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Ventricular Fibrillation in an Induced Myocardial Ischaemic Shock in Rats

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In an induced myocardial ischaemic shock in 43 rats, 21 died from ventricular fibrillation. The other (22) went into very severe systemic hypotension and A. V. block which later led to asystole. Marked ventricular ectopic activity, including isolated extrasystoles and a burst of ventricular tachycardia began to show around 5-7 minutes after coronary artery ligation associated with marked ST depression, in all the animals. The extrasystoles occurred between 5 and 18 minutes with a peak ectopic count of 211 per minute at around 11 minutes of ligation. By 30 minutes of ligation, the animals, which survived, returned to a stable sinus rhythm.

This study presents a useful model for assessing myocardial ischaemic investigations leading to a possible timing of clinical intervention during a sudden cardiac arrest.

Key words: *Fibrillation asystole, extra systoles, hypotension.*

INTRODUCTION

The commonest type of arrhythmia documented at the time of death is ventricular fibrillation [1]. Its major underlying aetiology includes occlusive coronary artery disease, congenital cardiac anomalies of the accessory pathways and idiopathic or secondary cardiomyopathies. Idiopathic ventricular fibrillation has been documented as a cause of death in the syndrome of nocturnal sudden death [2]. Additionally it has been seen that the development of ventricular fibrillation is often closely dependent on the heart rate [2]. Creamer, Edwards and Nightingale associated arrhythmias with the right ventricular infarction and linked the arrhythmias to the development of cardiogenic shock and further exacerbation of hypoxia [3]. Furthermore the severity of ventricular arrhythmias is also related quantitatively to myocardial injury [5, 6].

The development of ventricular fibrillation can be classified into 4 stages according to Toda [6]. Stage one is the phase in which fragmented activities are generated at a localized area of ventricular muscle. The genesis of these activities is attributed to strength of stimulus and underlying myocardial pathology. In stage two the localized activities propagate to the whole ventricular muscle, producing ventricular excitation. Stage 3 is characterized by the repetitive ventricular responses in a form of accelerating tachycardia, which disorganize ventricular excitations to finally degenerate into ventricular fibrillation in stage 4. In this last stage, ventricular fibrillation has fully developed. Stage one requires the existence of a rate-limiting stimulus for the extra systoles. The upper threshold above which the extrasystoles disappears and the lower threshold below which they are observed can vary according to changes in the autonomic nervous system balance.

At the cellular level, free intracellular calcium (Ca^{2+}) is said to govern directly the electrical activity of the heart [7] and changes in the intracellular Ca^{2+} have been proposed as an underlying mechanism of arrhythmogenesis [8, 9] A rise in intracellular Ca^{2+} might promote the induction of depolarizing membrane currents and an increased after-potential amplitude leading to the generation of premature beats and sustained triggered arrhythmias [10]. Depolarization by

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calcium-activated currents is further thought to produce initiating beat of ventricular fibrillation [10].

Although coronary artery blokade is considered the primary cause of ischaemic heart disease, Pasyk et al. [11] demonstrated a lack of ventricular fibrillation during an experimental occlusion of the coronary artery in the conscious dog. The aim of this study was to assess the continuous arrhythmia profile during a 30-minute period of coronary artery ligation in the rat in relation to time course, severity and mortality.

MATERIALS AND METHODS

Animal preparation

Male Sprag-Dawly rats weighing between 250-350 gm were used. Sodium pentobarbitone anesthesia 60mg/kg body weight was injected intraperitoneally. Artificial ventilation 1.5cc/100gm-rat and 54 strokes per minute was administered with a small animal pump (Nihon Kohden 21). Anesthesia was maintained by occasional intra-peritoneal administration of sodium pentobarbitone, 10-25mg/kg body weight.

Production of ischaemia and parameter measurements

After the achievement of the anaesthetic effect, a left thoracotomy was performed by cutting out at the 4th or 5th intercostal rib, 3-4cm from the sternum and a positive artificial ventilation with room air started immediately using a Howard small animal respirator, at a rate of 54 strokes per minute, 1.5cc/100gm-rat. After sectioning the 4th and 5th ribs, the pericardium was incised to facilitate access to the heart.

The heart was then exteriated by inserting a gentle downward pressure on the ribs and sternum. A 6/0 banded silk suture attached to a 10mm reverse cutting needle (Mersilk, W812 Ethicon) was placed under the left main coronary artery at a point close to its origin. The heart was returned to the chest cavity and blood pressure (BP) and electrocardiogram (ECG) were allowed to stabilize for 15 minutes. Any animal, which produced arrythmias or sustained fall in BP to less than 70mm Hg *immediately* after this procedure was discarded from the study at this point. After stabilization period, LAD was ligated by closing a knot using the suture already in place. All episodes of ventricular tachycardia and fibrillation were counted and their duration summed up.

RESULTS

Figure 1 shows a typical normal ECG tracing of the rat before surgery. After the occlusion there is a progressive rise in heart rate, and amplitude as shown in fig. 2

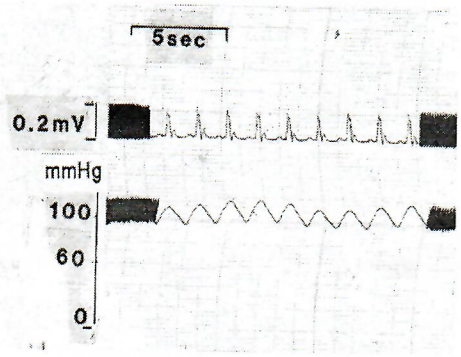

Fig 1; ECG pattern of the rat before surgery

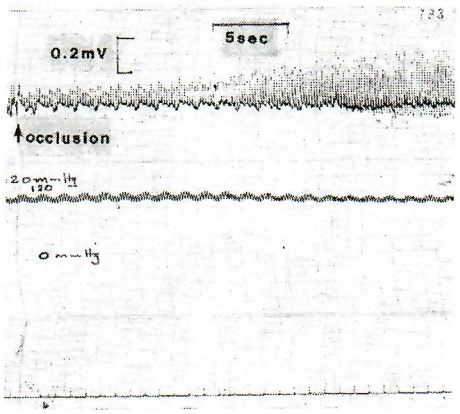

Fig 2: Characteristic ECG pattern immediately after the occlusion

Generally, within 5-7 minutes after ligating the coronary artery, the animals began to show marked ventricular ectopic activity, which included isolated extrasystole (Fig. 3), a burst of ventricular tachycardia (Fig. 4) and finally ventricular fibrillation and death. (Fig. 8).

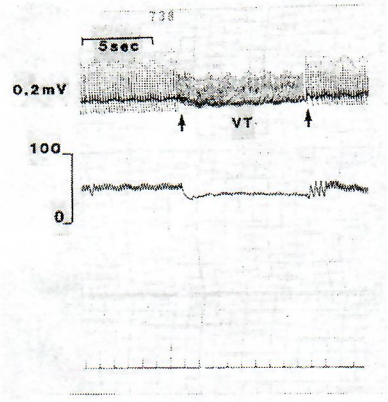

Fig 3: ECG pattern showing isolated extrasystoles (arrows)

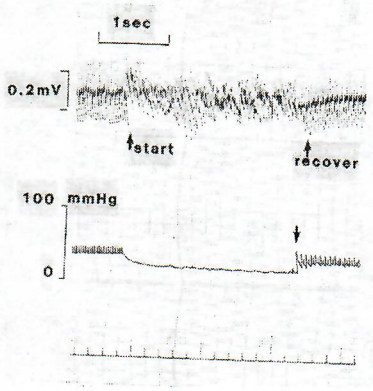

Fig 4; A burst of ventricular tachycardia

By 30 minutes of ligation, some animals usually returned to a spontenous reversion to a stable sinus rhythm and recovery (Fig 5).

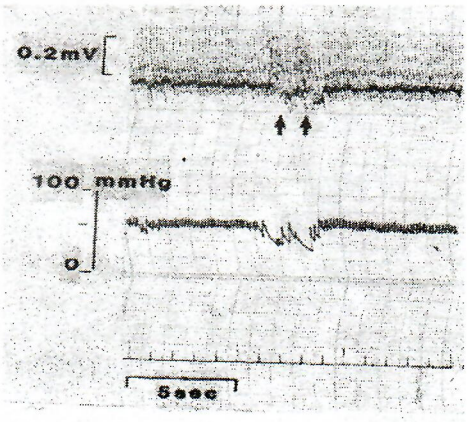

Fig 5: Reversion to sinus rhythm

Figure 6 shows characteristic lead II changes in the electrocardiogram (ECG) 15 minutes after the coronary artery ligation. There was development of deep Q-wave and marked S-T segment elevation (lower tracing) which was previously depressed from the onset of occlusion (upper tracing).

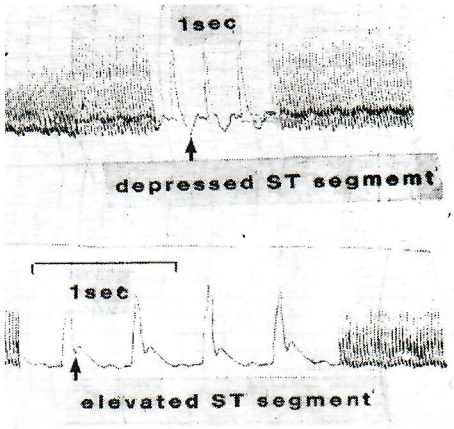

Fig. 6: Elevation and depression of S-T segmentation 15 minutes after the occlusion

The distribution of ventricular extrasystole over 30 minutes after ligation is shown in Figure 7. Most of the extrasystole occurred between 4 and 18 minutes following ligation with a peak ectopic count of 211 per minute at 11 minutes. After ligation, two distinctly active arrhythmogenic periods developed (11min), each followed by a quiescent phase which gradually decreased. The total mortality rate of 49% was found within these

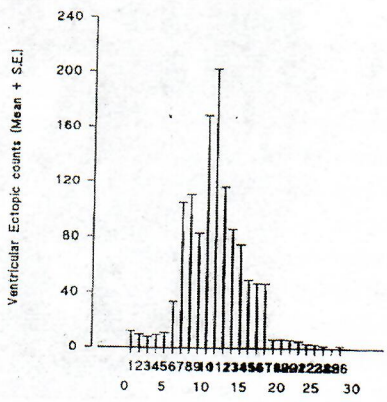

Fig. 7: Number of ectopic counts in the period of ligation

active periods, with 21 of 43 deaths. Non-survivors tended to have increased arrhythmia frequency and duration compared with survivors.

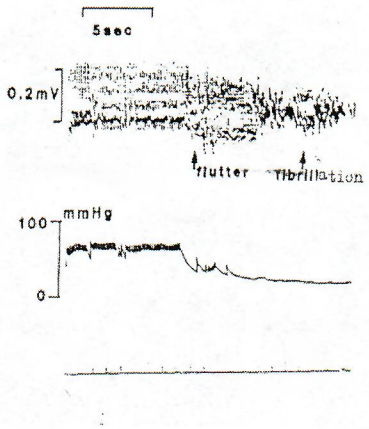

Fig. 8: Ventricular flutter and ventricular fibrillation leading to death

DISCUSSION

Ventricular fibrillation is a type of dysarrhythmia which shows no tendency towards a rhythm of any type and is the most common arrhythmia documented at the time of death [12]. Its cause is varried and includes congenital cardiac anomalies, accessory pathways and idiopathic or secondary cardiomyopathies. Ventricular fibrillation without obvious cardiac pathology also occurs and it has been documented as a cause of death in the syndrome of nocturnal sudden death [13]. Occlusive coronary artery disease, leading to ischaemia is considered a poor prognostic indicator of an arrythmia [5].

Figure 6 shows characteristic lead II changes in the electrocardiogram (ECG) 15 minutes after the coronary artery ligation. There was development of deep Q-wave and marked S-T segment elevation which was previously depressed from the onset of occlusion (Fig 6 lower tracing). This distortion of the S-T segment of the ECG pattern is evidence of myocardial ischaemia. Since complete polarization of the membrane cannot occur during this time, strong currents of injury flow from the infarcted area of the ventricles, leading to, first, depression and later, elevation of the S-T segment. Ischaemia brings about characteristic changes in the electrical properties of the myocardium. The characteristic changes are those of depolarizing process, witnessed by the early inversion of T waves and later the displacement of ST segment [6]. This is accompanied by the electrical instability, as there is now electrical potential difference between the normal and ischaemic cells of the heart. The term arrhythmia is not limited to irregularities of the heartbeat but is applied also to disturbances of rate and conduction. In this work both the heart rate and conduction was increased after the occlusion, which is shown in fig 2

Atrial arrhythmias such as very rapid atrial flutter and fibrillation associated with Wolff-Parkinson-White syndrome, may cause cardiogenic shock and may always end up in ventricular tachycardia and ventricular fibrillation. In this work hypoxia and death of rats were both taken as evidences for cardiogenic shock. Generally, by 5-7 minutes after ligating the coronary artery, the animals began to show marked ventricular ectopic activity which included isolated extrasystole (Fig. 3), a burst of ventricular tachycardia (Fig. 3) and (Fig. 4) finally ventricular fibrillation (Fig 7) and death.

The cycle of events can cause death in a variety of ways in myocardial arrhythmia. Uncontrolled arrhythmias result in the increase in myocardial oxygen consumption and may cause an infarction even in the presence of normal coronary arteries or in the presence of previously unrecognized coronary occlusion. Additionally rapid atrial arrhythmias in the setting of impaired pump function or in the setting of an obstructive pump, for example aortic stenosis, may occasionally result in altered circulatory dynamics especially when pump function is deprived of the usual compensatory increase in stroke volume associated with a slower rate [13].

Death can also come about in the following manner: the dead heart muscle becomes very thin during systolic stretch, hence this portion of the heart will bulge out until it ruptures to release blood into the pericardial spaces causing rapid development of cardiac tamponade. Secondly the contractile function of the ischaemic myocardium is markedly impaired by hypoxia. The prolonged

ischaemia with the resultant process of infarction creates necrosis in an area of ischaemia in tissue adjacent to the necrotic core [13].

The occlusion itself results in an asymmetric distribution of disordered contractility which alters the symmetry and synchrony of ventricular contraction and therefore reduces the formation of the myocardial pump. The heart becomes incapable of contracting with sufficient force to pump enough blood into the arterial tree and death can occur because of low perfusion of the vital organs. Pooling of blood in the venous system with the resultant pulmonary oedema and death can also come about because of pulmonary congestion and ventricular fibrillation so that not enough blood is supplied to the vital organs.

At the cellular level, free intracellular calcium (Ca^{2+}) is said to govern directly the electrical activity of the heart [9] and changes in the intracellular Ca^{2+} have been proposed as an underlying mechanism of arrhythmogenesis. A rise in intracellular Ca^{2+} might promote the induction of depolarizing membrane currents and increased after-potential amplitude leading to the generation of premature beats and sustained triggered arrhythmias [12]. Depolarization by calcium-activated currents is further thought to produce initiating beat of ventricular fibrillation [10] Thus the alteration of calcium metabolism represents a major factor in the etiology of triggered arrhythmias.

To summarise, this experiment is useful in assessing the different effects of therapeutic interventions on arrythmogenic periods and in the study of potential mechanisms for the spontenous resolution of ventricular ectopy and risk of sudden death. It can also be used to study antiarrhythmogenic properties of drugs.

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