The effects of hyperpotassaemia on cardiac performance

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AUTHORS' SYNOPSIS In order to evaluate the role of hyperpotassaemia in the development of circulatory failure at the late stage of renal failure, the effects of hyperpotassaemia on cardiac function were studied on dog hearts in situ. Aortic pressure, cardiac output, and heart rate were controlled at constant levels with the aid of an extracorporeal blood circuit. KCl solution was administered while the changes in left atrial pressure, maximal rate of left ventricular pressure rise, and the ECG were observed. Results suggested that the increase of plasma K is detrimental to cardiac function, particularly if the heart is in a diseased state, and that this is probably due to the direct effect of K on the myocardial contractile system.

Circulatory failure in patients with advanced renal failure has been attributed to three mechanisms: (1) left heart failure, (2) increased capillary wall permeability, and (3) excess fluid retention. The participation of a myocardial depressant factor has been postulated by many investigators but still remains controversial. This problem has been investigated by studying myocardial and haemodynamic performance in uremic patients with and without circulatory congestion. Several investigators have attempted to demonstrate the presence of a substance or factor which might impair myocardial performance in uremic patients (Raab, 1944). The present experimental study was designed to evaluate the effects of hyperpotassaemia, which is one of the most common and hazardous accompaniments of uraemia, on cardiac performance.

Methods

Studies were performed in 16 dogs weighing 10 to 14 kg. Anaesthesia was introduced by intravenous injection of 30 to 35 mg/kg of sodium pentobarbital and additional, supplemental doses were given as necessary. The chest was opened at the left fourth intercostal space, and the animals were ventilated with room air. After injection of 5000 U of heparin intravenously, the first four pairs of intercostal arteries were ligated. The descending aorta was dissected free and connected to an extracorporeal blood circuit, as shown in Fig. 1, comprising an electromagnetic flow meter probe, a Starling resistor, a reservoir, and an adjustable perfusion pump. The reservoir was primed with blood obtained from a donor dog and warmed to 38-39°C. Catheters were inserted into the aortic root through the right carotid artery and into the left atrium for pressure measurement. Left ventricular pressure was measured using a catheter inserted via the left subclavian artery, and the maximum rate of rise of left ventricular pressure (max dp/dt) was derived by electronic differentiation of left ventricular pressure. After all cannulae were in place, the arteries of aortic arch were ligated. The heart was paced electrically using a bipolar electrode sutured to the right atrium. Thus, aortic pressure, cardiac output, and heart rate could be controlled at constant levels throughout
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The effects of hyperpotassaemia on cardiac performance were studied in eight normal and eight acutely failing hearts. In three dogs, 5% glucose solution was substituted for the KCl solution and was administered at a rate of 3.75 ml/min. In this preparation, left atrial pressure, max dp/dt and lead II of the electrocardiogram remained stable for almost 3 hr.

Results

Effects of hyperpotassaemia on cardiac performance in intact hearts

An experimental record is shown in Fig. 2. In this experiment, an elevation of left atrial
pressure, a decrease of max dp/dt and a rise of left ventricular end-diastolic pressure began when serum K concentration reached 7.7 mmol/l. The first electrocardiographic change was peaking of the T wave with progressive increasing amplitude as the serum K concentration rose. The PR interval was prolonged when the serum K concentration reached 7.7 mmol/l and the QRS complex was widened at 9.0 mmol/l. Figure 3 shows the relationship between serum K concentration, left atrial pressure, and max dp/dt in eight intact hearts. Left atrial pressure rose and max dp/dt fell progressively as the serum K concentration rose above 7.8 mmol/l. The relationship between the serum K concentration and the electrocardiographic changes is shown in Fig. 4. Changes of the T/R ratio, prolongation of the PR interval, and widening of the QRS complex occurred when the concentration of serum K was increased up to about 4.5, 6.7, and 8.7 mmol/l, respectively. Figure 5 shows the relationship between changes of max dp/dt and QRS duration. In six dogs, the decrease of max dp/dt preceded the widening of QRS complex and in two, marked widening of QRS complex occurred before the fall of max dp/dt.

Effects of hyperpotassaemia on cardiac performance in failing hearts

Figure 6 shows a representative record of experiments conducted in animals with acute heart failure.
failure. When the concentration of serum K rose to 6.6 mmol/l, an elevation of left atrial pressure, a decrease of max dp/dt, and a rise of left ventricular end-diastolic pressure were observed.

On these experiments, the PR interval began to widen at a serum K concentration of 6.6 mmol/l and the QRS complex became prolonged at 7.4 mmol/l. Figure 7 shows the changes of left atrial pressure and max dp/dt as the serum K concentration rose in all eight failing hearts. At an average serum K concentration of 6.6 mmol/l, an elevation of left atrial pressure and a fall of max dp/dt were observed. The relationship between serum K concentration and electrocardiographic changes is shown in Fig. 8. These electrocardiographic changes did not develop at lower serum K concentration more in failing hearts than in normal hearts.

**Discussion**

In the present study, an elevation of left atrial pressure and a decrease of max dp/dt were observed when the concentration of serum K reached an average of 7.8 mmol/l in eight intact hearts and 6.6 mmol/l in failing hearts. This observation suggests that the increased serum K
concentration which occurs in uraemia may depress myocardial contractility and that, if the heart is diseased, the rise of serum K exerts even more deleterious effects on myocardial function. In addition, it was observed that there was no relationship between the impairment of cardiac performance and the electrocardiographic changes during hyperpotassaemia. The electrocardiographic changes of hyperpotassaemia developed at the same serum K concentration in both intact and failing hearts. The depression of cardiac pump performance expressed as a rise of left atrial pressure occurred in parallel with the decrease of myocardial contractility expressed in terms of max dp/dt.

The cardiac inotropic effect of hyperpotassaemia has been reported previously as either negative or inconsequential. In the isolated papillary muscle of the cat right ventricle, the contractile force was found to be minimally affected by the normal concentrations of serum K, whereas it was reduced significantly when the serum K concentration exceeded 11.3 (Garb, 1951) or 10.15 mmol/l (Green et al, 1952). Recently, Prasad et al (1971) observed a gradual and progressive depression of contractility of human papillary muscle as the K concentration was increased.

In the in-situ dog heart, Leight et al (1963) reported that K does not alter cardiac dynamics or right ventricular contractility estimated by the strain gauge arch, and Goodyer et al (1964) found that hyperpotassaemia to the point of impaired ventricular conduction at 10 to 11.5 mmol/l caused no measurable changes in either the pressure function curve or max dp/dt. Wallace and Mignone (1966), however, observed that at a serum K concentration of 7 to 8 mmol/l, left ventricular end-diastolic pressure was elevated, and substantial diminution of the force of contraction occurred with no diminution of conduction velocity. Surawicz et al (1967) studied the effects of slow and rapid administration of K on cardiac performance. A slow infusion of K (1.7 μmol/kg.s⁻¹) did not depress cardiac performance even when the serum K concentration reached 11.5 to 15.0 mmol/l, while a rapid infusion of K (6 to 30 μmol/kg.s⁻¹), led to depression of cardiac contractility. Sarnoff et al (1966) and Logic et al (1968) produced depression of myocardial contractility by injecting K selectively into a coronary artery. These results suggest that, although the rate of K administration is important, myocardial contractility may be depressed by an increase of serum K concentration. In a study of the effects of any drug or intervention on cardiac performance, it is important to differentiate direct effects on the heart from indirect effects exerted by changes in systemic haemodynamics. Therefore, in our experiment, we employed extracorporeal perfusion to maintain haemodynamic parameters constant. When extracardiac effects were excluded, cardiac performance was depressed consistently when the concentration of serum K was elevated above 7.8 mmol/l.

Another interesting and important finding from our experiment is that the negative inotropic effect of K was more striking in failing hearts. Clinically, K has been administered by some workers to patients with congestive heart failure to correct deficits of exchangeable body K. However, Flear and Cawley (1962) administered KCl of 30 mmol/24 hr to 125 heart failure patients without significant improvement. Kroetz and Ryan (1962) observed a decrease of cardiac output in patients with heart failure after intravenous injection of 60 mmol KCl. More recently Schwarzbach (1970) studied the cardiac effect of the oral administration of 80 mmol KCl in patients with heart failure and found that cardiac output and left ventricular max dp/dt decreased when the concentration of serum K rose above 5.6 mmol/l. Both our present experimental study and the clinical observations cited above suggest that elevated serum K concentration may have a more significant negative inotropic effect in the failing heart.

The negative inotropic effect of K may be due to changes of electrical activity of the myocardium or to direct effects of K on the myocardial contractile system. Goodyer et al (1964), Surawicz et al (1967), and Wallace and Mignone (1966) demonstrated that reduction of myocardial contractile force by hyperpotassaemia is not related to the electrocardiographic changes. The present study, confirming these observations, demonstrated that the appearance of hyperpotassaemic electrocardiographic changes was not accelerated in spite of earlier appearance of negative inotropic effect of K in failing hearts. Therefore the myocardial depression cannot be


attributed to abnormal intraventricular conduction induced by K. Langer and Brady (1966) suggested that hyperpotassaemia inhibits K ion efflux and results in a decreased influx of Ca ion leading in turn to decreased contractility. According to Prasad et al (1971), in a study of the effects of extracellular K concentration on the transmembrane potential and the contractility of human papillary muscle, the increase of K concentration produced a temporal increase and then decrease in the action potential duration, associated with a progressive decrease in the force of contraction. The physical state of extracted muscle protein is known to be extremely sensitive to changes of ionic strength (Hadju, 1953) and a very small increase of K concentration causes complete dissociation of the actomyosin complex (Szent-Györgyi, 1947). Although a direct effect of K on the contractile system of the myocardium may contribute to the decreased force of contraction, the exact mechanism still remains to be clarified.

Previously, we studied the clinical features of circulatory congestion in uraemic patients and pointed out that the decrease of cardiac performance must be one of the important factors in causing uraemic circulatory failure (Kaseno et al, 1971; Uraoka et al, 1972). In addition to the retention of so-called uraemic substances, hyperpotassaemia, acidosis, hypertension, severe anaemia, and fluid retention are commonly observed in the late stage of renal failure. Each of these has been known to affect cardiac performance to some extent. For example, acidosis is known to reduce ventricular contractility in dogs and cats, particularly after pretreatment with propranolol (Rocamora and Downing, 1969; Wildenthal et al, 1968). The negative inotropic effect of each of these individual factors may not be large. However, a diminution of myocardial contractile strength which may be well tolerated by a normal subject may be highly significant in patients with depressed myocardial function who have limited cardiovascular reserve. Since congestive failure in uraemic patients is not always associated with hyperpotassaemia, this cannot be regarded as the principal factor in the development of cardiac deterioration. However, it is the purpose of our present study to emphasize that hyperpotassaemia per se, particularly when it develops rapidly or when the heart is diseased, may contribute to the development of heart failure.

Conclusion

The effects of hyperpotassaemia on cardiac performance were studied in anaesthetized dogs in which cardiac output, aortic pressure, and heart rate were controlled. Myocardial contractility (left ventricular max dp/dt), cardiac pump performance (left atrial pressure), and the electrocardiogram were recorded as the concentration of serum K was progressively elevated. The results were as follows: (1) depression of cardiac performance was observed when the serum K concentration rose above 7.8 mmol/l in normal hearts. (2) In failing hearts, produced by administration of sodium pentobarbital, the negative inotropic effect of K was more conspicuous. (3) Changes of cardiac performance did not appear in parallel with electrocardiographic changes. These studies suggest that severe hyperpotassaemia may contribute to the development of heart failure.

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References


