Electrocardiographic Changes Produced by Potassium and Other Ions Injected into the Coronary Arteries of Intact Dogs

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MYOCARDIAL infarction produces characteristic electrocardiographic changes. Wiggers\textsuperscript{1} was the first to demonstrate that solutions of potassium chloride injected into the pericardial cavity or applied to the epicardium of dogs produced changes in RS-T segment similar to those present after coronary artery occlusion. Boyd and Scherf\textsuperscript{2} obtained similar results after a variety of mechanical and chemical stimuli applied to the epicardium. They concluded that this electrocardiographic response was not specific for potassium. Wolferth, Bellet, Livezey and Murphy\textsuperscript{3} applied these technics to define the gross anatomic site of the origin of RS-T displacements.

Recently, Guzman, West and Bellet\textsuperscript{4} demonstrated that injections of 1.15 per cent potassium chloride, sodium cyanide, strophanthin or pitressin into the circumplex coronary artery of the intact dog produced elevations of the RS-T segment and that these elevations could be temporarily reversed by injections of solutions of sodium salts. It is not clear from their abstract whether these elevations are systolic or diastolic and whether they are identical for all 4 substances; nor do they discuss whether electrocardiographic changes precede the appearance of these injury currents.

Our purpose was to determine whether the sequential electrocardiographic changes found in experimental subtotal and total occlusions of a coronary artery\textsuperscript{6} could be produced by changing the ionic concentration of blood within a coronary artery.

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Methods

Animals used in this study were mongrel dogs of 8 to 21 Kg. They were anesthetized with chloralose (100 mg./Kg.) and urethane (0.5 Gm./Kg.) by the intravenous route. The coronary arteries were catheterized by the method of West, Kobayashi and Guzman.\textsuperscript{5} In this method the chest is unopened and the coronaries unobstructed.

The pressure pulses and electrocardiograms were measured, as previously described.\textsuperscript{7} All injections were made within 1 second. Autopsy was performed after completion of each study.

Potassium chloride solution was dissolved in Ringer's solution to a concentration of 5 mg./ml. Doses varied from 2 jag./Kg. to 1.5 mg./Kg. Similar and even larger doses were used for lithium chloride, anhydrous calcium chloride and magnesium sulfate (calculated on an anhydrous basis). The solutions of these salts were made up to the same concentration as in the case of potassium.

Solutions of HCl and NaOH were made up to a molarity of 0.0134 to 0.0345. Carbon dioxide gas was bubbled through 1.3 per cent NaHCO\textsubscript{3}. This buffered solution was used when a solution of carbon dioxide was desired. These solutions had a pH of 6.87 to 6.95. When carbon dioxide was needed, 100 per cent gas was used. All solutions were injected into the circumflex branch of the coronary artery. Each experiment was repeated on at least 3 different dogs and many times on the same dog if the experiment was not lethal.

Results

Potassium Chloride

The injection of between 1 and 2 µg/Kg. changed the direction of the T wave within 1 second of the beginning of the injection. An initially upright T wave became diphasic (plus, minus) and, within 2 seconds, the T wave became negative. Nine seconds later, a diastolic injury current appeared. This was characterized by a shift of the diastolic base line away from and a rise of the S-T takeoff
Figure 1

Dog, 13.2 Kg., chloralose-urethane anesthesia. Upper record: lead II of EKG; middle record: femoral arterial pressure pulse; bottom record: signal of events. At signal 20 μg. KCl were injected into the left circumflex coronary artery. Record is continuous through all 3 strips. Time = 1 second. Calibration on blood pressure = mm. Hg.

towards the region of infusion. At the same time, the T wave became positive and tall. Within a few seconds, these changes disappeared and the trace assumed its preinjection pattern (fig. 1).

An injection of 6 μg/Kg. produced a more striking diastolic injury current. The S-T segment became cove-shaped as the injury current diminished in magnitude (fig. 2). The injection of 0.25 mg./Kg. produced an immediate diphasic T wave followed by a ventricular premature beat. This change was followed immediately by a diastolic injury current with high positive T waves. There was a minimal decrease in the voltage of R. In other experiments, 1 to 2 consecutive premature ventricular beats appeared before the elevation of the S-T takeoff. Within a few seconds, R returned to its original height, the diastolic injury current disappeared and the trace again reverted to its preinfusion pattern (fig. 3). There was no change in blood pressure in these 3 experiments.

The injection of 0.5 mg./Kg. produced an immediate increase in amplitude of the T wave. Within 1 second, 2 premature beats appeared, which were followed by a diastolic injury current and very large waves of much higher voltage than previously seen. Pulses alternans was produced for 4 consecutive beats. Again the trace reverted, within a few seconds, to its preinfusion pattern. The injection of 1 mg./Kg. usually produced an immediate diastolic injury current and even larger T waves, which were followed within 1 second by entirely positive monophasic QRS.
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Figure 2
Dog, 10.4 Kg., chloralose-urethane anesthesia. Records from above downward: upper record: femoral arterial pressure pulse (FA); second record: right ventricular pressure pulse (RV); third record: lead III EKG; fourth record: lead I EKG. At vertical arrow 60 µg KCl were injected into left circumflex coronary artery. Time = 1 second. Calibrations on pressure pulses = mm. Hg.

complexes slightly lower than the preinfusion rate. At this time, there was a slight drop and variation in arterial blood pressure. Two seconds later, the original contour of the QRS complex returned. Elevation of the S-T segment was preserved and large T waves were also observed. Within a few seconds, the trace returned to its preinfusion pattern. The largest dose used was 1.5 mg./Kg. and this dose produced identical changes with those of 1 mg./Kg., until the monophasic curve appeared. Six seconds later, this rhythm gave way to ventricular tachycardia which was terminated 3 seconds later by ventricular fibrillation and death.

Other Salts

Lithium chloride. No electrocardiographic change occurred until the dose reached 0.25 mg./Kg. Changes were then identical with those seen after the infusion of much smaller doses of potassium.

Calcium chloride. As much as 2 ml., containing 1 mg./Kg., produced a slow reversal of polarity of the T wave. The trace then returned to its preinfusion pattern.

Magnesium sulfate. Doses comparable to calcium produced only minor changes in voltage of both the QRS and T.

Hydrochloric acid. An injection of 2.5 ml. of 0.0134 M/Kg. produced within 2 seconds a minimal increase in voltage of the QRS and T. A larger dose (4.5 ml. of 0.0345 M/Kg.) produced an immediate but slight increase in voltage of T. This change was followed by ventricular premature systoles which within 2 seconds gave rise to ventricular tachycardia. Ventricular tachycardia persisted for 5 seconds and was terminated by ventricular premature beats in bigeminus and second degree heart block. This arrhythmia persisted for 2 seconds and was associated with elevation of the S-T takeoff with tall T waves. This latter abnormality persisted for a few seconds, after which sinus rhythm was restored.

Sodium hydroxide. Two ml. of 0.0134 M/Kg. produced after 1.5 seconds a premature ventricular systole. Eight seconds later, tachycardia with multiform ventricular complexes appeared. The trace returned to its preinjection form.

Animal Ringer's solution, pure carbon dioxide gas alone, and 1.3 per cent sodium bicarbonate solution saturated with CO₂ gas. Injections of such solutions produced minimal changes in the amplitude of T.

All of the above electrocardiographic changes were reproducible with but minor changes in dosage except for the amount of potassium necessary to produce ventricular fibrillation.
Discussion

Of all ions tested, the contour of the surface electrocardiogram was most sensitive to potassium. As little as 2 μg./Kg. almost instantaneously produced significant changes in the trace. These changes were characteristic and depended within a narrow range upon the concentration and quantity of potassium injected. The sequential changes are remarkably similar to those described by Bayley, LaDue and York after subtotal and total occlusion of a coronary artery.

The smallest effective dose of potassium produced diversion of T similar to that initially produced by temporary subtotal or total coronary artery occlusion. With a larger single dose of potassium, a diastolic injury current is produced and, like that following temporary subtotal or total occlusion of a coronary artery, is reversible.

With larger single doses of potassium, ventricular tachycardia occurred; with still larger single doses, ventricular fibrillation with a ventricular rate of about 1,200 per minute and death supervened. It is noteworthy that in most cases no decrease in ventricular electrocardiographic excitation was produced by intracoronary injections of potassium, except on rare occasions when transient complete ventricular standstill with undisturbed sino-auricular action occurred.

Lithium produced electrocardiographic effects identical with those of potassium, but the initial diversion of T was postponed and the dose necessary to produce it was many times that of potassium. These differences could be due to greater impermeability of myocardial tissue to lithium than to potassium or to potassium itself, the effect being due to the rate of displacement from the red blood cell of potassium by lithium.

Calcium chloride and magnesium sulfate in comparatively larger doses produced but minor changes in the final deflection of the ventricular complex.

Both acid and base produced primarily arrhythmias. Transient injury currents were seen only after termination of the arrhythmias.

The electrocardiographic effects of Animal Ringer’s solution and carbon dioxide gas were identical and negligible, whether given by the intravenous or by the intracoronary route. Animal Ringer’s solution is purposely composed so as not to alter the animal’s plasma concentration of ions. Carbon dioxide, as Roberts and Magida have pointed out, permeate cells so rapidly that almost instantaneous equilibrium is achieved between the extra- and intracellular compartments.

On the other hand, all other substances produced dissimilar effects when the intravenous route is used. Thus, Roberts and Magida found that similar electrocardiographic alterations could be produced by intravenous administration of potassium chloride and acids.

Intravenous administration of potassium chloride, calcium chloride and magnesium sulfate produced results identical with those reported by Winkler, Hoff and Smith. Intra-aortic injection of potassium central to an aortic clamp, with or without an extra corporeal pump, also produced dissimilar electrocardiographic effects. These effects were variable, although the dose and duration of injection were constant. Total cardiac arrest, ventricular arrest followed by atrial arrest, atrial arrest with intraventricular rhythm, widened, deformed ventricular complexes of uncertain origin and intraventricular block resembling that originating from the right or left ventricle were some of the responses. Apparently identical injections in the same dog can at one time produce ventricular complexes...
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of apparent right ventricular origin, and at other times of left. At no time was the sequence of electrocardiographic changes identical with those seen when solutions of potassium chloride were injected directly into a coronary artery. Deviations of the RS-T segment always occurred with intraventricular block and appeared to be secondary changes during systole.

It is well known that contrast substances so introduced may fail to visualize both patent coronary arteries. This failure is due to unequal distribution of the contrast substance. It is possible that potassium chloride, injected into the ascending aorta, may at times be unequally distributed to the coronary arteries. This may be the reason for the variable electrocardiographic responses. It is possible that on rare occasions the catheter may be so placed that initially only 1 coronary artery is injected with potassium. In such an instance, one would anticipate initial sequential changes identical with those seen after intracoronary injections. We have never encountered the accident. It is also possible, as the coronary arteries are subsequently reinfused with blood, that unequal distribution may become manifest. This possibility may have a bearing on some of the untoward effects of elective cardiac arrest with potassium. The peculiar dialyzable currents of injury occasionally seen in advanced potassium intoxication may also be due to unequal concentration of the ion.

Finally, it is noteworthy that of the substances used, only potassium in microgram doses is capable of producing an injury current. Only potassium, and with much larger doses, lithium can produce such a current without a preceding arrhythmia.

Summary

Ions injected into the circumflex branch of the left coronary artery of the intact dog produce sequential electrocardiographic changes different from those produced by exposure of the entire heart to these ions. Of all substances tested, the contour of the surface electrocardiogram is most sensitive to potassium. The electrocardiographic sequence of alterations produced by potassium so injected are characteristic and similar to those produced by subtotal and total occlusion of a coronary artery.

Summario in Interlingua

Iones injicite in le branca circumflexe del arteria coronari sinistre de canes intacte produce sequentialmente alterationes electrocardiographic que differe ab illos producite per le exposition del corde integre a leste mismo ions. Le contorno del electrocardiogramma de superficie es plus sensible a kalium que a non importa le qual del altere substantias testite. Le sequentia electrocardiographic de alterationes producite per kalium assi injicite es caracteristic simil al alterationes producite per occlusion subtotal o total a un arteria coronari.

References

9. McKusick V.: Effect of lithium on the electrocardiogram of animals and relation of the effect to the intracellular and extracellular con-


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