

Circulatory effects of potassium, glucose and insulin following open-heart surgery

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The cardiovascular effects of an acute infusion of potassium, glucose and insulin (PGI) were investigated in 10 subjects following valve replacement surgery. All required circulatory support with isoprenaline and no additional improvement in cardiac function could be demonstrated following PGI. Pressures in both atria rose out of proportion to the volume infused and there were biochemical changes which suggested that haemodilution had occurred. These findings were attributed to the administration of hypertonic dextrose solution and this also resulted in hyperglycaemia, glycosuria and an osmotic diuresis.

Therapy with potassium, glucose and insulin has been advocated in the treatment of myocardial infarction (Mittra, 1965; 1968). The rationale for its use is based on the possibility that within an area of myocardial injury, there are not only irreparably damaged fibres but also some which are only partially depolarized and which could be restored to normal by forcing potassium re-entry with glucose and insulin (Sodi-Pallares, Testelli, Fishleder, Bisteni, Medrano, Friedland, and De Micheli, 1962; Sodi-Pallares, Bisteni, Medrano, De Micheli, Ponce de Leon, Calva, Fishleder, Testelli, and Miller, 1966). However, a review by Surawicz (1968) and the report by the Medical Research Council Working Party (1968) on the treatment of myocardial infarction both conclude that there is no evidence that this therapy either decreases the mortality or reduces the incidence of arrhythmias in male or female patients with myocardial infarction.

The possibility that repolarization of partially depolarized fibres may increase contractile force and improve myocardial efficiency has received some experimental support (Fishleder, 1964; Calva, Mújica, Bisteni, and Sodi-Pallares, 1965) and was the basis for suggesting that the therapy might be of value in other cardiovascular conditions (Sodi-Pallares and Polansky, 1961; Sodi-Pallares, Bisteni, Medrano, Testelli, and De Micheli, 1963). Infusion of potassium, glucose and insulin (PGI) was recommended by Braimbridge, Clement, Brown, Sabar, and Mendel (1969) to

improve myocardial function in patients following triple valve replacement when there had been an inadequate clinical response to isoprenaline.

In the present study, the circulatory effects of an infusion of PGI were observed in patients who had undergone open-heart surgery for valvular disease within the previous 24 hours. The clinical conditions of all subjects had given rise to concern for at least some part of this period and each had required an infusion of isoprenaline. This therapy was continued undisturbed throughout the period of study because hypotension or bradycardia followed its withdrawal in the majority of subjects and it was therefore felt unjustified to attempt a comparison of the effects of PGI with those of isoprenaline. The trial was performed to observe whether any additional benefit followed the infusion.

METHODS

Ten patients were studied on the first day after valve replacement surgery. Clinical details are given in Table I.

The subjects lay supine throughout with the upper half of the body tilted head-up by about 20°. All were maintained on intermittent positive pressure ventilation with oxygen-enriched air through an oral endotracheal tube, and suitable sedation (papaveretum) was administered at constant rate from an infusion pump. All the subjects were receiving an infusion of isoprenaline (10–250 µg./hour) and numbers 7 and 9 were also receiving lignocaine (1.0 and 1.7 mg./min. respectively) to control ventricular ectopic beats. Both these drugs were continued at a constant rate from the infusion pump.

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TABLE I
CLINICAL DETAILS OF PATIENTS STUDIED

No.	Age and Sex	Body Surface Area (m. ²)	Operation
1	59 F	1.62	Open mitral valvotomy (and aortic incompetence)
2	48 F	1.60	Aortic valve replacement; mitral valvotomy
3	56 M	1.96	Mitral valve replacement
4	52 F	1.68	Aortic valve replacement
5	40 F	1.50	Aortic and mitral valve replacement
6	56 F	1.52	Aortic and mitral valve replacement
7	55 F	1.45	Mitral valve replacement
8	49 F	1.40	Aortic and mitral valve replacement
9	54 F	1.66	Aortic and mitral valve replacement
10	52 M	1.64	Aortic valve replacement

Pressure recordings were made using Statham P23Db transducers and an Elema-Schonander recorder. Zero for the pressure measurements was taken from the sternal angle and both dynamic and mean pressures were recorded on each occasion. Left atrial pressure was measured through a Teflon catheter (I.D. 0.4 mm.) placed in situ at operation and right atrial pressure through a catheter in the right internal jugular vein. Systemic arterial pressure was recorded from either the radial or brachial artery, and pulmonary arterial pressure was measured using a flow-guided nylon catheter (Bradley, 1964).

Cardiac output was determined by the thermal dilution technique (Branthwaite and Bradley, 1968), each value being the mean of three injections. The pulse rate was recorded over 20-second periods during the performance of each cardiac output determination. Cardiac index, stroke volume, stroke work and pulmonary and systemic vascular resistance were calculated from standard formulae.

Plasma sodium, potassium and calcium concentrations were analysed with a flame photometer, osmolality by depression of freezing point, blood and urine sugar by the method of Middleton and Griffiths (1957) and haematocrit by direct measurement using a microcentrifuge.

Three sets of data were recorded on each subject over a period of one to one and a half hours to establish that stable baseline conditions existed (period I). The trial solution, consisting of 100 ml. 50% dextrose with 10 mEq potassium (as KCl) and 10 units of soluble insulin, was then infused through a caval catheter over 30 to 45 minutes. The observations were repeated either immediately after this infusion or during the last few minutes that it was running (period II) and final values were obtained at the end of a further hour (period III).

On each of these five occasions (three control values, immediately after and one hour after the infusion), right and left atrial and pulmonary and systemic arterial pressures were recorded together with the cardiac output, pulse rate and plasma potassium concentration. During the first recording in period I, and in periods II and III, blood was also taken for the estimation of sodium, calcium,

osmolality, haematocrit and blood sugar. The volume of urine draining through an indwelling catheter was recorded and the urinary glucose concentration was measured. The volume collected in the control period was analysed separately from that collected during and after the PGI infusion.

RESULTS

Detailed results are given in Table II. There were no significant changes ($P>0.1$) in any of the variables during the three control recordings in period I, thus demonstrating that the baseline conditions were stable.

TABLE II
HAEMODYNAMIC AND BIOCHEMICAL CHANGES FOLLOWING INFUSION OF POTASSIUM, GLUCOSE, AND INSULIN

	Period I (Control)	Period II		Period III	
	Mean \pm SD	Difference from Control Abso- lute	% Change	Difference from Control Abso- lute	% Change
CI	2.2 \pm 0.56	+0.2	+9.1	0.0	0.0
SV	36.0 \pm 11.4	+3.0	+8.3	0.0	0.0
HR	99.0 \pm 11.8	+2.0	+2.0	+1.0	+1.0
LVSW	32.0 \pm 11.2	+2.0	+6.2	0.0	0.0
RAP	4.0 \pm 4.5	+2.7	+62.5	-0.3	-7.5
LAP	9.0 \pm 5.9	+3.7	+41.0	-0.6	-6.7
PAP	24.0 \pm 11.2	+4.5	+18.8	-1.0	-4.2
SAP	74.0 \pm 7.8	+3.0	+4.1	0.0	0.0
PVR	4.8 \pm 2.8	-0.2	-4.2	-0.3	-6.3
SVR	22.0 \pm 7.4	-2.0	-9.1	0.0	0.0
K ⁺	4.2 \pm 0.7	+0.2	+4.1	0.0	0.0
Na ⁺	138.0 \pm 4.8	-2.3	-1.7	-1.8	-1.3
Ca ⁺⁺	10.4 \pm 1.6	-0.8	-8.0	-0.5	-3.8
Osm.	296.0 \pm 6.7	+14.0	+5.0	+4.0	+1.4
PCV	43.5 \pm 1.6	-2.0	-4.7	-0.5	-1.2
BS	113.0 \pm 24.9	+290.0	+257.0	+111.0	+98.0

Key:	
Period I	Three control values
Period II	Immediately after infusion
Period III	One hour after infusion
CI	Cardiac index (l/min./m. ²)
SV	Stroke volume (ml.)
HR	Heart rate (beats/min)
LVSW	Left ventricular stroke work (g./m.)
RAP	Mean right atrial pressure (mm. Hg)
LAP	Mean left atrial pressure (mm. Hg)
PAP	Mean pulmonary arterial pressure (mm. Hg)
SAP	Mean systemic arterial pressure (mm. Hg)
PVR	Pulmonary vascular resistance (units)
SVR	Systemic vascular resistance (units)
K ⁺	Plasma potassium concentration (mEq/l.)
Na ⁺	Plasma sodium concentration (mEq/l.)
Ca ⁺⁺	Plasma calcium concentration (mg%)
Osm.	Plasma osmolality (mOsmole/kg)
PCV	Haematocrit (%)
BS	Blood sugar (mg.%)

HAEMODYNAMIC EFFECTS Immediately following the infusion there were small (<10%) increases in pulse rate, cardiac index, stroke volume, left ventricular stroke work and systemic arterial pressure, a rather greater increase (18.8%) in pulmonary arterial pressure and considerable increases in both right and left atrial pressure (62.5% and 41% respectively). Both systemic and pulmonary vascular resistance fell slightly (<10%).

Variance analysis showed that the increase in right atrial pressure was significant ($P < 0.01$), the increases in left atrial pressure and cardiac index were probably significant ($P < 0.05$), and the other changes were not significant ($P > 0.1$).

One hour after the completion of the infusion, all variables were close to the control values, and none of the differences was significant ($P > 0.1$).

BIOCHEMICAL EFFECTS In the immediate post-infusion period there was a small (4.1%) and probably significant ($P < 0.05$) increase in plasma potassium, but one hour after the infusion was complete there was no significant difference from the control value ($P > 0.1$).

In all subjects, plasma sodium, calcium, and the haematocrit fell significantly ($P < 0.01$) and there was a significant rise in osmolality and blood glucose ($P < 0.01$). These changes were still present at the end of one hour although the values were all tending to return to the control figure.

Hyperglycaemia was sufficient to cause glycosuria in all subjects in whom urinary glucose concentration was recorded (cases 3 to 10) and was associated with an increased rate of urine secretion (+234%).

DISCUSSION

Quantitative definition of myocardial performance is difficult, particularly in the critically ill human subject. Sarnoff and Mitchell (1962) define an increase in contractility as an increase in external stroke work for any given end-diastolic pressure. Rushmer (1964) prefers the term initial ventricular impulse to describe the dynamic properties of ventricular ejection. This is manifested as the rate of rise of intraventricular pressure and the acceleration of blood into the aorta, but the siting of the catheters and the frequency response of the recording system used here precluded any observations on these functions.

Using the criteria of Sarnoff and Mitchell, the administration of potassium, glucose and insulin in these circumstances produced no demonstrable improvement in myocardial performance, there being no significant increase in stroke volume or left ventricular stroke work in spite of an increase in both atrial pressures. An impaired ability to change stroke volume in response to alterations in filling pressure is characteristic of the failing heart (Ross and Braunwald, 1964), and it is suggested that the changes seen in this study are a manifestation of heart failure rather than a reflection of

a frankly deleterious effect of potassium, glucose and insulin.

The absence of functional improvement following an acute infusion of the solution is in agreement with the work of Dixon, Hyde, Leonard, and Schlant (1965), who demonstrated that potassium, glucose and insulin failed to modify the consequences of acute coronary artery ligation in dogs. However, Sheldon, Sabar, and Braimbridge (1970) have shown transitory improvement in the performance of the failing, isolated dog heart following the addition of potassium, glucose and insulin to the coronary perfusate. It is possible that when the myocardium is 'in extremis', restitution of intracellular potassium can be achieved with consequent improvement in performance.

The acute infusion of PGI solution produced several biochemical changes. It is suggested that the decreased concentration of sodium and calcium and the fall in haematocrit were manifestations of haemodilution caused by the increased osmolality of a high blood sugar, and it seems likely that this osmotic effect was largely responsible for the observed increases in atrial pressure which were out of proportion to the volume infused. The alteration in plasma potassium concentration may reflect movement of the ion into cells and a probable increase in urinary loss, in addition to the effect of the dose infused and the occurrence of haemodilution.

It may be concluded that no improvement in cardiac function could be demonstrated following the administration of potassium, glucose and insulin to patients following open-heart surgery who were already receiving an infusion of isoprenaline. There was biochemical evidence of haemodilution, probably associated with a sudden increase in blood volume, together with hyperglycaemia, glycosuria and an osmotic diuresis. In some subjects these changes could be undesirable.

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