The Initiation of Ventricular Tachycardia and Fibrillation in Isolated Hearts by Potassium Chloride

By L. Grumbach, Ph.D.

In collaboration with L. K. Tanner, B.S. and J. Winibert, A.M.

An accelerating tachycardia ending in fibrillation can be initiated in isolated hearts by injections of KCl after the administration of epinephrine, but not in untreated hearts. KCl acts in two ways to do this. First, it causes an A-V block that enables epinephrine to cause a paroxysmal ventricular tachycardia. Secondly, it causes the latter to accelerate by delaying the recovery of excitability so that at least one premature systole can fall into the recovery phase of a preceding impulse. This event is necessary and sufficient for the initiation of a self-sustaining accelerating tachycardia that can end in fibrillation.

PROCaine is an effective antifibrillatory agent, as shown by suitable tests in experimental animals and, in addition, has been successfully used clinically for this purpose. However, in certain circumstances it can cause ventricular arrhythmias, both in experimental animals and in isolated hearts. The mechanisms involved in this action of procaine have been analyzed in the latter case. In order to determine whether these mechanisms are peculiar to antifibrillatory agents of the local anesthetic type, the ability of potassium salts to initiate ventricular arrhythmias in isolated hearts has been studied. They have long been known to have antifibrillatory actions and to cause ventricular fibrillation in intact animals.

METHODS

The electrical activity of isolated rabbit hearts perfused with Krebs-Henseleit solution in a Langendorff apparatus was recorded by a previously described method. Epinephrine solutions were made up in 1 per cent ascorbic acid to prevent oxidation. The vehicle alone had only a transient effect on the T wave which in control experiments was found to have no bearing on the phenomena to be described. KCl in a 0.77M solution was used for producing rapid alterations in the K+ concentration of the tissue fluid.

RESULTS

Injections of KCl into the perfusion stream never produced ventricular arrhythmias when the hearts were well washed with perfusion fluid. The typical sequence of events caused by a KCl injection is shown in figure 1, part 1a and consists of a slowing of the sinus rate and of atrioventricular and intraventricular conduction. The latter is more clearly seen in figure 2, part 2b which shows the lengthened P-R interval and widened QRS complex produced by KCl. These effects are entirely similar to those produced by procaine which are shown in fig. 2, part 1b and figure 2, part 1c.

In hearts that have been treated with epinephrine, on the other hand, KCl injections can cause an accelerating ventricular tachycardia that more or less rapidly ends in fibrillation. The fibrillation shown in part 2a of figure 1 continued for 5 minutes at which time it was stopped by an injection of 0.8 ml. of 0.77M KCl. That shown in part 3 of figure 1 ended spontaneously a short time after it began. In general, spontaneous reversions occurred within a minute; past that time, fibrillation usually continued indefinitely until stopped by some antifibrillatory treatment. When this was done, a normal sinus rhythm was resumed (cf. part 2b with 1b of figure 1).

Certain characteristic effects of rapid KCl injections on the electrocardiogram were noted. One effect was the production of A-V blockade.
both in normal and in epinephrine-treated hearts, as can be seen in parts 1a, 2a and 3 of figure 1. This also occurs with procaine injections (fig. 2, part 1b). A second effect that was seen only in epinephrine-treated hearts was the occurrence of premature ventricular systoles. These made their appearance coupled to the first supraventricular impulses to pass the depressed A-V node. They are indicated at the arrows in parts 2a and 3 of figure 1. The runs of accelerating ventricular tachycardia produced by KCl injections after epinephrine appear to consist of analysis of fast records of a series of premature ventricular systoles coupled to the first and apparently emanating from the same focus giving rise to the first one.

The rapidity with which the ventricular tachycardia accelerates and ends in fibrillation depends on the amount of KCl used. With larger amounts of KCl the oscillations are initially slow and regular and their acceleration is gradual (part 3 of fig. 1). With smaller amounts the acceleration is more rapid and fibrillation supervenes more quickly (part 2a of fig. 1).

The results just described were obtained in two out of every three hearts (the total number studied was 21). The negative result was usually an abortive train of premature systoles which nonetheless was not counted as successful. However, in some hearts treated with epinephrine the only effect of KCl was to slow the rate and conduction as described for untreated hearts at the beginning of this section.

KCl was also tested for its ability to replace epinephrine in the epinephrine-procaine sequence of injections that leads to an accelerating ventricular tachycardia ending in fibrillation. The procedure was the same as that just described for the epinephrine-KCl sequence. Part 2a of figure 2 shows the effect on the electrocardiogram 25 seconds after an injec-
tion of 0.2 ml. of 0.77M KCl solution. Record 2b demonstrates the effect of 0.4 ml. of 2 per cent procaine solution given 5 seconds later. Record 2c, taken 20 seconds later, shows a series of irregular idioventricular beats followed by a regular accelerating tachycardia which ended abruptly, as shown in 2e, 65 seconds later. The electrocardiograms of the reverted beats 15 seconds afterwards (2f) showed that that heart was still depressed by the combined effect of excess K+ and procaine. The strongly depressant effect of the combination of procaine with excess K+ was undoubtedly responsible for the fact that the result shown in part 2 of figure 2 was hard to obtain.

Part 3 of figure 2 shows that acetylcholine can also substitute for epinephrine in the epinephrine-procaine sequence of injections if the heart is atropinized. The acceleration of the sinus rate and the appearance of a U deflection in the ventricular complex seen in part 3b indicates that a considerable amount of a sympathomimetic substance was released. In parts 3c, d, e it can be seen that enough was liberated to allow procaine to
initiate ventricular tachycardia and fibrillation in the usual manner.

**Discussion**

The results of KCl injections in epinephrine-treated hearts are entirely analogous to those obtained with procaine injections in the same circumstance. The first action of both substances in initiating ventricular tachycardia and fibrillation is the production of some degree of A-V block which allows a latent action of epinephrine to become manifest, namely, that of initiating premature ventricular systoles either singly or in trains of constant frequency. A second action of procaine and KCl is to transform this paroxysmal tachycardia into an accelerating one. Fibrillation occurs when the latter reaches a critical frequency. The essential feature of this second action of KCl is that recovery of excitability is delayed without a concomitant decrease in the frequency of the premature ventricular systoles. As a result successive impulses fall into the recovery phase of the impulses just preceding each one. This is sufficient for the acceleration of a paroxysmal tachycardia and the eventual initiation of fibrillation.

The concept developed here, that KCl can only produce an accelerating ventricular tachycardia and fibrillation in hearts that have been treated with epinephrine, and that it does so in this circumstance by depressing conduction and recovery of excitability, does not accord fully with older interpretations of the mechanism of K+ fibrillation in experimental animals. In some cases the injection of KCl followed by a suitable amount of procaine caused an accelerating ventricular tachycardia. Our interpretation of this result is that KCl caused the release of an epinephrine-like substance from the chromaffin tissue of the heart. Hoffmann and his collaborators showed that measurable amounts of such a substance were released when acetylcholine was injected into isolated, atropinized hearts.

**Summary**

The ability of KCl to initiate ventricular arrhythmias was studied electrocardiographically in isolated rabbit hearts perfused with Krebs-Henseleit solution in the Langendorff apparatus.

In about two-thirds of the hearts studied, an accelerating ventricular tachycardia could be initiated by injections of KCl into the perfusion stream after treatment of the hearts with epinephrine, but not in untreated hearts. In the majority of cases the tachycardia ended in a transient or persistent fibrillation.

The mechanism by which KCl produces this result is entirely similar to the mechanism by which procaine effects the same result in similar circumstances. First, it causes an A-V block which permits epinephrine to initiate a paroxysmal ventricular tachycardia. Secondly, it transforms the latter into an accelerating tachycardia by delaying the recovery of excitability so that at least one epinephrine-induced premature ventricular systole can fall into the recovery phase of a preceding impulse.

KCl can also replace epinephrine in the epinephrine-procaine sequence of injections that leads to the initiation of ventricular tachycardia and fibrillation. Evidence was adduced to support the view that this excitatory effect of KCl is an indirect one, being on intracardiac adrenergic structures and not on cardiac tissue proper.

**Summario in Interlingua**

Le capacitate de chlorido de kalium de initiari arrhythmias ventricular eseva studiate electrocardiographicamente in isolate cordes de conilio perfundite con le solution de Krebs-Henseleit in le apparato de Langendorff.

In circa duo tertios del cordes studiate, il eseva possibile initiari un tachycardia ventricular accelerative per injic chlorido de kalium in le currente perfusional post que le cordes habeva esse tractate con epinephrina. In cordes non essi tractate le mentionate effecto non se produceva. In le majoritate del casos le tachycardia se terminava in un fibrillation transiente o persistente.

Le mechanismo per que chlorido de kalium produce iste effecto es integmente simile al mechanismo per que procaina effectua le mesme resultato sub simile conditiones. Primo,
illo causa un bloque atrio-ventricular que permite al epinefrina de iniciar un tachycardia ventricular paroxysmal. Secundo, illo transform le tachycardia ventricular paroxysmal in un tachycardia accelerative per retardar le recuperation del excitability de manera que al minus un prematur systole ventricular inducido per epinefrina occurre in le phase de recuperation del impulso precedente.

Chlorido de kalium pote etiam prender le placia de epinefrina in le sequentia de injectiones de epinefrina e procaina que duce al initiation de tachycardia e fibrillation ventricular. Es presentate datos in supporto del conception que le effecto excitatori de chlorido de kalium es un effecto indirecte que age super structuras adrennergic intracardiac e non super histos cardiac per se.

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L. GRUMBACH

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