In connection with this, there is an increased danger of harming the chest tissue, especially the skin.

The investigations that we performed do not allow us to say categorically that it is possible to use ultrasound practically in clinics for defibrillation of the heart. The most likely area for its use is prevention of arrhythmias in cases of infarct myocardium and in other diseases of the cardiovascular system where there arises the danger of arrhythmia, especially ventricular fibrillation.

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