Relation Between Coronary Sinus Plasma Potassium and Cardiac Arrhythmia

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Infusion of insulin glucose which reduces the level of potassium in the coronary sinus blood will prolong the life of dogs after coronary ligation.

It appears to be rather widely accepted that ventricular fibrillation very often follows premature ventricular beats occurring singly, or more often in a rapid series. The premature beat is most likely to lead to fibrillation if it occurs during repolarization of the ventricle (vulnerable period). The extra systoles resulting from coronary occlusion can well be the cause of the ventricular fibrillation which often results in the fatal termination of this condition.

Since the injection of cardiac tissue extract or of potassium solution into the coronary stream elicits extrasystoles and since anoxic cells liberate potassium, Harris suggested that the potassium released from the ischemic myocardium might act as an excitatory factor at the boundary of the infarction and establish ectopic foci.

These considerations led us to experiment with the possibility that infusions of insulin-glucose or sodium bicarbonate which are said to counteract the release of potassium from the cells might have an effect on the genesis of extrasystoles and the advent of ventricular fibrillation. It was also possible to analyze electrocardiographically the nature and timing of the beat which preceded the onset of fibrillation.

METHODS

Mongrel dogs were anesthetized with 10 mg./Kg. of morphine subcutaneously and an intravenous dose to 15 mg./Kg. of sodium pentobarbital. One jugular vein was cannulated for infusion. The left thorax was opened at the fourth or fifth interspace. A Courand catheter was introduced into the coronary sinus by direct manipulation and its retention was confirmed at autopsy. The chest was temporarily closed and control samples of coronary sinus blood were taken. Control electrocardiograms were recorded in simultaneous pairs usually from lead I and II with an occasional recording of unipolar chest leads.

As soon as the control observations and samples were made the dogs were treated in either of two ways: In 9 control dogs the chest was again opened and the descending branch of the left coronary was ligated at a point 5 to 10 mm. from the left atrial appendix. The ligature often included the vein and a small strand of myocardium and its occlusion of the artery was confirmed at autopsy. The chest was closed, the electrocardiogram was continuously monitored and samples were taken of the coronary sinus blood. During the first 10 min. the samples were taken continuously, thereafter every 15 min. They were centrifuged immediately and analyzed for potassium with a Beckman flame photometer.

Sixteen experimental dogs were given a slow infusion of either insulin-glucose or a sodium bicarbonate solution to reduce the potassium plasma levels. Four hundred milliliters of 50 per cent glucose in water with 70 or 200 units of insulin given to most of the animals over a period of 2 to 3½ hours. Some animals received 100 or 200 ml. of 5 per cent sodium bicarbonate alone or added to the insulin-glucose.

Two hours after the insulin glucose infusion was started and/or 15 to 30 min. after the beginning of the sodium bicarbonate infusion, the chest was opened as in the control and the coronary ligation was performed. The thorax was then closed, the electrocardiogram monitored and blood samples taken as described above. In addition simultaneous samples were taken of systemic venous blood in 6 animals.

RESULTS

Control Dogs. In 5 of the 9 control dogs the mean plasma potassium level was 3.9 mEq./L. Immediately after coronary ligation there was a sharp increase in the potassium level which
was accompanied by a rapid series of extrasystoles that ended in ventricular fibrillation 5 min. after the ligation (fig. 1 A).

In 3 animals the potassium level rose and a short burst of extrasystoles occurred. The level of potassium in the coronary sinus blood then began to decrease and the extrasystoles were suppressed to return again as the level once more rose and finally terminated in ventricular fibrillation 16 to 20 min. after ligation. These animals illustrated a pattern that was to recur again and again. The extrasystoles usually occurred when the level of potassium in the coronary sinus blood was rising (fig. 1 B).

The ninth control dog (fig. 1 C) showed no rise in potassium level in the coronary sinus blood. There were a few early ventricular extrasystoles probably from stimulation attendant upon ligation. The potassium level did not rise though the occlusion was complete at autopsy, and there was a regular sinus rhythm. The animal was sacrificed at the end of 3 hours.

Experimental Dogs. The infusions (insulin-glucose, and sodium bicarbonate) acted equally to reduce the coronary sinus potassium levels to about half the control figure. Before the ligation the electrocardiogram showed a typical hypokalemic pattern in some cases but there was a regular sinus rhythm. After the ligation there were wide fluctuations in the potassium level. For example, in one experiment from group D figure 2, the potassium level rose immediately after the ligation. This rise was accompanied by numerous extrasystoles which ceased as the potassium level fell. There was a regular sinus rhythm during this descent at levels which, when the coronary sinus potassium was rising, gave numerous ventricular extrasystoles. During a second rise in potassium level the extrasystoles terminated in ventricular tachycardia and ventricular fibrillation.

The experimental animals divided themselves into 4 groups. Average trends and values are given in the figures. Five animals (fig. 2 C) showed a prompt increase in coronary sinus blood potassium, extrasystoles, ventricular fibrillation and death. These animals could be distinguished from the controls only in that the potassium levels were low. They were infused for 2 hours and until the ligation was made.

Two animals (fig. 2 D) survived the first
up surge in coronary sinus potassium level and had a regular sinus rhythm until the level rose for a second time. These animals were infused 2 hours and until the ligation was made. They survived for 90 min. after ligation and after the cessation of infusion.

The 6 animals illustrated in figure 2A had infusions lasting 2 hours and up until the time of ligation. The potassium level stayed constant and there were few extrasystoles during the first hour. After that, the potassium level rose and there extrasystoles terminating in ventricular fibrillation.

The 3 animals shown in figure 2B were infused for 3½ hours, 1½ hours after ligation. They maintained a low potassium level and a regular rhythm until sacrificed at the end of 3 hours.

In the 6 animals whose systemic blood was sampled it was found that the infusion lowered the potassium level as it did the coronary sinus blood. After ligation the systemic blood potassium tended to rise but maintained levels well below those in the coronary sinus.

Electrocardiographic Patterns. The electrocardiograms of 10 control and 9 experimental animals were studied. Dogs that developed heart block were excluded. The premature ventricular contractions were divided into 4 types; Type 1 was an rS pattern with a wide RST in lead I. The mean electric axis of this complex is downward and to the left and could result from an excitation wave originating in the apex of the heart and spreading toward the base. Type 2 was a wide qRS with inverted T in lead I and wide Rs with inverted T in lead II. The mean axis of this complex is downward and to the left and could result from a basal focus. Type X was different from previous types and not constant.

In table 1 is a compilation of the ventricular extrasystoles and ventricular tachycardia beats in the control dogs. In no cases did ventricular fibrillation follow a normal cycle. The type of premature ventricular contraction which preceded ventricular fibrillation was type 1 or type 1' in all cases.

Table 2 gives parallel data for the treated groups. In a great majority of cases the electric pattern of the preterminal extrasystole was type 1. In one case, the fatal arrhythmia was ushered in by a single type 1 extrasystole which had been preceded by a protracted sinus rhythm interrupted by one type 2 extrasystole at the time of ligation. In another dog a type X premature ventricular contraction preceded the ventricular fibrillation. The electric axis of this beat was directed downward and to the left. It probably originated in the base of the ventricle. This was the dominant type of arrhythmia in this animal during the latter half of his post ligation survival.

In some cases 3 precordial leads were recorded during type 1' extrasystoles. The mean electric forces seemed to be directed posteriorly and to the left because leads at the left mam-
millary line and fifth intercostal space showed an rS pattern while a lateral lead at the left midacillary line and the same horizontal level showed an R pattern, and a lead at the posterior axillary line at the same level showed a qR pattern.

When the premature ventricular contractions followed a normal beat they did not produce ventricular fibrillation. None of the extra beats fell in the interval between Q and the beginning of T. Twenty such beats began after the wave and twelve were seen to begin during the T wave, but ventricular fibrillation did not follow.

During a series of premature ventricular beats ventricular excitation usually began after the T wave but in some cases it began before the end of T.

In 8 of the dogs studied electrocardiographically it was impossible to tell just where the rhythm changed from ventricular tachycardia to ventricular fibrillation. In 6 of the 10 dogs the shape of the electric pattern changed to one indicating fibrillation at the end of QRS or at the beginning of T of the last coordinated ventricular beat and in 5 dogs it changed after the peak of T.

**DISCUSSION**

Evidence from these experiments seems to confirm the viewpoint of Harris that release of potassium from cells made anoxic by coronary ligation is associated with ventricular extrasystoles and fibrillation. There is no evidence to justify speculation as to details of cellular mechanisms involved, but the association of arrhythmia, with a rising coronary sinus potassium level will, we believe, play a role in our final understanding of the fatal outcome of coronary occlusion.

The infusion of insulin-glucose or of sodium bicarbonate lowers the plasma potassium level and causes the ischemic myocardium not to release this ion after ligation to the same degree that it does in the controls without infusion. The result is that the coronary sinus blood of most of the dogs that had been infused and had suffered coronary ligation either remained low in potassium or showed wide fluctuations in the potassium level. When the level remained low there were very few extrasystoles, no ventricular tachycardia, or fibrillation. When the potassium level fluctuated extrasystoles were hardly seen when the potassium level was going down. Rapidly recurring extrasystoles, ventricular tachycardia and ventricular fibrillation were only seen when the potassium level in the coronary sinus blood was rising.

Thus it would seem that when the infusion hindered the anoxic outpouring of potassium from the myocardium it also reduced the incidence of arrhythmia. One can account for the variability of the results on the supposition that some hearts have more collateral circulation than others and that the occlusion produces a smaller or larger ischemic bed through which some blood flows carrying potassium into the coronary sinus stream.

Electrocardiographic evidence indicates that the electric axis of the ventricular extrasystoles that elicit ventricular fibrillation usually points upward and slightly to the right or left. Extrasystoles with an electric axis in the opposite direction were seen a few times and were predominant in only 1 of the 19 dogs studied. Thus, the usual extrasystole originates at the apical edge of the ischemic area and sweeps upward over the myocardium. These extrasystoles were not observed to elicit ventricular fibrillation when they followed a normal beat even though they occurred in the so-called vulnerable period. Ventricular fibrillation usually occurred after a paroxysm of ventricular tachycardia.

**SUMMARY**

The descending branch of the left coronary artery was ligated. The plasma potassium level of coronary sinus blood increased promptly in 7 of 8 control dogs and these 7 died with ventricular fibrillation within 20 min. The 16 experimental dogs had infusions of insulin-glucose and/or NaHCO₃ solutions for 2 hours which lowered the coronary sinus plasma potassium level to about half the control value. In 5 animals the potassium level rose immediately after coronary ligation and fibrillation came on promptly as in the controls. In the others the level remained low and the cardiac rhythm regular for an hour or more (6 animals) or for
3 hours until sacrifice (3 animals whose infusion was continued for 1½ hours after ligation). In 2 animals, the potassium level fluctuated but they survived the ligation 90 min. or more. Premature ventricular contractions, developing into ventricular tachycardia, preceded, in all cases, ventricular fibrillation. These contractions usually originated in the apex, probably at the margin of the infarction and occurred only when the potassium level was rising.

SUMMARY IN INTERLINGUA

Le branca descendente del sinistre arteria coronari esseva ligate. Le nivello de kalium in le sanguine del sinus coronari se augmentava promptemente in 7 ex 8 canes de controlo, e omne le 7 moriva con fibrillation ventricular intra 20 minutas. Le 16 canes del gruppo experimental recepiva infusiones de insulina-glucoosa e/o NaHCO₃ in solution durante periodos de 2 horas. Isto resultava in un reduction del nivello de kalium in le plasma del sanguine del sinus coronari a circa un medietate del valor de controlo. In 5 animates le nivello de kalium montava immediamente post le ligation coronari, e fibrillation superveniva promptemente, como esseva le caso in le casos de controlo. In le alteres, le nivello remaneva basse e le rhythm cardio remaneva regular durante un hora o plus (6 animates) o durante le 3 horas usque al sacrificio del animates (3 cases, in que le infusion esseva continuante durante 1½ horas post le ligation). In 2 animates le nivello de kalium fluctuava, sed ambes superviveva le ligation per 90 minutas o plus. Le fibrillation ventricular esseva precedite in omne casos per prematur contractiones ventricular que se disveloppava in tachycardia ventricular. Iste contractiones habeva lor origine usualmente in le apice, probablemente al margin del infarimento. Illos occurreva solmente quando le nivellos de kalium se trovava in stato de crescentia.

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