Interactions of Quinidine and Potassium on Atrioventricular Transmission

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ABSTRACT

The effects of quinidine and its interactions with potassium (K) on atrioventricular (A-V) conduction were studied in isolated, perfused rabbit hearts, utilizing microelectrode techniques. Quinidine gluconate (10 mg/liter) was added to perfusion fluid containing either normal [K+] (4.5 mEq/liter), low [K+] (1.5 mEq/liter), or high [K+] (7.5 mEq/liter). The following observations were made: (A) The marked prolongation of A-V conduction time produced by quinidine was antagonized by low K+ and enhanced by high K+ concentration. (B) Quinidine or high K+ concentration prolonged the A-V interval by slowing intra-atrial and His-Purkinje-ventricular conduction. (C) Low K+ concentration depressed conduction in the N region of the A-V node. (D) Lowering K+ concentration in the presence of quinidine shortened the A-V interval by enhancing His-Purkinje-ventricular conduction. (E) Quinidine and high K+ concentration increased the action potential amplitude in the nodal and the node-His regions of the A-V node while low K+ concentration showed opposite effects. Hence, different regions of the A-V conducting system were selectively influenced by these agents. A-V conduction in the presence of low K+ and quinidine depends upon the net results of their antagonism within individual fiber types. The importance of these interrelationships in pharmacologic approach to A-V conduction disturbances is stressed.

ADDITIONAL KEY WORDS

A-V node A-V block conduction transmembrane potentials perfused rabbit hearts

The effects of potassium on A-V transmission have been the subject of numerous clinical and experimental reports since the classical observations of Mathison in 1911 (1). Recently, a detailed experimental study by Paes de Carvalho and Langan (2) showed an optimal range of extracellular potassium concentration for A-V transmission and impairment of conduction outside this concentration range. These investigators further suggested that delay in A-V transmission when the potassium concentration is low (< 2.7 mM/liter) was due to slowing of conduction within the A-V node while the delay when the potassium concentration is high (> 7 mM/liter) was related to the depression of atrial and subnodal conduction (2). However, they made no attempt to explain the electrophysiological events engendering these changes or to localize the site of conduction delay within the various regions of the A-V node. Other studies have demonstrated the interrelationship of potassium with vagal stimulation, acetylcholine or digitalis, although some confusion still exists in the interpretation of these observations (2-5).

The effects of quinidine on A-V transmission and especially its interactions with potassium have been studied far less extensively (6, 7). Utilizing conventional electrocardiographic recordings in the dog, Bennett et al. concluded that both quinidine and hyperkalemia produced slowing of intra-atrial, atrioventricular and intraventricular conduction but their effects were neither additive nor synergistic (7). In view of our previous observations on

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ventricular fibers (8), the present experimental study was undertaken to reevaluate the electrophysiologic antagonism and synergism of potassium and quinidine on A-V transmission.

**Methods**

Experiments were carried out on isolated, perfused rabbit hearts. The basic technique of isolation and perfusion was previously reported (9). The rate of perfusion was usually between 15 and 20 ml/min. A bipolar ventricular electrogram was recorded between two small surface electrodes, one attached to the right ventricular apex and the other to the left ventricular base. A small bipolar electrode with an interelectrode distance of 1 mm was attached adjacent to the S-A node to record an atrial electrogram. Two flexibly mounted glass microelectrodes were utilized to record transmembrane potentials from various portions of the A-V junctional region. Voltages were amplified through a neutralized input capacity amplifier and Tektronix type D and M amplifiers, and displayed on two Tektronix type 532 oscilloscopes. Photographs were taken from one oscilloscope with a Grass Kymograph Camera (Model C4-K) at a paper speed of either 50 or 100 mm/sec.

During the initial control period of 45 to 60 min, transmembrane potentials were recorded from various A-V junctional fibers, in order to map and time normal A-V transmission. The site of microelectrode impalement was observed through a dissecting microscope and plotted on a chart with reference to various anatomical landmarks. Subsequent alterations of the perfusate divide the experiments into three groups. In 13 experiments (group 1), quinidine gluconate (10 mg/liter) was added to the perfusate. After 30 to 45 min, the potassium concentration of the perfusate was lowered from 4.5 to 1.5 mEq/liter while the same concentration of quinidine was maintained. In a second series of 13 hearts (group 2), the experimental order was reversed. Following the initial control period, potassium concentration was lowered from 4.5 to 1.5 mEq/liter. After 30 to 40 min, quinidine (10 mg/liter) was added to the low potassium perfusate. In the last series of 11 experiments (group 3), interactions between quinidine and high potassium concentration (7.5 mEq/liter) were studied. During perfusion of each test solution, numerous transmembrane potentials of the A-V conducting fibers were recorded to study the changes in the spread of excitation as well as the configuration of the action potential.

Obviously, the impalement of these fibers by the microelectrodes could not be maintained during the control and test perfusions. However, activation times as well as the configuration of the action potential in the atrial and the node-His fibers in the presence of a steady A-V interval were quite reproducible in serial impalments. Hence, possible involvement of large errors due to slight differences in electrode position can be ruled out (10). Only gross changes in the maximal rate of depolarization were observed because of the difficulty of holding microelectrodes inside nodal cells.

In the majority of the experiments, the heart was allowed to beat spontaneously throughout the entire period of observation. A smaller number of experiments in each series (4 in group 1, 3 in group 2 and 1 in group 3) were carried out with the heart being electrically driven at a selected frequency through a small, bipolar stainless steel electrode attached to the right atrial appendage. Electrical stimuli produced by a laboratory stimulator (American Electronic Laboratories, model 104A) were in the form of a square pulse of 2 msec duration and 1.5 times the threshold intensity, and applied through a stimulus isolation unit. Various fiber types in the A-V junction as identified by location and configuration of the action potential have been classified according to Paes de Carvalho (11): AN (atrionodal), N (nodal) and NH (node-His).

**Results**

**A-V Conduction Time**

In the experiments utilizing spontaneously beating hearts, the A-V conduction time remained remarkably constant during the initial control period. The heart rate also remained constant in the majority of instances (21 hearts); it decreased slightly in 8 hearts. A typical time course of the A-V conduction time in those experiments of groups 1 and 2 is shown in Figure 1.

Group 1. Following the addition of quinidine (10 mg/liter) to the control perfusate, the A-V conduction time was markedly and progressively prolonged in all instances. There was a concomitant decrease in heart rate. Prolongation of the A-V interval often reached a plateau within 30 to 40 min. In 10 of the 13 experiments, the A-V conduction time approximately doubled; in the other 3 hearts, the prolongation was less marked. When the perfusate was replaced by a low potassium solution ([K+] = 1.5 mEq/liter) with the same
Typical time course of the A-V conduction time during perfusion with different test solutions.
Black line represents a group 1 experiment and dotted line a group 2 experiment. Shortening of the A-V interval due to low potassium perfusion in the presence of quinidine is evident. Low potassium concentration alone causes little prolongation of the A-V interval.

Concentration of quinidine, the A-V conduction time was shortened (Fig. 1, upper curve). This shortening of the A-V conduction time was accompanied by a slight reduction in the heart rate, usually less marked than in the presence of quinidine alone. In hearts driven at a constant rate, shortening of the A-V interval following lowering of potassium concentration was less and more transitory (not shown).

Group 2. Initial lowering of the potassium concentration to 1.5 mEq/liter did not produce significant changes in the A-V conduction. In some hearts, the A-V interval remained unchanged (Fig. 1, bottom curve); in others it became gradually longer. Lowering of [K+] usually caused a slight decrease in the heart rate. In some experiments, transient second degree A-V block was observed immediately following the start of low potassium perfusion, with restoration of 1:1 conduction several minutes later. Furthermore, it was apparent that the level of extracellular K+ was crucial for A-V transmission, since second degree or higher grades of A-V block rapidly developed in 3 experiments where [K+] was lowered to less than 1.2 mEq/liter. The addition of quinidine (10 mg/liter) to a perfusate with a low [K+] produced a progressive prolongation of the A-V conduction time, although the prolongation often reached a plateau earlier than in the presence of a normal potassium concentration (Fig. 1, bottom curve).

In another experiment of group 2 (Fig. 2), prolongation of the A-V interval due to quinidine in the presence of low potassium solution reached a plateau after about 30 min. Returning potassium concentration to the control level (4.5 mEq/liter) in the presence of the same quinidine concentration caused a rapid and marked prolongation of the A-V conduction time.

Group 3. High potassium concentration (7.5 mEq/liter) alone often caused a prolongation of the A-V interval (not shown). The combined effects of quinidine and high potassium concentration on the A-V conduction time are shown in Figure 3. In this instance, prolongation of the A-V interval reached a plateau after 30 min of quinidine perfusion. When the [K+] of the perfusate

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was then elevated to 7.5 mEq/liter, in the presence of quinidine, rapid and unusual prolongation of the A-V conduction time ensued. An A-V interval of 540 msec was recorded before second degree A-V block occurred. The heart rate gradually decreased following the addition of quinidine and during the perfusion with high potassium and quinidine. A return to the control perfusate without quinidine resulted in an increased heart rate and shortening of the A-V conduction time to 220 msec within 30 min.

**SITE OF MAJOR CONDUCTION DELAY**

The time of activation of various points within the A-V junctional region was determined in the presence of control as well as test solutions. In Figure 4, the change in conduction time due to quinidine is shown at four representative points. At each point, the numbers above the line represent A-V conduction time during the control period and those below the line during the infusion of altered perfusion fluid. The two numbers above and below the line represent the time of activation of the fiber with reference to the atrial electrogram, plus the time interval from depolarization of the fiber to the onset of ventricular activation. Thus, the total A-V interval during the control period ranged from 86 (54 + 32) to 91 (45 + 46) msec, with an average of 89 msec. Quinidine prolonged the A-V conduction time to 188, 194, 195 and 197 msec, an average increase of 103 msec. It can be seen that the conduction time from the S-A nodal region to an atrial fiber bordering the A-V node was prolonged by 21 (52 - 31) msec following quinidine perfusion. Similarly, the conduction time from a distal NH fiber to the ventricles was increased by 77 (109 - 32) msec. Hence, the delay in the intra-atrial and in the His-Purkinje conduction due to quinidine was 98 (21+77) msec, and accounted
Changes in the A-V conduction time due to quinidine and high potassium perfusion (group 3 experiment).

for most of the A-V conduction delay of 103 msec. Conduction time across the major portion of the A-V nodal tissue was not prolonged by more than 5 msec. These findings indicate that the marked prolongation of the A-V conduction time in the presence of quinidine is mainly due to slowing of conduction in the atrial and His-Purkinje conducting system while conduction time through the A-V nodal region remains relatively unaffected.

Figure 5 shows changes in conduction time due to low extracellular potassium concentration. During the control period, the total A-V conduction times were 105, 105, 106 and 108 msec. The conduction time between an atrial fiber adjacent to the A-V node and an NH fiber close to His bundle was 41 (76 - 35) or 42 (71 - 29) msec. When perfusion with low potassium prolonged the A-V conduction time by approximately 20 msec, the time interval between these two fibers was between 51 (83 - 32) and 61 (101 - 40) msec. Hence, the conduction time across the A-V nodal region was prolonged by 10 to 20 msec which could account for most of the increase in A-V transmission time. In contrast, conduc-
Changes in the activation time of various fibers due to quinidine (group 1 experiment), as plotted on a map of the A-V nodal region. CS = ostium of coronary sinus; RA = right atrium; AVR = fibrous atrioventricular ring; IVS = interventricular septum; HB = His bundle. The upper numbers show conduction time from the S-A node to a given fiber plus that from the fiber to the ventricles during the control period. The lower numbers represent similar time values following quinidine perfusion. Detailed discussion in text.

Figure 6 illustrates 1 experiment in group 3 in which high extracellular [K+] caused an unusually marked prolongation of the A-V conduction time. In this instance, the total A-V interval during the control period was between 110 (50 + 60) and 128 (32 + 96) msec, while that following high potassium perfusion reached 330 (75 + 255) to 342 (135 + 207) msec, an increase of approximately 215 to 220 msec. Intra-atrial conduction was obviously slowed by high potassium, as the time of activation of an atrial fiber was delayed by 54 (75 – 21) msec, and that of an AN fiber by 62 (94 – 32) msec. Similarly, conduction time from the NH region to the ventricles was markedly prolonged by 144 (198 – 54) to 147 (207 – 60) msec. Hence, out of 220 msec of total delay, almost 200 to 210 msec resulted from slowing of transmission within the atrial and His-Purkinje conducting system. The conduction time across the A-V nodal region was prolonged by only 10 to 15 msec.

These observations are illustrated graphi-
Changes in the activation time of various A-V functional fibers due to low potassium perfusion (group 2 experiment). See text for discussion.

Changes in the activation time of A-V junctional fibers due to high potassium perfusion (group 3 experiment). Detailed discussion in text.
cally in Figure 7. The total A-V conduction time is subdivided into intra-atrial (A), intranodal (N) and His-Purkinje (HP) conduction time during each test perfusion. The results of representative experiments from groups 1, 2, and 3 are shown. In group 1, the addition of quinidine to the control perfusate caused a marked delay in the intra-atrial and the His-Purkinje transmission, while the intranodal conduction time remained unchanged. Subsequent lowering of potassium concentration in the presence of the same quinidine concentration resulted in a slight shortening of the A-V interval. This shortening was due to a decreased His-Purkinje conduction time, whereas the intranodal conduction time was actually prolonged. Hence, an increased conduction velocity in the His-Purkinje system appears to occur by lowering potassium concentration. Furthermore, initial lowering of potassium concentration in group 2 experiments caused a prolongation of the intranodal conduction time, which could explain the total delay in A-V conduction. The addition of quinidine to the low potassium solution prolonged both the intra-atrial and the His-Purkinje conduction times but prevented further prolongation of the intranodal conduction time.

Group 3 experiments have clearly demonstrated that the effects of a high potassium concentration on A-V transmission are similar to those of quinidine. Marked prolongation of the A-V interval was due to a delay in the intra-atrial and the His-Purkinje conduction without significant change in the intranodal conduction time.

**ACTION POTENTIAL CONFIGURATION**

**Group 1 experiments.** Following perfusion with quinidine, the atrial fibers showed a decrease in the amplitude of the action potential (Table 1). Although no quantitative

![Figure 7](http://circres.ahajournals.org/)

*Changes in conduction time across individual regions of the A-V conducting system. A, N and HP represent intra-atrial, intranodal and His-Purkinje conduction time, respectively. Total A-V interval equals the sum of these conduction times. Cont. = control perfusate, K = 4.5 mEq/liter; Quin. = quinidine, 10 mg/liter; low K = low potassium perfusate, K = 1.5 mEq/liter; High K = high potassium perfusate, K = 7.5 mEq/liter. Discussion in text.*
measurement could be made, a decrease in the rate of depolarization was apparent. The action potential duration (at 80% of repolarization) was significantly prolonged in both driven and spontaneously beating hearts (Table 1). In the N and NH fibers, on the other hand, quinidine caused a significant decrease in both the driven and spontaneously beating hearts. The rate of repolarization was decreased in the N fibers, increased in the NH fibers, and unchanged in the N and NH fibers. The rate of depolarization was increased in the N fibers, increased in the NH fibers, and unchanged in the N and NH fibers. The duration of the action potential of the NH fibers showed little change. Furthermore, failure of A-V conduction, A-V block, and local responses did not develop. The action potential duration was observed in both driven and spontaneously beating hearts. The action potential duration was observed in both driven and spontaneously beating hearts.

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>No. of hearts</th>
<th>Condition</th>
<th>Atrial and AN fibers</th>
<th>N and NH fibers</th>
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<tr>
<td></td>
<td></td>
<td>Action potential amplitude (mv) (mv)</td>
<td>Action potential duration (msec) (msec)</td>
<td>Action potential amplitude (mv) (mv)</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>Control</td>
<td>76.9</td>
<td>117.7</td>
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<tr>
<td></td>
<td></td>
<td>Quinidine (10 mg/liter)</td>
<td>71.0 -7.7%</td>
<td>165.5 +40.8%*</td>
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<tr>
<td></td>
<td></td>
<td>+ low K+ (1.5 mEq/liter)</td>
<td>78.0 +9.9%</td>
<td>194.0 +17.2%</td>
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<tr>
<td>11</td>
<td>13</td>
<td>Control</td>
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<td>121.4</td>
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<tr>
<td></td>
<td></td>
<td>Low K+ (1.5 mEq/liter)</td>
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<td>130.5 +7.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ quinidine (10 mg/liter)</td>
<td>76.0 -2.9%</td>
<td>192.4 +47.3%</td>
</tr>
<tr>
<td>L11</td>
<td>7</td>
<td>Control</td>
<td>76.3</td>
<td>120.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High K+ (7.5 mEq/liter)</td>
<td>74.5 -2.4%</td>
<td>140.9 +17.2%</td>
</tr>
</tbody>
</table>

*Changes statistically significant (P < 0.05).

†Consistent prolongation of the action potential duration was observed in both driven and spontaneously beating hearts.

Group 2 experiments. Lowering of potassium concentration caused a minimal prolongation of the action potential duration in the atrial fibers. The amplitude of the action potential duration in the NH fibers appeared to be slightly increased in the presence of quinidine in the NH fibers. The rate of depolarization in the NH fibers was decreased in the presence of quinidine in the NH fibers. The rate of repolarization was increased in the NH fibers. Failure of A-V conduction, A-V block, and local responses in the NH fibers did not develop. Failure of propagation and second degree A-V block occurred in both driven and spontaneously beating hearts. The action potential duration was prolonged in the NH fibers in the presence of quinidine. Failure of A-V conduction, A-V block, and local responses in the NH fibers did not develop. Failure of propagation and second degree A-V block occurred in both driven and spontaneously beating hearts.
depolarization appeared decreased in the atrial and the NH fibers, while that in the N fibers remained essentially unchanged.

**Group 3 experiments.** Following elevation of the potassium concentration, the atrial fibers showed a decrease in the rate of depolarization. The duration of the action potential was slightly but insignificantly prolonged. In the N and the NH fibers, on the other hand, both amplitude and duration of the action potential were significantly increased (Table 1). The rate of depolarization in these fibers appeared relatively unchanged.

Similar to quinidine, second degree A-V block due to high potassium was associated with normal intranodal conduction, with the maintenance of good action potentials up to the distal NH region and failure of propagation below this area.

In addition to these changes in the action potential configuration of various fibers, slowing of intra-atrial and intraventricular conduction due to quinidine or high potassium was manifested by widening of the atrial and ventricular electrograms.

**Discussion**

In the present study of isolated perfused rabbit hearts, quinidine (10 mg/liter) consistently and markedly prolonged the A-V conduction time (Figs. 1 and 3). A quinidine concentration of 10 mg/liter in plasma is considered a toxic level (12). Approximately 80% of quinidine in plasma is bound to plasma albumin. Therefore a concentration of 10 mg/liter of protein-free perfusate, as utilized in this study, is even higher than the toxic concentration of free quinidine in human plasma. However, Bennett et al. observed similar degrees of prolongation of the P-R interval (twofold the control value) with a 8 to 10 mg/liter of plasma quinidine concentration in dogs (7). Furthermore, in our laboratory, concentrations of 6 to 8 mg/liter in preliminary experiments produced inconsistent results in perfused rabbit hearts. Hence, species difference may account for the requirement of a higher level of quinidine to produce toxic effects in rabbit as compared to dog or man.

Localization of the effects of quinidine within the A-V conducting system has never been attempted by previous investigators. In addition, the interactions of quinidine and potassium within the three regions of the A-V node have not been studied. In the present experiments, it was clearly demonstrated that the prolongation of the A-V interval due to quinidine resulted from a slowing of intra-atrial and His-Purkinje-ventricular conduction, while conduction across the A-V node (especially its N region) remained unaffected (Figs. 4 and 7). Slowing of intra-atrial transmission was accompanied by a decrease in the amplitude of the action potential and the rate of depolarization in the atrial fibers. Prolongation of the His-Purkinje and intraventricular conduction time can be attributed to a similar reduction in the rate of depolarization in Purkinje (13) and ventricular (8, 13, 14) fibers. Quinidine significantly increased the action potential amplitude in the N and the NH fibers, with little change in the rate of depolarization in the N fibers (Table 1). These findings could satisfactorily explain the maintenance of 1:1 A-V conduction in the presence of extremely prolonged A-V intervals due to quinidine as normal conduction is preserved through the crucial N region of the A-V node. The present study is not in keeping with a previous preliminary report by Sano et al. (6) demonstrating alterations of the configuration of the action potential of the A-V junctional fibers by quinidine. However, the functional subdivisions of the three regions of the A-V node (11) were not known at that time, and a precise interpretation of the earlier results cannot be made.

In some instances, high potassium concentration (7.5 mEq/liter) was without appreciable effect on A-V transmission. However, when high potassium prolonged the total A-V interval, the transmission delay occurred predominantly in the intra-atrial and His-Purkinje conducting system, while normal conduction was preserved across the A-V node (Figs. 6 and 7). Similar observations were
previously reported by Paes de Carvalho and Langan (2). However, correlation of these findings with the changes in the action potential configuration was not described. In this regard, the present study demonstrated a significant increase in the amplitude of the action potential in the N and the NH fibers following high potassium perfusion (Table 1). The action potential amplitude and the rate of depolarization in the atrial fibers decreased. Hence, the effects of high potassium concentration on A-V transmission were quite similar to those of quinidine, and the effects of these two agents may be additive (Fig. 3).

Second degree A-V block due to excessive quinidine, high potassium, or combination of both was characterized by failure of transmission below the NH region or in the His-Purkinje-ventricular conducting system. Lowered potassium concentration alone selectively depressed conduction through the N region of the A-V node (Figs. 5 and 7). Intra-atrial as well as His-Purkinje-ventricular transmission were relatively unaffected. These findings are again in keeping with the previous report (2). Most of these changes in conduction can be explained by the following effects of low potassium on the action potential configuration: (A) a significant decrease in the amplitude of the action potential and the rate of depolarization in the N fibers, (B) a slight decrease in the rate of depolarization in the NH fibers, and (C) no appreciable change in these parameters in the atrial fibers (Table 1). These results as well as the development of local response and failure of propagation in the N and the NH regions in second degree A-V block are quite similar to those with digitalis (10).

Antagonism of quinidine and low potassium concentration on A-V transmission was demonstrated in the experiments of groups 1 and 2. Lowering of potassium concentration in the presence of quinidine resulted in a shortening of the A-V conduction time, while the addition of the same amount of quinidine often produced less marked prolongation of the A-V interval when potassium was low than when normal (Fig. 1). Return from a low to normal potassium concentration in the presence of quinidine caused a marked prolongation of the A-V conduction time (Fig. 2), further illustrating antagonism of low potassium and quinidine.

Low potassium-induced shortening of the A-V interval in the presence of quinidine resulted predominantly from a shortened conduction time in the His-Purkinje-ventricular conducting system (Fig. 7). In these experiments, action potentials of Purkinje fibers were not studied. However, our previous observations showed that quinidine decreased the rate of depolarization in ventricular fibers and subsequent lowering of the potassium concentration restored it toward normal (8). Similar antagonism may well take place in the His-Purkinje conducting system. The rate of depolarization in the atrial fibers was also increased by low potassium, in the presence of quinidine. Hence, it can be generalized that the toxic doses of quinidine used in these experiments depressed conduction in the atrial and His-Purkinje-ventricular transmission system while low potassium enhanced conduction in those tissues. The beneficial effects of slowing of the heart rate in the spontaneously beating hearts must be considered, as the shortening of the A-V interval due to lowering of potassium concentration was less significant in the electrically driven hearts. However, the decrease in the heart rate following the lowering of potassium concentration in the presence of quinidine was usually less marked than during the preceding period of quinidine perfusion. Hence, low potassium-induced acceleration of His-Purkinje conduction in the presence of quinidine cannot be explained by the heart rate change alone. Furthermore, the present study demonstrated that the amplitude of the action potential and the rate of depolarization in the N fibers were increased by quinidine, whereas low potassium perfusion showed an opposite effect (Table 1). Thus, low potassium depressed while quinidine apparently protected conduction through this crucial region of the A-V node, a finding which stands
in sharp contrast to other portions of the A-V conducting system.

From these observations, it is easily understood that the combined effects of quinidine and low potassium result from a complex interplay of their effects on each component of the A-V conducting system. Whether the net results of the antagonism in a particular region would be depression or enhancement of conduction may depend on the relative concentration of quinidine and potassium. Hence, the following statements may summarize the interactions of low potassium and quinidine: When quinidine effects predominate over those of low potassium, the A-V interval may be markedly prolonged, with maintenance of 1:1 A-V conduction. When low potassium effects predominate, the A-V interval may remain relatively unchanged before second degree A-V block develops within the A-V node.

However, dissimilar sensitivity of different fiber types to these agents as well as the influence of other localized electrophysiologic derangements would obviously affect the overall response of A-V conduction in individual hearts. Under certain conditions, the effects of low potassium and of quinidine may even become additive, as the former depresses A-V nodal conduction and the latter slows intra-atrial and His-Purkinje transmission. Actually, in the terminal stage of some of the experiments, advanced second degree A-V block was observed with failure of propagation both within the A-V node (N-NH regions) and below the NH region (or in the His-Purkinje system) (15). Since it has been demonstrated that the effects of low potassium on A-V transmission appears quite similar to those of digitalis (10), the above statement may well apply to the interactions of digitalis and quinidine (or high potassium).

On the contrary, combination of high potassium concentration and quinidine appeared additive in depressing intra-atrial and His-Purkinje transmission (Fig. 3). These results are in agreement with our previous report on ventricular fibers (8). The combined effects of digitalis and low potassium concentration in depressing intranodal conduction may also be inferred from these and previous studies (10). These findings on the interrelationships of quinidine and potassium may support or deny important clinical decisions in the use of these agents.

Addendum
Since the completion of this manuscript, Wallace et al. (Circulation Res. 19: 960, 1966) demonstrated no change in atrial-His bundle conduction following quinidine infusion (5.4 to 10.6 mg/liter) in intact awake dogs. The present study shows that quinidine may selectively affect intra-atrial and intranodal transmission. Hence, measurement of the atrial-His interval is not sufficient to characterize conduction across the A-V node.

References


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