Effect of Lidocaine on Atrioventricular Response Via the Accessory Pathway in Patients with Wolff-Parkinson-White Syndrome

MASOOD AKHTAR, M.D., CAROL J. GILBERT, R.N., AND MOHAMMAD SHENASA, M.D., PH.D.

SUMMARY Electrophysiologic effects of i.v. lidocaine were evaluated in 10 patients with Wolff-Parkinson-White (WPW) syndrome during atrial fibrillation (AF) (eight of 10) or programmed atrial stimulation (nine of 10). The shortest RR intervals during AF were 190–415 msec (mean 271.8 ± 64.5 msec) before lidocaine and decreased to 250.0 ± 85.4 msec (range 180–435 msec, p = NS) after the drug. In six of eight patients, the shortest RR interval decreased and in the remaining two patients it increased by 20 msec after lidocaine. After lidocaine, the average RR intervals during AF for all eight patients decreased from 351.1 ± 45.9 msec to 335.6 ± 68.0 msec (p = NS). After lidocaine, the RR interval shortened in all of eight patients, lengthened in two and did not change in one. In two of eight patients, acceleration of ventricular rate after lidocaine was accompanied by hemodynamic deterioration, necessitating DC cardioversion in one. The control effective refractory period of the accessory pathway (ERP-AP) was 300 msec or less in all patients, and lidocaine prolonged this variable in only one case. In the remaining patients, after lidocaine the ERP-AP either shortened (two of nine), did not change (two of nine) or atrial refractoriness precluded its determination. Similarly, during incremental pacing, the atrial cycle length that produced block in the AP shortened in five patients, lengthened in one and did not change in the others.

In patients with WPW syndrome and relatively short ERP-AP (i.e., ≤ 300 msec), lidocaine generally has no significant effect or produces acceleration of ventricular response during AF. In patients with AF and a rapid ventricular rate due to antegrade conduction over the AP, lidocaine is unlikely to have beneficial effects and may be deleterious.

ATRIAL FIBRILLATION (AF) can be a life-threatening arrhythmia in patients with the Wolff-Parkinson-White syndrome. The rate of preexcited ventricular responses during AF in these patients is primarily determined by the electrophysiologic properties of the AP in the antegrade direction. Several investigators evaluated effects of various pharmacologic agents upon the functional properties of the AP. Most studies so far have dealt with the responses of AP during programmed cardiac stimulation. Rarely have the efficacy and possible deleterious effects of a given drug been assessed during actual AF in patients with ventricular preexcitation. Surprisingly, rather limited data are available dealing with the response of AP to the commonly used antiarrhythmic agents during AF. With the exception of a single case report, even the effects of lidocaine have not been tested in this setting.

The present study was undertaken to systematically evaluate the effect of lidocaine on the electrophysiologic properties of the AP, with particular emphasis on ventricular response during AF in 10 patients with WPW syndrome.

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Table 1. Clinical and Electrophysiologic Data

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<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
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<th>WPW type</th>
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All values pertaining to electrophysiologic data are expressed in milliseconds.

*After an i.v. bolus of 2 mg/kg.

Abbreviations: MVP = mitral valve prolapse; C = control; L = after lidocaine; BCL = basic cycle length; ERP = effective refractory period; FRP = functional refractory period; AP = accessory pathway; ACL = paced atrial cycle length.

Methods

Electrophysiologic studies were performed in a postabsorptive, nonsedated state in 10 patients with ventricular preexcitation. The nature of the procedure was explained to all patients and signed consents were obtained. Under local anesthesia with lidocaine (1% without epinephrine), two or three multipolar electrode catheters were percutaneously introduced into peripheral veins. All 10 patients received a total of less than 150 mg of lidocaine and nine received less than 100 mg. With fluoroscopic guidance the catheters were positioned in the high right atrium, left atrium (via patient foramen ovale or coronary sinus), right ventricle and atrioventricular (AV) junction to record local electrical activity or for local pacing.18

All intracardiac electrograms (filter frequency 30–500 Hz), three surface ECG leads (I, II and VI) and time lines were simultaneously displayed on a multichannel oscilloscope and recorded on a magnetic tape for later reproduction. Electrical stimulation was accomplished with a digital stimulator delivering rectangular impulses with adjustable amplitude and duration. All equipment was carefully grounded and patient isolation existed during the conduct of these studies. Electrophysiologic properties of the atrium and AP were evaluated with incremental atrial pacing and atrial premature stimulation as previously described.18 After baseline programmed stimulation, atrial fibrillation (AF) was induced with rapid atrial pacing. After the AV response over the AP during AF had been observed for 5 minutes or longer, lidocaine was administered initially as an i.v. bolus (2 mg/kg), followed by an i.v. infusion (3–4 mg/min) (table 1), and the studies were repeated. The sequence of repeat study depended upon the response of induced AF. If AF was of short duration and self-terminating, programmed atrial stimulation was repeated first and AF was induced later. When AF was sustained for more than 10 minutes, lidocaine was administered during the AF and programmed atrial stimulation was repeated if AF spontaneously ceased before termination of the study. In most instances, the repeat study was completed within 15 minutes after lidocaine administration. Blood for determination of lidocaine levels was drawn immediately before and 5–10 minutes after lidocaine administration. Plasma lidocaine concentrations were measured by gas chromatography at 180°C with a flame ionization detector that has a reproducibility of ± 10%. Statistical analysis was done using the test for paired data.

Definition of Terms

Atrial Effective Refractory Period (ERP): The longest $S_1S_2$ interval ($S$ representing stimulus artifact) where $S_2$ fails to produce an atrial ($A_3$) response.

Atrial Functional Refractory Period (FRP): The shortest $A_1A_2$ interval in response to progressively shorter $S_1S_2$.

$ERP_{-AP}$: The longest $A_1A_2$ where $A_2$ fails to conduct via the AP.

In addition, the shortest $V_1V_2$ interval in response to the full range of $A_1A_2$ was measured during conduction over the AP.

During AF, the average RR cycle length/minute as well as the shortest RR intervals were analyzed. The average RR cycle lengths were measured over several minutes if AF was sustained. When AF was of short duration, the RR intervals were measured during several episodes of 30 seconds or longer and averaged. To obtain the shortest RR interval the entire recorded episode of AF was analyzed. For measurement of the shortest RR interval, the earliest detectable portion of the QRS complex on the surface ECG or intracardiac
electrogram tracing closest to the AP was used. For all of the RR measurements mentioned above, the analysis was made when AV response occurred over the AP without an interposed QRS complex of normal morphology.

Results

The clinical, electrocardiographic and electrophysiologic data in the 10 patients are summarized in table 1. At the time of study all patients were in sinus rhythm and had been off cardioactive medications for more than 72 hours. Electrophysiologic studies revealed a right-sided AV AP in patients 3, 6, 8, 9 and 10 and a left-sided AP in the remaining five. Pacing from both right and left atria was performed in nine of 10 patients; however, the data in table 1 are from pacing and recording sites closer to the AP.

Observations During AF

The AF was sustained for longer than 10 minutes in patients 1-4 and for more than 5 minutes in patients 5 and 6. In patients 8 and 9, the episodes of AF were short and it was necessary to induce AF repeatedly to evaluate the ventricular response over the AP. In the remaining two cases (patients 7 and 10), AF spontaneously terminated within a few cycles and the ventricular response during AF could not be adequately assessed.

The shortest RR interval for these eight patients was 271.8 ± 64.5 msec (mean ± sp) (range 190–415 msec) before and 250.0 ± 85.4 msec (range 180–435 msec) after lidocaine (p = NS) (fig. 1A). Six of the eight patients (nos. 1–6, table 1) showed a decrease in the shortest RR interval after lidocaine, whereas the remaining two cases (nos. 8 and 9) showed an increase

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Shortest (A) and mean (B) RR values via the accessory pathway (AP) in eight patients during atrial fibrillation (AF) before and after lidocaine. Patients who showed a decrease in the RR intervals after lidocaine generally had the shortest control values. The patients who had an increase in RR intervals after lidocaine had the longest control values. The mean values are indicated by the interrupted line and were not significantly different.

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**Table 1.** (Continued)

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<th>ERP atrium</th>
<th>Incremental atrial pacing</th>
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<td>V',V via AP</td>
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in this measurement. The decrease in the shortest RR interval after lidocaine was more pronounced in patients 1-3 (table 1); a representative tracing is shown in figure 2.

For all eight patients, the mean RR interval over the period of measurement was 351.1 ± 45.9 msec (range 293-434 msec) during the control period. Lidocaine produced an overall shortening of this value to a mean of 335.6 ± 68.0 msec (range 276-458 msec, \( p = \text{NS} \)) (fig. 1B). In patients 1-5, the average values for RR intervals decreased, whereas in two of seven it increased after lidocaine (fig. 1B). Average RR values in the remaining patient (no. 6) showed minimal change (≤ 5 msec) after lidocaine. In patients 1-3, lidocaine produced an obvious shortening in the average RR interval (fig. 2, table 1), whereas in patient 9 lidocaine resulted in antegrade block in the AP during AF (fig. 3).

In three of five patients with sustained AF during the study, the blood pressure measurements did not change after lidocaine. Patient 1, who otherwise tolerated AF throughout the episode, had a decrease in systolic blood pressure of 20 mm Hg (120 to 100 mm Hg) 2 minutes after lidocaine. The remaining patient (no. 2) had tolerated long episodes of AF on several occasions and was stable until lidocaine was given. Within 3 minutes of drug administration, however, significant hemodynamic deterioration (hypotension with no recordable blood pressure) was noted, necessitating immediate DC cardioversion. In
both cases acceleration of ventricular response was observed before the hypotensive episodes.

None of the patients in this series experienced any documented episodes of VF before, during or after the electrophysiologic studies.

**Observations During Atrial Premature Stimulation**

**ERP-AP**

The ERP-AP could be determined in six of 10 patients during the control period and ranged from 270-300 msec (mean 283.3 ± 13.6 msec). In the other three cases (nos. 1, 4 and 5) the atrial FRP was encountered before the ERP-AP could be reached. After lidocaine, the ERP-AP was measured in five patients (nos. 6-10), and showed no change in two, a decrease of 10-20 msec in two and an increase of 50 msec in one (table 1). Even though the exact values could not be determined in the remaining three cases, the ERP-AP did not increase after lidocaine.

**Atrial ERP**

Atrial ERP could be tested in eight of 10 patients (nos. 1 and 4-10, table 1) before and after lidocaine, and showed no change in three of eight, shortened by 10 and 50 msec in two and increased by 10 msec in the remaining three.

**Observations During Incremental Pacing**

After lidocaine, the atrial cycle length that produced block in the AP decreased in five patients, remained unchanged in two and increased in one.

**Plasma Lidocaine Concentrations**

Control plasma lidocaine levels were available in eight of 10 cases and averaged 0.60 mg/l (range...
0.25-1.0 mg/l). Lidocaine concentration after the bolus and infusion ranged from 3.8-7.4 mg/l (average 4.9 mg/l) in the eight patients in whom the levels were available.

**Discussion**

The results of this study indicate that lidocaine in therapeutic doses generally does not prolong the refractoriness of the AP in patients with WPW syndrome. The results of other studies evaluating the effect of lidocaine on the AP suggest that lidocaine has a depressant effect on refractoriness of the AP.5, 17 Rosen et al.8 tested the response of the AP during incremental pacing in six patients. In four of these patients, lidocaine had a depressant effect on the AP and AP block occurred at a relatively long paced atrial cycle lengths (average 409 msec, range 375-750 msec) during the control period. In the other two patients, who had no block in the AP up to the paced atrial cycle length of 300 msec, lidocaine had no depressant effect. The ERP-AP was determined in two patients: One patient with a control value of 520 msec showed an increase, whereas the other showed a decrease (280 to 270 msec). These findings are compatible with ours.

In the only case report available showing the effect of lidocaine on the AP during AF, the results of incremental atrial pacing and premature stimulation and the shortest RR values during AF were not provided.17 If the tracing shown is representative of the average RR intervals at the time of study (460 msec), these are appreciably longer than the average RR intervals in the present study.17 The two patients (nos. 8 and 9) in the present series who had average control RR intervals measuring ≥ 380 msec also showed slowing of the ventricular response after lidocaine. Patients with AP block at paced atrial cycle lengths of less than 300 msec seem less likely, therefore, to show depressant effects of lidocaine as seen in this study and in the study by Rosen et al.8 Similar observations have been made previously, indicating that patients with control ERP-AP < 270 msec are less likely to demonstrate lengthening of ERP-AP after therapeutic agents known to prolong this measurement.19

During premature atrial stimulation, lidocaine either shortened the ERP-AP or had no effect, except in patient 9, whose ERP-AP was prolonged. Similarly, during AF, when the average RR was less than 360 msec or the shortest preexcited RR was ≤ 275 msec or less, lidocaine generally shortened those values. It appears that when a therapeutic agent is most needed, lidocaine is less likely to be effective and could be potentially deleterious, as in patient 2. Whether lidocaine exerts a differential effect on AP with long vs short refractory periods is uncertain and cannot be determined from the relatively small number of patients in this study.

Results of this and a previous study indicate that both the average and the fastest ventricular responses during AF cannot always be predicted from the values obtained during programmed atrial stimulation.14 Therefore, the drug efficacy during AF in patients with WPW syndrome should also be directly tested by induction of AF when feasible.14, 18

Before meaningful conclusions can be drawn from data such as these, problems inherent in this type of investigation should be considered. It may be argued that true control values as reported here and in other studies do not exist, as local lidocaine anesthesia is universally employed before insertion of the catheters. A recent report indicated that after local anesthesia with lidocaine (initial dose 100-250 mg, average 191 mg; subsequent doses 0-215 mg, average 74 mg), detectable blood levels of the drug were achieved.20 The whole blood levels were generally less than 1.0 mg/l, but the peak concentration in six patients was in a therapeutic range, i.e., 1-1.6 mg/l, which corresponds to a plasma concentration of 1.5-2.4 mg/l.20 It is not known if these subtherapeutic levels of lidocaine influence the AP. We attempted to minimize the amount of local anesthetic used, and in none of our patients did the plasma lidocaine level exceed 1 mg/l before the i.v. drug administration. In other reports, neither the control nor the study lidocaine levels were mentioned.

Sustained AF with moderate or rapid ventricular response may lead to anxiety, hypotension and reflex sympathetic stimulation, which might increase the ventricular response via the AP coincident with lidocaine administration. It is clear, however, that lidocaine in most of these patients did not have any depressant effect on the AP with or without concomitant sympathetic stimulation.

Another problem is the possibility of catheter-induced trauma to the AP.11 Local trauma to the AP during initial placement of catheters might cause prolonged refractoriness of the AP, and its recovery coinciding with the timing of study after lidocaine. With catheter-induced trauma to the AV bypass tracts, one would expect failure of conduction along the AP at least for a few beats, but this was not observed in most cases during either sinus rhythm or AF. Only patients 8 and 9 showed normalization of QRS complex during AF, and prolongation rather than shortening in the average and shortest RR intervals was noted after lidocaine. Thus, it is unlikely that catheter-induced trauma significantly contributed to the results obtained, particularly in patients with left-sided AP.

**Clinical Implications**

None of the patients in this series had suffered from VF, and the arrhythmia did not develop during the study. Sellers et al.16 reported VF related to digitalis in patients with control shortest RR values of 220 msec or less.15 Patients 1 and 3 in this series, with control shortest RR values of 230 msec or less, showed a further shortening of these values, to 180 msec, after lidocaine. Whether achievement of such short RR intervals after lidocaine could precipitate VF, or whether the drug will prevent its occurrence despite shortening of the RR interval, is unknown. In patients with a short
ERP-AP and a rapid ventricular response during AF, lidocaine will be expected to have no effect on or result in acceleration of ventricular rates. Lidocaine should not be administered to such patients unless facilities for immediate cardioversion are available, as the drug could have a deleterious effect.

References

Effect of lidocaine on atrioventricular response via the accessory pathway in patients with Wolff-Parkinson-White syndrome.
M Akhtar, C J Gilbert and M Shenasa

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