Editorial

Effect of Potassium on A-V Conduction

"When the potassium is injected slowly, after a time the heart gradually slows to perhaps half its normal rate, the auricle and ventricle being markedly dilated but still contracting synchronously. This is an example of sinus slowing, and is probably due to the direct action of the salt upon what Lewis has termed the 'pace-maker' of the heart; it is not due to stimulation of the vagus endings, since it is still produced after administration of atropine. . .

"In other cases an abrupt slowing of the pulse rate occurs, due to dissociation of the auricular and the ventricular rhythms, a condition of 2:1 or of complete heart block being produced. This dissociation is sometimes seen in a heart that is in quite good condition and, upon discontinuing the injection of potassium salts, recovery soon takes place. It cannot be produced with any degree of certainty; since marked sinus slowing, stoppage in diastole, or ventricular fibrillation frequently ensue without this type of heart block being manifested. . .

"In the present state of our knowledge it is legitimate to infer from these results that the block is due to a depression of the conductivity of the auriculoventricular connections from the direct action of the potassium salts upon the musculature. The block is produced in the hearts of animals that have been treated with atropine, so that stimulation of the vagus mechanism is not an essential factor."—Mathison.1

This statement summarizes succinctly our present-day knowledge of the effect of hyperkalemia on atrioventricular (A-V) conduction. However, the realization that these observations and conclusions were made by Mathison as early as 1911 may come as a surprise to many. It is also of interest that his conclusions were based on direct visual observation of the behavior of the atria and ventricles without the benefit of the electrocardiograph. Following the original studies of Mathison, the question of the effect of potassium (K+) on the A-V conduction received little attention, with some notable exceptions.2,3 until the late 1950s. Reawakening of interest in the effect of K on the overall electrical properties of the heart was in large measure due to the recognition of the importance of this cation in its interrelationships with digitalis, the relative ease and reliability with which plasma K+ can be presently measured, the widespread use of the ECG, and the advances in methodology applicable to electrophysiologic investigation.

Potassium when infused intravenously first accelerates then depresses A-V conduction. Acceleration of A-V conduction by K+ has been demonstrated in a Langendorff preparation of the rabbit heart, by intravenous infusion in the vagotomized dog, and by direct injection into the coronary arteries of

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<th>Plasma K⁺</th>
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<th>Clinical</th>
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<tr>
<td>Reduced</td>
<td>Depressed</td>
<td>No change</td>
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<td>1°, 2°, 3° block</td>
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<td>Elevated</td>
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<td>(Sino-ventricular conduction?)*</td>
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*This has never been demonstrated in the presence of recognizable atrial activity (P waves) but may be operative when atrial activity is suppressed.

the dog. Clinically the accelerating property of mild and moderate hyperkalemia has been shown to improve A-V conduction in patients with sinus rhythm and A-V block, and in patients with atrial fibrillation it may result in acceleration of the ventricular rate. From the practical standpoint, however, K⁺ is rarely, if ever, used to enhance A-V conduction in patients with heart block.

Potassium may accelerate A-V conduction by one, or a combination of, the following mechanisms: (1) blocking vagal action, (2) reducing the magnitude of the resting potential, and (3) increasing the rate of rise of phase 0 of the action potential independently of any change in the resting potential.

The antivagal effect of mild hyperkalemia at the A-V junction has been demonstrated with intravenous and direct intracoronary infusion of the cation and by its ability to inhibit the action of exogenous acetylcholine. Reduction of the magnitude of resting potential narrows the difference between the resting potential and the threshold potential resulting in a reduction in the strength of the stimulus required to elicit a propagated response, and thus, A-V conduction may be enhanced. Preliminary results from our laboratory also suggest that prior to any changes in the level of the resting potential there is a significant augmentation of the rate of rise of phase 0 of the action potential which may prove to be a factor in acceleration of A-V conduction.

Continued elevation of plasma K⁺ in dogs frequently results in prolongation of the P-R interval followed by higher degrees of A-V block. All varieties of A-V conduction delay and block, some of which could be interpreted only by involving the concept of "supernormality" of conduction and concealed conduction, have been observed.

The exact site of K⁺ induced A-V block remains unsettled. The high resistance of the A-V node per se to hyperkalemia is well known. In fact, it has been shown that ventricles may be driven by the sinus pacemaker at plasma K⁺ levels sufficiently high to depress atrial activity and to eliminate P waves from the electrocardiogram. Such direct sinoventricular propagation was ascribed to specialized atrial conduction pathways which are said to be particularly resistant to depolarization by K⁺. Frequently, however, the atrial tissue, the idioventricular focus, and the ventricular myocardium are more resistant to K⁺ than the weakest link of the A-V transmission system, and classical complete A-V block is recorded. One of the possible variables responsible for the difference in the relative sensitivity of the various tissues from experiment to experiment may well be the rate of infusion, with the traditional forms of A-V block being recorded at faster rates of infusion of K⁺.

Electrophysiologic studies of the A-V junction indicate that the depression of conduction by K⁺ occurs largely at the atrionodal, nodal-His, or His-Purkinje regions and that the true nodal or N region is quite resistant to the depressing effect of K⁺.

The uniformity with which one can induce A-V block experimentally, at least in dogs, is...
in striking contrast to the paucity of such observations in man. Scattered cases of high degree of A-V block have been observed after administration of large doses of K⁺ for the treatment of arrhythmias or as replacement therapy.⁰ To our knowledge, however, A-V block, other than simple prolongation of P-R interval, has not been demonstrated as yet in patients with “spontaneous” hyperkalemia. This discrepancy between the experimental and clinical incidence of high degree of A-V block can be explained by the fact that experimental hyperkalemia represents a “pure” effect of K⁺, while in patients, who may have renal failure as the underlying disturbance, disorders of acid-base balance and of electrolytes, factors other than K, probably play an important role in the alteration of electrophysiologic properties. Furthermore, the rate of administration is a variable. While in patients with uremia the K⁺ level rises slowly, in the occasional patient in whom high degree of A-V block has been recorded, the cation was administered rapidly and in large doses.¹⁰

The mechanisms by which K⁺ may cause prolongation of conduction include (1) reduction of resting potential to the point of inexcitability,⁷ (2) potentiation of the vagal action,¹¹ and (3) according to our preliminary observations, a direct depressing effect on the rate of rise of phase 0.

Recognition of the ability of K⁺ to depress A-V conduction is clinically important when treating digitalis induced arrhythmias. Potassium, when given in the face of digitalis toxicity, has been shown to potentiate the effect of the glycoside on A-V conduction.¹² It is equally important, however, to recognize that such depression of A-V conduction occurs at K⁺ levels considerably higher than those necessary to suppress ectopic rhythms. With this margin of safety, provided the cation is administered with the usual precautions, K⁺ can be given to patients in whom depressed A-V conduction is manifest only by prolongation of the P-R interval. The potentiation of the depressive effect of digitalis on A-V conduction by exogenous K⁺ is related to the more rapid rise of plasma K⁺ at any given dose in the presence of digitalis. This steep rise of plasma K⁺ is probably due to decreased ability of K⁺ to move intracellularly in the presence of digitalis toxicity.

Reduction of plasma K⁺ levels has been shown to prolong A-V conduction in pigs fed a low K⁺ diet, and in the isolated frog, turtle, and rabbit hearts when exposed to low K concentration.⁴-¹³ In contrast, large numbers of ECGs recorded in patients with low K⁺ have failed to demonstrate statistically significant changes in the P-R interval.¹⁴

It appears superficially that, with the exception of the potential enhancement of the action of digitalis and the occasional effect of the rapid administration of K⁺ alone, the alterations of A-V transmission brought about by this cation are of interest largely to the investigator and, at least for the present, are of limited clinical utility. The fact is, however, that there is much to be learned about K⁺, A-V conduction, and the patient. As an example, the possible important role of K⁺ in the genesis of heart block complicating myocardial infarction needs clarification. It has been shown that coronary sinus K⁺ rises appreciably and relatively rapidly following acute myocardial infarction and calculations based on these figures suggest that the extracellular K⁺ in or about the ischemic or infarcted area may be as high as 10 to 12 mEq/L.¹⁵ Potassium levels of this magnitude will induce A-V conduction defects either by direct effect on the conduction tissue or by potentiating vagal action¹¹ or both.

One may safely conclude that our knowledge of action of K⁺ is fragmentary and that considerable information about its contribution to, and insight into, the mechanism of its action in various clinical disorders of conduction remains to be elucidated.

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References

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