The Effectiveness of Hypertonic Glucose in Resuscitation of the Hypothermic Heart Following Potassium Chloride Arrest

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Cardiac arrest was produced by coronary perfusion of potassium chloride in hypothermic dogs during sinus rhythm and during ventricular fibrillation. Resuscitation of rhythmic beats was facilitated by injection of hypertonic glucose when the ventricles responded to a light tap (responsive phase).

One method of overcoming ventricular fibrillation is to produce cardiac arrest by perfusion of the coronary circulation with potassium and restoring a normal rhythm by cardiac massage. Resuscitation of the hypothermic heart after potassium arrest frequently requires prolonged massage, but if hypertonic glucose is administered intravenously when the myocardium is in the "responsive phase", spontaneous contraction occurs more quickly and the heart recovers sooner.

The effectiveness of potassium in arresting ventricular fibrillation produced by faradic stimulation in normothermic animals has been studied by Wiggers. Cardiac arrest in diastole was produced by injecting potassium chloride solution directly into the ventricles. A normal cardiac beat could be frequently obtained by cardiac massage and the injection of calcium chloride. The potassium ion produces a depression of conduction of the myocardial fibers (Fenn). Wiggers concluded that fibrillation resulted with small amounts of potassium, when some areas of the myocardium escaped depression, and cardiac arrest occurred when all areas were depressed by larger doses.

Swan and his associates abrogated fibrillation in the hypothermic heart by perfusing the coronary circulation with potassium chloride solution. Thereafter, spontaneous ventricular contraction could be produced with calcium chloride and manual massage. In our hands the use of calcium chloride was less effective.

METHODS

Forty-six dogs were anesthetized with pentothal sodium, then hypothermia was induced to a rectal temperature of 26 C. by surface cooling. Respirations were controlled with positive pressure oxygen at a rate of 24 per minute, a carbon dioxide absorber being added to the closed circuit during cooling. The animals were subjected to right thoracotomy and underwent varying periods of caval occlusion. All dogs had cardiac arrest induced by the intraaortic injection of potassium chloride solution, 1 mEq./ml.; the aorta being clamped distal to the site of the injection. In this way, aided by cardiac massage, the coronary arterial circulation was perfused. The potassium chloride solution was injected until electrocardiographic cardiac arrest had been produced, the amount required varied considerably. In 10 dogs potassium arrest followed ventricular fibrillation of varying periods, in the remainder it was induced in the presence of sinus rhythm, either at the onset of caval occlusion or at the end, as an initial step in resuscitation.

After removal of the caval clamps resuscitation was undertaken either by massage alone or by massage along with 50 per cent glucose given intravenously in 10 Gm. doses when the ventricles were in the "responsive phase." Crystalline insulin was also given intravenously after the glucose.

Arterial and venous pressures were recorded as required via polyethylene catheters inserted to the arch of the aorta and the inferior vena cava via the femoral vessels. These catheters were attached to...
Hypertonic glucose in cardiac resuscitation

Experimental Results. Potassium produced cardiac arrest of the hypothermic heart results in a characteristic sequence of events. During the period of caval occlusion the myocardium has been ischemic and anoxic. Immediately after arrest the myocardium is flabby, has poor muscular tone and appears cyanotic. After a few minutes of massage, when the caval clamps have been removed, the muscle tone improves remarkably; the myocardium appears pink and the arterial pressure can be easily maintained. The myocardium then enters a “responsive phase,” when stimulation, such as a massage, or a light tap at any point on the myocardium, will result in a spontaneous ventricular contraction followed by asystole. The “responsive phase” appears to be a very important period in cardiac resuscitation after arrest with potassium chloride, and can be readily recognized. In our experience, hypertonic glucose must be given soon after the myocardium first responds to stimulation. Glucose is less effective if administered before this phase, or after it has been present for five or more minutes.

If 50 per cent glucose is injected into the vena cava (10 to 30 Gms. of glucose) early in the “responsive phase,” sustained spontaneous ventricular contractions develop more quickly than with massage alone. In 15 animals the average time which elapsed between potassium arrest and spontaneous ventricular recovery with massage alone was 22.8 minutes. The time required before the electrocardiogram appeared normal was 62.6 minutes. In 15 dogs glucose was given as described with a ventricular recovery time of 10.2 minutes and an electrocardiographic recovery time of only 17.9 minutes. In 16 animals glucose was given before or after the early “responsive phase” and was less effective.

Figure 1 shows the arterial and venous pressure patterns which are characteristic of the recovery phase in these animals. Following potassium arrest and massage there is an abrupt rise in arterial pressure at the time when the myocardium regains its muscle tone. During the “responsive phase,” and at the time when glucose is given, the pressure remains at the usual hypothermic level (50 to 60 mm. Hg) with a transient rise at the beginning of idioventricular rhythm. The venous pressure is high at the beginning of massage and falls when an adequate arterial pressure has been attained, but it does not return to normal until after sinus rhythm has developed. The gradual fall in venous pressure after spontaneous cardiac contraction has been established is regarded as a good prognostic sign.

Figure 2 shows the electrocardiographic changes due to a persistently elevated potassium plasma concentration resulting from large doses of potassium, and the rapid improvement after further glucose administration. Dog 55-196 received 68 mEq. of potassium and 60 ml. of 50 per cent glucose intravenously. The caval occlusion time was 15 minutes. Figure 2A shows the ventricular complexes 8 minutes after the onset of idioventricular rhythm and after an initial dose of 40 ml. of 50 per cent glucose. The plasma potassium was 7.2 mEq/liter, the arterial and venous pressures 56 and 8 mm. Hg and the rate 30/
minute. Figure 2B shows the dog when rewarmed in a water bath at 47 C. The plasma potassium was 6.4 mEq, with the same rate and pressures as at A. The electrocardiograms at C and D were taken after rewarthing and still show a high potassium pattern. The plasma potassium at this time was 6.8 mEq., the arterial and venous pressures were 98 and 7 mm. Hg and the cardiac rate 80/minute. Figure 2C shows what happened when, at 4:48 p.m., 20 ml. of 50 per cent glucose was administered. The plasma potassium at 5:00 p.m. was 4.6 mEq., arterial and venous pressures were 115 and 3 mm. Hg and the rate 130. The return of P waves and a sinus rhythm with subsequent uneventful recovery of the dog is shown.

Figure 3 shows the improvement in cardiac action when arrest has been produced with a small dose of potassium, and glucose is given in the "responsive phase." Dog 55-228 had a 15 minute period of caval occlusion and arrest was induced by 8 mEq. of potassium. The ventricles recovered in 4 minutes after massage and, at A, the plasma potassium level was 7.9 mEq./liter. Twenty ml. of 50 per cent glucose were given intravenously at B., the arterial pressure was 46 mm. Hg. At C, the plasma potassium level was 6.4 mEq., plasma glucose 800 mg. per cent and arterial pressure was 80 mm. Hg. The electrocardio-

gram at C still shows evidence of high potassium, but at D has returned to normal. The potassium level at 1:37 p.m. was 4.34 mEq.

DISCUSSION

In the experiments reported, perfusion of the coronary circulation of the hypothermic heart with potassium chloride resulted in cardiac arrest in the presence of either ventricular fibrillation or sinus rhythm. Following potassium arrest and massage the myocardium develops what appears to be a "responsive phase" when any stimulation causes ventricular contraction followed by asystole. If 50 per cent glucose is administered intravenously at this time, spontaneous ventricular contractions (idioventricular rhythm) result within a shorter time, maintaining an adequate arterial pressure. This phase is followed within a short time by a sinus rhythm.
The mechanism by which glucose accelerates the return of normal sinus rhythm following potassium arrest is not yet evident. The heart loses potassium during the period of inflow occlusion. This negative potassium balance has been demonstrated by simultaneous determination of the potassium concentration in the coronary sinus and in aortic blood during occlusion. The coronary sinus has a much higher concentration than the aorta. Hooker has shown that ventricular fibrillation in the perfused heart can be converted to a normal rhythm by adding potassium to the perfusate. He believes this is due to a replenishment of intracellular potassium in the myocardium. A high concentration of potassium in the myocardium is necessary to produce arrest. The high potassium level is, however, harmful and must be reduced before complete cardiac recovery is obtained (fig. 2). Fenn has shown that potassium enters skeletal muscle with glucose. In these experiments the improvement following glucose is correlated with a decrease in circulating potassium. The beneficial effect of glucose may, therefore, be related to the transfer of extracellular potassium into the cells of skeletal muscle and myocardium. It is also possible that the large amount of glucose available to the myocardium has some other beneficial effect. Further experiments are in progress attempting to evaluate the role of hypertonic glucose in this problem.

The venous pressure changes following inflow tract occlusion are a helpful guide during resuscitation. In our experiments removal of the superior caval clamp alone often resulted in a fall in the inferior caval pressure but both clamps had to be removed to obtain adequate venous return. Cardiac massage following potassium arrest adequately maintained the arterial pressure but the venous pressure did not return to normal until sinus rhythm had been established. An abrupt fall of venous pressure with massage indicated peripheral circulatory failure and was an indication for whole blood transfusion.

**Summary**

Cardiac arrest has been produced by coronary artery perfusion with potassium chloride in the hypothermic dog during normal sinus rhythm or ventricular fibrillation. Resuscitation of the heart by massage is more readily accomplished if hypertonic glucose is injected intravenously. The beneficial effect of glucose appears to be related to a reduction of the circulating potassium.

**SUMMARIO IN INTERLINGUA**

In canes hypothermic, arresto cardiac esseva producite per perfuder le arteria coronari con chlorido de kalium durante le normal rhythmo sinusal o fibrillation ventricular. Le resuscitacion del corde per massage es plus facilmente effectuabile si glucosa hypertonic es injicite intravenosemente. Le effecto benefic de glucosa es apparentemente connectite con un reduction del kalium circulante.

**REFERENCES**

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