Effect of Digitalis on Atrioventricular Conduction and Circus-Movement Tachycardias in Patients with Wolff-Parkinson-White Syndrome

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SUMMARY
During regular driving of the right atrium using the single-test stimulus method, atrioventricular conduction and initiation of tachycardias were studied in six patients with the Wolff-Parkinson-White syndrome (W-P-W), before and 45 min after the administration of ouabain (0.75-1.5 mg into the right atrium).

Following ouabain (1) all patients showed shortening of the refractory period of their anomalous pathway; (2) at least five of them showed lengthening of the refractory period of the A-V nodal-His pathway; and (3) all patients showed prolongation of the A-V nodal transmission time (prolongation of the A-H interval). In four patients who suffered from circus-movement tachycardias these changes resulted in two patients in marked shortening of the range of premature beat intervals during which a tachycardia could be initiated and complete inability to initiate a tachycardia in the other two. These results suggest that digitalis can be of prophylactic value in patients with the Wolff-Parkinson-White syndrome and circus-movement tachycardias.

Additional Indexing Words:
Electrical stimulation  Accessory pathway  Ouabain  Refractory period

As demonstrated by epicardial excitation mapping,1-3 electrical stimulation of the heart,4-6 His bundle recordings,7 and outcome of surgical interventions8, 9 two pathways between atria and ventricles are present in patients with the Wolff-Parkinson-White (W-P-W) syndrome. These connections (the A-V nodal-His pathway and the accessory A-V pathway) differ in their electrophysiologic properties, which can lead to alterations in QRS complex configuration following changes in heart rate and atrial premature beats. The differences in properties are essential in the genesis of circus-movement tachycardias in patients with the W-P-W syndrome. As shown,4-6 a critically timed atrial premature beat can find one pathway (pathway B) refractory and be conducted to the ventricles by way of the other pathway (pathway A). If this is followed by ventriculoatrial conduction by pathway B, and subsequent atrioventricular conduction by pathway A, a circus movement is completed. A movement of this type may also follow a critically timed ventricular premature beat if a similar response pattern occurs. Perpetuation of such a circus movement results in a tachycardia. Usually atrioventricular conduction during such a tachycardia is by way of the A-V nodal-His pathway and ventriculoatrial conduction via the accessory pathway.

Both the atrioventricular conduction by the two pathways and the mode of initiation of tachycardias in patients with the W-P-W syndrome can be studied by applying premature stimuli to the atrium during regular driving of the atrium. The same method can also be used to investigate the effect of drugs on atrioventricular conduction and on initiation of tachycardias in patients with this syndrome. Ouabain was the drug used in this study.

METHODS
Six patients were studied (table 1). All had the characteristic findings of the W-P-W syndrome (P-delta interval of 0.12 sec or less, a delta wave, and a QRS width of 0.12 sec or more). According to Rosenbaum's classification10 four had type A W-P-W and two type B. Four patients suffered from tachycardias. By use of the Seldinger technic electrode catheters were passed under
local anaesthesia through the femoral veins and positioned at the desired intracavitary location. A bipolar catheter was used for stimulation of the right atrium. With help of another bipolar catheter the intracavitary atrial complex was registered. A tripolar catheter was used to record the electrogram of the His bundle. A description of the stimulator has been given previously. In all patients atrioventricular conduction was studied by way of a premature stimulus to the right atrium once after eight beats of a regular driven atrial rhythm. The interval between the last beat of the regular driven rhythm and the induced premature beat (the premature beat interval) was thereby gradually shortened until the atrium became refractory to stimulation. The premature beat interval at which the anomalous pathway and the A-V nodal-His pathway became refractory, and the range of premature beat intervals during which a tachycardia could be initiated were carefully determined.

The same measurements at exactly the same driving frequencies were made 45 min following 0.75–1.5 mg ouabain given directly into the right atrium. Both before and after ouabain these measurements were repeated three times. Care was taken not to move the stimulating and recording electrodes from the position they had prior to the administration of ouabain. The results of our stimulation studies were observed in the ECG of leads I, II, III, V1, and V6, the His bundle lead and the bipolar intratrial lead. The His bundle lead and the bipolar intratrial recordings were made with the help of an Elemen amplifier-type EMT 12. The electrocardiograms were registered on an eight-channel high-frequency direct-writing Elema recorder and stored on magnetic tape with an Ampex FR 1300 tape recorder.

**Results**

As shown in table 2, prior to ouabain injection the anomalous pathway became refractory before the A-V nodal-His pathway in five patients. In patient D atrioventricular-His conduction was blocked at a premature beat interval shorter than 350 msec. The ventricular complex following an atrial premature beat given after an interval of 350 msec showed conduction by way of the anomalous pathway. We could not exclude the possibility that at that premature beat interval A-V conduction also took place by way of the A-V nodal-His pathway with the His bundle electrogram buried in the ventricular complex. In patients A, B, C, and F the A-V nodal-His pathway was able to conduct the atrial premature beat up to the refractory period of the atrium. In the same four patients an atrial premature beat given after an interval shorter than the refractory period of the anomalous pathway initiated a tachycardia.

The mode of initiation and the configuration of the QRS complexes during the tachycardia were compatible with a circus movement, with A-V conduction via the A-V nodal-His pathway, and ventriculoatrial conduction by way of the anomalous bypass. Although it is theoretically possible that A-V nodal reentry was the mechanism of the tachycardia, this seems unlikely in view of the fact that all premature beats given in the interval range between the refractory period of the anomalous pathway and the refractory period of the A-V nodal-His pathway, were followed by a tachycardia.

The phenomenon of a reentry zone during which premature beats initiate a tachycardia with no tachycardia following very early premature beats, which is frequently found in A-V nodal tachycardias, was absent in our patients. In one patient the simultaneous recording of left and right atrial activation showed that during the tachycardia (in this patient with W-P-W type A) left atrial activation preceded right atrial activation by 90 msec.

The range of atrial premature beat intervals during which a tachycardia could be initiated measured 50, 90, 80, and 80 msec, respectively. Following ouabain all patients showed shortening of the refractory period of their accessory pathway.

**Table 1**

**Description of Patients Studied**

<table>
<thead>
<tr>
<th>Pt</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Type W-P-W</th>
<th>Taehy</th>
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<tbody>
<tr>
<td>A</td>
<td>M</td>
<td>34</td>
<td>A</td>
<td>+</td>
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<tr>
<td>B</td>
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<td>+</td>
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<td>F</td>
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<td>A</td>
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</tr>
<tr>
<td>E</td>
<td>F</td>
<td>41</td>
<td>B</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>F</td>
<td>27</td>
<td>A</td>
<td>+</td>
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</tbody>
</table>

**Table 2**

**Effect of Ouabain Injections on the Refractory Period of the Anomalous Pathway, Atrioventricular-His Conduction, and Right Atrium in Six Patients**

<table>
<thead>
<tr>
<th>Time</th>
<th>A</th>
<th>R</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>b</td>
<td>230*</td>
<td>300*</td>
<td>270*</td>
<td>350*</td>
<td>360*</td>
</tr>
<tr>
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<td>350</td>
<td>285</td>
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<tr>
<td>AVH</td>
<td>b</td>
<td>180</td>
<td>210</td>
<td>190</td>
<td>≥350</td>
<td>280</td>
</tr>
<tr>
<td>a</td>
<td>≥210</td>
<td>≥260</td>
<td>250</td>
<td>≥390</td>
<td>≥350</td>
<td>270</td>
</tr>
<tr>
<td>RA</td>
<td>b</td>
<td>180</td>
<td>210</td>
<td>190</td>
<td>230</td>
<td>275</td>
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<td>220</td>
<td>180</td>
<td>210</td>
<td>270</td>
<td>240</td>
</tr>
</tbody>
</table>

Abbreviations: b = before ouabain injection; a = after injection; AP = anomalous pathway; AVH = A-V nodal-His pathway; RA = right atrium.

*Basic cycle length during atrial pacing was 600 msec.
†Basic cycle length during atrial pacing was 700 msec.

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Figure 1

Patient E. Lead II and the His bundle lead are shown. Prior to ouabain during right atrial pacing (basic cycle length 600 msec) the anomalous pathway becomes refractory at a premature beat interval (S2-S1) of 360 msec (A), and the A-V nodal-His pathway at a S2-S1 interval of 280 msec (C). The right atrium was refractory to S1-S2 intervals shorter than 275 msec.

ranging from 10 to 50 msec (table 2). Lengthening of the refractory period of the A-V nodal-His pathway was observed in five patients (ranging from 30 to 70 msec). In patient D the latter could not be determined for reasons given above. As described under Methods, the refractory periods of the two pathways and the range of tachycardia-initiating premature beat intervals were determined in three consecutive scans before and after ouabain administration. The differences in values never measured more than 5 msec. The two identical figures are given in table 2. As shown in this table the refractory period of the anomalous pathway became shorter or at least equal to that of the A-V nodal-His pathway in three patients (A, B, and F) (figs. 1 and 2). It was also observed that the transmission time through the A-V node increased (prolongation of the A-H interval). Measurements of the A-H interval became impossible when at short premature beat intervals the His bundle electrogram became buried in the QRS complex. The combination of shortening of the refractory period of the anomalous pathway, lengthening of the refractory period of the A-V nodal-His pathway, and prolongation of the A-H interval resulted in: (1) A greater amount of preexcitation following ouabain if one compared QRS complexes at identical atrial pacing rates and after equal atrial premature beat intervals before and after ouabain administration. (2) A marked reduction of the premature beat interval range during which tachycardias could be initiated in patients C and F (from 80 and 80 msec, respectively, to 10 and 15 msec) and inability to initiate a tachycardia in patients A and B, the refractory period of the A-V nodal-His pathway now being equal or longer than that of the anomalous bypass (figs. 3 and 4).

Figure 2

Patient E. After ouabain the refractory period of the anomalous pathway measured 350 msec (A). No A-V conduction was seen at shorter premature beat intervals. The right atrium was refractory to atrial premature beats with S1-S2 intervals shorter than 270 msec (C). Like in figure 1 the basic cycle length during atrial pacing was 600 msec.

Figure 3

Patient B. Lead I and the His bundle lead are shown at four different premature beat intervals. Prior to ouabain the anomalous pathway becomes refractory at an S1-S2 interval of 300 msec (C). This is followed by conduction via the A-V nodal-His pathway and a circus-movement tachycardia. The same was observed (D) until the atrium became refractory to stimulation (S1-S2 interval 210 msec). The basic cycle length during right atrial pacing was 600 msec.
Patient B. Following ouabain. Same leads as in figure 3. The anomalous pathway now becomes refractory at an S₂-S₃ interval of 290 msec (C). The refractory period of the A-V nodal-His pathway could not be measured because no His bundle complex could be identified in the QRS complex at S₁-S₂ intervals < 320 msec. Note that the S₁-H₃ interval at a S₃-S₄ interval of 340 msec now measured 180 msec as compared to 155 msec prior to ouabain (fig 3).

In two patients (C and F) where tachycardias still could be initiated, the frequency of the tachycardia decreased due to an increase in A-H interval (20 and 30 msec, respectively). No change in the interval between QRS complex and atrial activation was seen. In one patient (patient A) we observed a reduction in the time interval between the atrial complex and the beginning of ventricular activation by way of the anomalous pathway when we compared these intervals before and after ouabain administration at identical pacing rates (fig 5).

Discussion

Already in 1943 Fox et al.12 observed that in a patient with the W-P-W syndrome the degree of preexcitation increased following digitalis. They attributed this finding to depression of the function of the A-V node. Damato and co-workers10,14 using the single-test stimulus method reported that in the human heart digitalis increased the refractory period of the A-V node and prolonged the A-V conduction time (by prolonging the A-H interval). This is in agreement with the microelectrode studies by Watanabe and Dreifus.15 We also found lengthening of the refractory period of the A-V node and prolongation of A-V nodal transmission time after digitalis administration in our patients with the W-P-W syndrome. Unfortunately following early premature beats measurement of the A-H interval became impossible, the His bundle electrogram being lost in the ventricular complex. We therefore do not have exact figures on the changes in the functional and effective refractory periods of the A-V node after ouabain. The refractory period of the anomalous pathway shortened.

For the initiation and maintenance of the circus-movement tachycardia critical time relations are necessary between conduction velocity and refractory periods of the different parts of the tachycardia circuit. It has been generally accepted that changes in these time relations following the administration of digitalis can stop the tachycardia. As our findings indicate, changes in the electrophysiologic properties in two parts of the tachycardia circuit, the A-V nodal-His pathway, and the anomalous pathway following digitalis administration can result in prevention of circus-movement tachycardias in patients with the W-P-W syndrome.

An example is given by patient B. He was completely incapacitated from tachycardias that could not be controlled by quinidine, pronestyl, or β-blocking agents given alone or in combination. Surgical dissection of one of his atrioventricular connections was seriously considered. Based upon the outcome of our study we placed him on a
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prophylactic regimen of digoxin. He did not have a single attack of tachycardia for the past 7 months. In the failing heart with W-P-W, digitalis, apart from influencing the electrophysiologic properties of the different part of the tachycardia pathway, may be helpful by reducing cardiac dimensions (the tachycardia circuit) and preventing ectopic activity. Our results seem to enforce caution in the use of digitalis in patients with W-P-W syndrome who suffer from atrial fibrillation.

As documented by Dreifus et al., this arrhythmia in the presence of an anomalous bypass with short refractory period can be life threatening. This makes digitalis a hazardous drug to use in patients with atrial fibrillation and a short refractory period of the anomalous pathway. A further reduction of the refractory period of the anomalous pathway following digitalis might lead to an increase in ventricular rate during atrial fibrillation. In those with a long refractory period of their accessory pathway a reduction of the refractory period by 10–50 msec will not lead to a serious increase in ventricular frequency and digitalis might still be beneficial. We feel that if one considers digitalis on a prophylactic basis one should be informed about the type of tachycardia present in a particular patient.

Ideally the properties of the A-V conduction system and the mechanism of the tachycardias should be studied before making a definite decision. The changes in electrophysiologic properties of the anomalous bypass and the A-V nodal-His pathway after ouabain argue for structural differences between the two pathways. In our patients the refractory period of the right atrium did not change significantly following ouabain administration, which is in accordance with data from Moe and Han. As pointed out by Hoffman digitalis shortens the refractory period of the ventricular myocardium and Purkinje fibers. In our patients we did not systematically measure the refractory period of the ventricle before and after ouabain. Therefore, although in our patients the anomalous pathway did not behave like atrial muscle, we do not know whether its electrophysiologic properties are more like those of the ventricle.

References


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