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Experimental Studies on the Electrocardiographic Effect of Low Potassium Solution on the Injured Heart Surface

AN APPROACH TO THE PROBLEM OF LONG-PERSISTING ST-ELEVATION
AFTER THE ATTACK OF THE MYOCARDIAL INFARCTION

By

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INTRODUCTION

For many years it has been known that the ST-elevation is generated by the application of potassium solution on the intact heart surface, and disappears easily and reversibly when Ringer's solution is poured on that area to wash out the potassium (1).

When an acute coronary occlusion occurs, the leads from the infarcted area show the ST-elevation. This electrocardiographic finding is attributed to the localized transmural ischemia and is supposed to be brought on by the biochemical or bioelectrical changes occurring in the lesion. The ST-elevation is also produced when the heart surface is experimentally injured by burning, crushing, pressure, or by application of toxic substances such as alcohol, nitric acid, and other chemical agents (2).

Some authors (3, 4) suggest that the high potassium concentration in the extracellular fluid around the infarcted or experimentally injured muscle tissue is the cause of the ST-elevation, which results from the potassium liberation from the damaged muscle cells. In our experiments previously reported (5), it was observed that the potassium content of the coronary venous blood was increased simultaneously with the appearance of the ST-deviation, when the coronary arterial flow was reduced. Such a finding leads us to conclude that the excess potassium in the extracellular space is the cause of the ST-deviation.

In such a circumstance, however, the intracellular potassium is reasonably decreased as a result of its liberation from the inside of the cells, as already confirmed by autoptical or experimental data. To discuss the relation between the ST-elevation and the potassium in the damaged heart, therefore, the change in the relation of the intracellular to extracellular potassium content must be

considered.

It has been pointed out in clinical and experimental observations that the changes in the electrocardiogram are not always correlated with the serum potassium level (6-10), but the altered difference of the potassium concentration between inside and outside of the cells plays an important role in producing the ST-deviation (11-13).

When the damaged area, in which the potassium content decreased, is covered with potassium-free or potassium-diminished solution, an altered ratio will occur between the intracellular and extracellular potassium. It is not difficult to suppose that such an alteration of the ratio may have an effect on the ST-elevation. However, there have been only a few reports relating to the effect of potassium on the electrocardiogram in the presence of the local myocardial damage (14, 15). From this standpoint the following experiments were performed.

METHOD

Eighteen toads were used. Wide exposure was accomplished by removing the frontal chest wall. The pericardium was cut open carefully, so as not to injure the heart surface. Then the heart muscle was injured by burning or by the application of 95% alcohol solution. To apply the latter, intramyocardial injection or contact with the heart surface was performed. The injured surface of the heart was covered with the previously prepared samples of the potassium solution and the direct unipolar leads were taken through it. A needle electrode wrapped with moist cotton was employed as the different one (Fig. 1). The indifferent electrode was placed on the right arm. The elevation of the ST-junction was used as a criterion of the elevation of the ST-segment. The samples containing the same constituents as Ringer's solution

Fig. 1. Experimental Method

except for potassium were prepared, in which the potassium concentration was altered from 0 mEq/L to 10 mEq/L.

RESULT

Immediately after a local injury was given to the epicardial surface, a typical monophasic curve was recorded from this area, whether the covering solution was Ringer's or potassium-free one. Sooner or later came the moment when the ST-elevation was no longer recorded if potassium-free solution was used. The time interval from the injury to that moment was variable according to the methods of injury. It was somewhat longer in burning than in contact with the alcohol cotton or intramyocardial alcohol injection, as shown later in Figs. 4 and 5. After this instant it was necessary to use samples of higher potassium concentration in order to generate the ST-elevation, and at last even

the normal Ringer's solution had no effect.

Fig. 2 shows an instance of the course in the burning injury. Until twenty-six minutes after the injury the ST-elevation was always recorded by use of potassium-free as well as 4 mEq/L solution. At 26 minutes the potassium-free solution did not produce the ST-elevation. At 28 minutes 1 mEq/L and at 31 minutes 3 mEq/L had no effect on the ST-segment. On the other hand, 4 mEq/L at 29 minutes, 6 mEq/L at 32 minutes produced the ST-elevation. In a further course 5 mEq/L at 46 minutes, 6 mEq/L at 43 minutes, 7 mEq/L at 44 minutes, and 10 mEq/L at 46 minutes were unable to produce the ST-elevation, whereas 7 mEq/L at 40 minutes had the effect. In this figure the white spots represent the ST-elevation and the black ones are used for no ST-elevation. A boundary line between these white and black spots may be drawn as seen in the Figure.

Fig. 3 was obtained in another case in which alcohol injury was given, and a similar line as in Fig. 2 was drawn. Such lines were obtained in each experiment performed (Figs. 4 and 5). They are nearly straight and their slopes are almost the same in every experiment, whether the injury was given by burning or by alcohol application. In the upper side of the gained line in these figures the ST-elevation will be recorded, while in the lower

Fig. 2. A course of the change in the ST-deviation after burning of the localized area of the epicardial surface. The injured area was covered with potassium solutions of various concentrations and the direct unipolar electrocardiogram was taken from there. The white spots indicate the ST-elevation, the black spots no deviation. Details in text.

Fig. 3. A course of the change in the ST-deviation after alcohol application to the epicardial surface. Details in text.

side no ST-elevation will be obtained. In other words, the samples of higher potassium concentration are needed in order to gain the ST-elevation after the instant when the potassium-free solution was unable to elevate the ST-segment. This fact shows that there exists a kind of threshold of potassium concentration to generate the ST-elevation and its value rises as time passes after injury.

When the injured area was recovered, the threshold value returned to 6–7 mEq/L or a little higher; that is, samples of a little higher concentration than before the injury were needed to produce the ST-elevation at the end of recovery. After the injured region was completely recovered, this threshold value, of course, returned again to 6–7 mEq/L. Careful observation of such an “overshooting” was performed only in some cases, as indicated in Figs. 4 and 5. In other cases the observation was

Fig. 5. Same as in Fig. 4. Cases of alcohol injury.

discontinued after the threshold value rose beyond the previous level, but it was observed that the value returned to the former level within thirty minutes in every case. Fig. 6 shows an instance of the relation.

DISCUSSION

1. The effect of low potassium solution on the ST-elevation generated by injury, and the ratio between intra and extracellular potassium content.

If the outflux of potassium from the injured myocardial tissues is concerned in producing the ST-elevation, three situations may be considered as its cause, as shown in Fig. 7.

- (a) An increase in the extracellular potassium (Fig. 7b)

Fig. 4. Boundary lines obtained in each experiment. Cases of burn injury.

Fig. 6. The change in the threshold value in a case of alcohol injury. At the end of recovery the value returned to the previous level after rising beyond it.

Fig. 7. The ratio of intracellular to extracellular potassium and its relation to the ST-elevation:

- The normal ratio of 150:5. No change in the ST-segment, as seen in normal electrocardiogram.
 - The extracellular potassium increases so that the ratio is, for instance, 150:10. The ST-segment is elevated.
 - The extracellular potassium does not increase, while the intracellular one decreases. The ST-elevation may occur.
 - Immediately after injury. The potassium inside the myocardial fibers decreases, while outside increases. The ST-segment is elevated.
 - To eliminate the ST-elevation in the situation d, it is necessary to reduce the extracellular potassium severely.
- (b) A decrease in the intracellular potassium (Fig. 7 c)
- (c) An altered ratio between the intracellular and the extracellular potassium (Fig. 7 d)

It is well known that, when the extracellular potassium is increased locally by the application of potassium solution on the intact surface of the heart, the ST-elevation appears. A curve mistaken for the acute myocardial infarction or pericarditis has been recently reported in clinical cases of potassium intoxication and it disappeared by dialysis with the artificial kidney (16). In these cases, the ST-elevation seems directly or indirectly due to the increased potassium content in the extracellular fluid.

The electrocardiographic findings in the cases of the reduced myocardial potassium content have not been studied in detail (17). Currens and Crawford (18), as well as Ljunggren and associates (19), supposed from the indirect evidence obtained by analysis of clinical cases that the intracellular potassium concentration may be correlated with the electrocardiographic changes rather than the extracellular content. Weller and associates (20) emphasized in their study on the effects of acute removal of potassium from dogs, that no changes occurred in the electrocardiogram, if myocardium did not participate in the potassium loss. Kuehns (21) observed the hyperpotassemic changes in the electrocardiogram in the presence of normal serum level, while no changes in the electrocardiogram in the presence of severe hypopotassemia, when the serum potassium level was experimentally

elevated or reduced in dogs pretreated with DOCA. Iseri (22) and other authors observed a decrease in the intracellular potassium in the heart of the myocardial infarction at autopsy, but they had no comment in relation to the electrocardiographic findings. In the experimentally injured hearts the intracellular potassium has been found also to decrease and this may be supposed as a result of its liberation to the outside of the cells (23, 24).

In this view, the ratio of intracellular to extracellular content must be taken into consideration.

The ratio in the normal heart muscle is nearly 150 : 5 (25). When it shows this value, the ST-segment lies in the level of the baseline, as seen in the usual normal electrocardiogram (Fig. 7a). When the external potassium increases, so that the ratio changes to 150 : 10, for instance, the ST-deviation occurs, as observed in the clinical and experimental hyperkalemia (Fig. 7b).

On the one hand, the decrease in the intracellular potassium also may cause the ST-elevation as indicated in Fig. 7c. Accordingly, when the potassium increases in the outside and decreases in the inside of the cell, the ST-segment may elevate. Fig. 7d shows the relation.

In the latter situation it is considered that, in order to eliminate the ST-elevation, it is necessary to reduce the extracellular potassium severely (Fig. 7e). For this purpose it was attempted to pour potassium-free solution on the damaged surface. The disappearance of the ST-elevation could not be observed immediately after injury in our experiments, probably because of short duration of the effect of the solution. But, as time passed, it was observed that the potassium-free solution eliminated the ST-elevation. This fact indicates that the intracellular potassium is reduced as a result of damage, in accordance with the consideration mentioned above.

As more time passed, higher concentration was needed to produce the ST-elevation; it was observed that the potassium solution of a certain concentration had no effect, while a little higher concentration had the effect. The threshold value to produce the ST-deviation was elevated gradually. At last Ringer's solution again had no effect to elevate the ST-segment as before injury. This suggests that the intracellular potassium was restored gradually and to the previous level.

The concept that the ST-deviation observed in myocardial damage is caused by potassium changes,

is not yet generally accepted. However, our observation that the decrease in the potassium concentration in the covering solution eliminates the ST-elevation, strongly supports this concept.

2. *Explanation for the long-persisting ST-elevation in the old myocardial infarction.*

The finding in our experiments may be used to explain the long-persisting ST-elevation in the myocardial infarction. The infarcted area is considered to become scarred soon after the acute stage, after which the electrocardiographic findings must return to normal. It is not rare, however, that the ST-elevation persists for years after the attack, as experienced in clinical cases.

There have been a few arguments as to the explanation for this clinical observation. In 1938, Parkinson and associates (26), obtained in the cases of ventricular aneurysm the tracing consistent with the infarction of the anterior wall. Ford and Levine (27) observed, that the ventricular aneurysm is frequently associated with the electrocardiographic appearance interpreted usually as the acute myocardial infarction. Scherf and Boyd (28), and Schlichter (29) reported similar observations. Rosenberg and Messinger (30) showed that in all eight patients with the persisting elevation of the ST-segment as well as Q waves in the precordial leads after the acute stage of the myocardial infarction, the ventricular aneurysm was discovered autoptically or by other examinations.

Nevertheless some authors published their opinion that there is no characteristic electrocardiographic pattern with the ventricular aneurysm, and in the literature the patients with the ventricular aneurysm autoptically confirmed did not always show the persisting ST-elevation (31, 32).

Another explanation is that of Mayer and Hiller (33). They claimed that the persisting ST-elevation in the precordial leads after the acute stage of the anterior infarction, is caused by hypertrophy of the posterior wall of the heart lying opposite to the lesion. The old infarcted area is supposed to be electrically inert. If the cardiac wall opposite to the area is hypertrophied, its electrical effect will be manifest through the intervening inert tissues. They reported also that the most significant ST-elevation was seen in the heaviest of their examined hearts.

Now a new proposal is presented by us in view of the change in the ratio of the intracellular

to extracellular potassium content. If the intracellular potassium content in the infarcted area remains reduced for many years, the normal blood circulating through this region may cause the ST-elevation after the acute phase of the myocardial infarction. This situation is similar to Fig. 7c. The fact that the potassium content in the infarcted area is reduced has been shown autoptically or experimentally by some authors, as above mentioned.

In clinical cases of acute myocardial infarction, the elevation of plasma potassium level is observed within a few days, and returns to the normal value thereafter. Fig. 8 shows a course in one of the

potassium level returned spontaneously toward the control value within one hour and a half. The heart muscle examined at that stage revealed a surprising potassium increase of 12% on the average in comparison with the control series. This finding may be related to our observations.

SUMMARY AND CONCLUSION

1. In order to study the electrocardiographic effect of low potassium solution on the damaged area of the heart surface, the ventricular surface of a toad was injured by burning or application of alcohol solution, and the injured area was covered with low potassium solution.

Fig. 8. Changes in the plasma potassium level after the attack of acute myocardial infarction. A 61-year-old woman.

cases; the ST-elevation persisted even after the return of the plasma potassium level to the normal (34, 35).

3. Overshooting phenomena of the potassium threshold.

After the return of the "potassium threshold" to the previous level its further elevation was observed in our experiments as previously shown in Fig. 6. It may be regarded as a kind of "overshooting". Since higher potassium concentration is required to elevate the ST-segment, the intracellular potassium concentration must be considered to be higher than normal. It is supposed that the damaged cells take up potassium in excess for their improvement.

In this regard, the report of Nichopoulos and Hoffman (36) on the effect of acute hypopotassemia on the intracellular potassium and on the electrocardiogram may be noted with interest. The dogs were rendered acutely hypopotassemic by hemodialysis. After the cessation of dialysis, serum

2. Immediately after the injury the ST-elevation appeared in the unipolar lead taken from the damaged area. The elevation was not eliminated by changing the covering solution to the potassium-free. As time passed, however, it was necessary to use samples of higher concentration in order to produce the ST-elevation. At last even the normal Ringer's solution had no effect. This fact shows that there exists a kind of threshold of potassium concentration to produce the ST-elevation and its value rises as time passes after injury.

3. These findings may be explained by the supposition that the intracellular potassium is gradually restored after injury, so that the higher concentration is needed to produce the ST-elevation. The ratio of the intracellular to extracellular potassium concentration plays an important role in the ST-deviation.

4. These observations may be applied to the explanation for the long-persisting ST-elevation after the attack of the myocardial infarction.

If the intracellular potassium in the infarcted area remains reduced for many years, the normal blood circulating through this region may cause the ST-elevation.

5. At the end of recovery, the "threshold value" of the potassium for the ST-elevation arises beyond the previous level. This fact may be explained as a result of the excessive increase in the intracellular potassium in comparison with the level before the injury.

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