Procainamide, Disopyramide and Quinidine: Discordant Antiarrhythmic Effects During Crossover Comparison in Patients With Inducible Ventricular Tachycardia

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A crossover comparison of intravenous procainamide, disopyramide and quinidine was made in 32 patients. All three drugs had dosage-related effects on electrocardiographic intervals, refractory periods and cycle length of ventricular tachycardia. Significant linear relations between serum drug levels and changes in refractory periods and ventricular tachycardia cycle length were also observed. Ventricular tachycardia was no longer inducible on at least one drug in 11 patients but concordance of this effect on both of the others was 36% and on either of the others it was 45%. Ventricular tachycardia remained inducible on at least one drug in 28 patients and concordance of this effect on both of the others was 75% and on either of the others was 79%.

Classification of antiarrhythmic agents into pharmacologically related subgroups is useful, particularly for the purpose of teaching. The most widely used classification scheme is based on the effects of drugs on cardiac action potentials of single cells from normal animal hearts (1). In this system, procainamide, disopyramide and quinidine are grouped together in class 1A. Such schemes have limitations and their clinical applicability is unproved. The effects of these drugs on single cell action potentials of normal cardiac tissue are not the same (2). Other potential limitations (3,4) include: 1) different direct cardiac effects on normal and diseased myocardium; 2) different indirect cardiac effects (vasodilation, autonomic blockade); and 3) different pharmacokinetic characteristics (protein binding, formation of active metabolites). These considerations have prompted retrospective clinical studies with conflicting results (5–7). These studies utilized a mixture of intravenous and oral dosage forms that are not always equivalent (8,9) and probably contributed to their conflicting results. Accordingly, a prospective crossover study was undertaken to assess the concordance of electrophysiologic and antiarrhythmic effects of these three drugs in patients with inducible ventricular tachycardia (10). To optimize the assessment of concentration-response relations and to minimize pharmacokinetic confounders such as active metabolite formation, the drugs were administered as a series of loading and maintenance intravenous infusions.

Methods

Selection of patients. Thirty-two patients with inducible, ventricular tachycardia/fibrillation at an antiarrhythmic drug-free catheter electrophysiologic study participated in this investigation. Inclusion required informed consent, reproducible (≥ twice) ventricular tachycardia/fibrillation in-
duction at baseline and repeat ventricular tachycardia/fibrillation induction immediately before each drug infusion. Patients without documented spontaneous ventricular tachycardia/fibrillation were included only when sustained unimorphic ventricular tachycardia was induced and the patient’s symptoms were reproduced.

**Study design.** Concentration-response relations were determined for all three drugs (procainamide, disopyramide and quinidine). After a baseline drug-free evaluation, each patient received each medication on separate days. Drugs were not administered in any particular order but their administration was not formally randomized. Testing of each drug was separated by a minimum of 24 and a maximum of 72 hours. Only when repeat testing of the next drug was performed 24 hours after the previous one were serum levels of the first drug measured at the second test. The previous drug was detectable in the serum of only two patients, and in these two the levels were well below the lower limit of the therapeutic range. The electrophysiologic effects and antiarrhythmic activity of each drug were assessed by transvenous catheter electrophysiologic study using the same pacing site (right ventricular apex in all instances) at which ventricular tachycardia was induced just before drug administration. Each antiarrhythmic drug was administered as a series of loading and maintenance intravenous infusions designed to produce two stable serum concentrations. The higher dose was administered only if ventricular tachycardia remained inducible on the low dose. The concordance of antiarrhythmic activity was assessed in this crossover design.

**Procedures.** Electrophysiologic testing was performed using commonly employed pacing and extrastimulus techniques. Patients were studied in the fasting state after all medications with known electrophysiologic effects had been discontinued for at least five half-lives. Surface electrocardiographic leads I, aVF and V_1_ were recorded simultaneously with intracardiac electrogroans from the high right atrium, His bundle site and right ventricular apex. Standard definitions were used to determine electrocardiographic intervals obtained at a paper speed of 100 mm/s. The rate-corrected QT interval was calculated from the formula QTc = QT/VRR(s). Ventricular effective and functional refractory periods were determined for single (S_2_), double (S_3_) and triple (S_4_) extrastimuli at basic pacing cycle lengths of 600, 500 and 400 ms. The S_2_S_3_ interval was progressively shortened by 10 ms until ventricular capture was lost. It was increased again (usually by 10 to 20 ms) until reliable ventricular capture was reestablished and then the S_2_S_3_ interval was progressively shortened by 10 ms until ventricular capture was lost. The same process was followed with the S_3_S_4_ interval after similarly setting the S_2_S_3_ interval.

**Ventricular tachycardia/fibrillation induction** was attempted with a protocol using right ventricular stimuli of 2 ms duration and an intensity of at least 10 times diastolic threshold. We have shown in a previous study (11) that no change in ventricular tachycardia inducibility accompanied changes in stimulus intensity from twice to 10 times the threshold. Single, double and triple extrastimuli were applied at basic pacing cycle lengths of 600, 500 and 400 ms. If necessary, bursts of rapid ventricular pacing at cycle lengths of 300 to 240 ms were used after completion of the extrastimulus portion of the protocol. This protocol is similar to that used by a number of other laboratories (12,13).

**Sustained ventricular tachycardia/fibrillation induction was defined** as a continuous ventricular rhythm with a cycle length of <500 ms, lasting for >30 seconds or requiring premature termination because of serious hemodynamic compromise. During drug therapy, completion of the entire induction protocol without production of five or more consecutive ventricular depolarizations at a cycle length of <500 ms was taken to indicate a complete antiarrhythmic response. Partial antiarrhythmic response was defined as an increase in the number of extrastimuli required to induce ventricular tachycardia/fibrillation. Completion of the extrastimulus portion of the protocol with subsequent ventricular tachycardia/fibrillation induction by rapid burst pacing was also considered to be a partial antiarrhythmic response. The term “harder to induce” will refer to either of these partial responses. The term “easier to induce” will refer to the observation that fewer extrastimuli were required to induce ventricular tachycardia/fibrillation. No patient required rapid burst pacing to induce ventricular fibrillation at the drug-free study.

**Drugs.** The lower dosage procainamide infusions were 0.25 mg/kg per min for 30 minutes, then 0.05 mg/kg per minute for a minimum of 15 minutes. The higher dosage procainamide infusions were an additional 0.15 mg/kg per min for 10 minutes, then 0.075 mg/kg per min for a minimum of 15 minutes. Similarly, the lower dosage disopyramide infusions were 0.14 mg/kg per min for 25 minutes, then 0.01 mg/kg per min for at least 15 minutes. The higher dosage disopyramide infusions were an additional 0.06 mg/kg per min for 5 minutes, then 0.015 mg/kg per min for at least 15 minutes. The higher dosage of disopyramide was not given when the drug-free left ventricular ejection fraction (gated nuclear angiogram) was <35%. The quinidine infusions were the same as those used in previous studies from this laboratory (14). Briefly the lower dosage quinidine infusions were 0.22 and then 0.11 mg/kg per min, each given for 25 minutes. The higher dosage disopyramide infusions were an additional 0.06 mg/kg per min for 5 minutes, then 0.015 mg/kg per min for at least 15 minutes. The higher dosage of disopyramide was not given when the drug-free left ventricular ejection fraction (gated nuclear angiogram) was <35%. The quinidine infusions were the same as those used in previous studies from this laboratory (14). Briefly the lower dosage quinidine infusions were 0.22 and then 0.11 mg/kg per min, each given for 25 minutes. The higher dosage quinidine infusions were an additional 0.17 and then 0.14 mg/kg per min, each given for 25 minutes.

**Electrophysiologic measurements** began no sooner than 15 minutes after the start of the last infusion for each dosage level. To verify constant serum levels, samples were obtained at the beginning and end of each series of electrophysiologic measurements. The serum drug levels reported
here and used for statistical purposes are the average of these two determinations. Procainamide, disopyramide and quinidine were measured using EMIT assays.

Data analysis. Continuous data are reported as the mean ± 1 SD. Proportions are presented ± SEE. Standard deviations and standard errors of the estimate are omitted from the figures when they overlap. Statistical analysis was done by chi-square technique for paired dichotomous data (Cochran's and McNemar tests). To compare continuous data within one drug treatment, the paired t test using Bonferroni's correction (15) was used on complete data (that is, data available for baseline, low and high drug dosages) and one-way analysis of variance and Tukey's test was used to include all data. To compare continuous data between drug treatments, multivariate analysis of variance using Bonferroni's correction for multiple comparisons was applied. The relations between serum drug levels and electrophysiologic measurements were examined by linear regression and linearity was tested by analysis of residuals. Programs from the Statistical Package for Social Sciences (version SPSS) (16) were utilized in data analysis. The null hypothesis was rejected when probability (p) was < 0.05.

Results

Study patients. All 32 patients had reproducibly induced ventricular tachyarrhythmias as the main criterion for entry into the study. Their clinical characteristics are outlined in Table 1. Most patients were men with coronary artery disease.

Inducibility of ventricular tachyarrhythmias: response rate. The overall antiarrhythmic activity of the three drugs, as determined by effects on ventricular tachycardia/fibrillation inducibility, were not significantly different. Cumulative response rates at low and high concentrations of each of the three drugs are depicted in Figure 1. The total number and proportion of patients who had a complete response to each drug were: five (16 ± 7%) for procainamide, six (19 ± 7%) for disopyramide and nine (28 ± 8%) for quinidine. Eight patients with a very low left ventricular ejection fractions (<0.35) did not receive the higher disopyramide dosage. In addition to the complete responders, there were some patients who had a "partial" response in that a greater number of extrastimuli (or burst pacing in two patients) were required to induce ventricular tachycardia/fibrillation (see Methods). The cumulative numbers and proportions of patients with a partial response to each drug were: six (19 ± 7%) for procainamide, six (19 ± 7%) for disopyramide and six (19 ± 7%) for quinidine. Combination of complete and partial responders results in cumulative numbers and proportions of patients who had potential antiarrhythmic effects as follows: 11 (34 ± 7%) for procainamide, 12 (38 ± 9%) for disopyramide and 15 (47 ± 9%) for quinidine. The remainder of the patients showed no evidence of a potential antiarrhythmic response to any of the three drugs.

No difference in the potential for a proarrhythmic effect was seen in comparison of the cumulative numbers and proportions requiring fewer extrastimuli to induce ventricular tachycardia (procainamide, seven [22 ± 7%]; disopyramide, six [19 ± 7%]; quinidine, seven [22 ± 7%]). The drug-free ventricular tachyarrhythmia cycle length and refractory periods tended to be shorter in those patients who were complete responders to each of the three drugs, but significant differences were seen only in the comparison of disopyramide responders and nonresponders (Table 2).

Table 1. Clinical Characteristics of Study Population

| No. of patients | 32 |
| Age (yr) | 56 ± 14 |
| Sex | 5F/27M |
| Cardiac diagnosis | |
| Coronary artery disease | 25 |
| Valvular heart disease | 3 |
| Arrhythmogenic right ventricular dysplasia | 2 |
| Primary electrical disease | 2 |
| Presentation | |
| Ventricular tachycardia, sustained | 12 |
| Recurrent syncope with inducible sustained ventricular tachycardia | 10 |
| Ventricular tachycardia, nonsustained | 6 |
| Ventricular fibrillation | 5 |

F = female; M = male.
Table 2. Drug-Free Electrophysiologic Measurements

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Response to Procainamide</th>
<th>Response to Disopyramide</th>
<th>Response to Quinidine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NI (n = 5)</td>
<td>I (n = 27)</td>
<td>NI (n = 6)</td>
</tr>
<tr>
<td>QRS interval</td>
<td>116 ± 36</td>
<td>115 ± 31</td>
<td>104 ± 33</td>
</tr>
<tr>
<td>QTc interval</td>
<td>448 ± 22</td>
<td>450 ± 29</td>
<td>452 ± 21</td>
</tr>
<tr>
<td>VTCL</td>
<td>217 ± 21</td>
<td>244 ± 42</td>
<td>208 ± 20*</td>
</tr>
<tr>
<td>VERP</td>
<td>224 ± 24</td>
<td>243 ± 48</td>
<td>215 ± 22</td>
</tr>
<tr>
<td>VFRP</td>
<td>257 ± 16</td>
<td>271 ± 29</td>
<td>246 ± 15*</td>
</tr>
</tbody>
</table>

*p < 0.05 NI versus I. All values are ms ± SD and were obtained just before drug administration. Patients are grouped according to subsequent antiarrhythmic response to each drug. I = remained inducible on this drug; NI = became noninducible on this drug; VERP = ventricular effective refractory period of S2 at pacing interval of 500 ms; VFRP = ventricular functional refractory period of S2 at pacing interval of 500 ms; VTCL = ventricular tachyarrhythmia cycle length.

Inducibility of ventricular tachyarrhythmias: discordance of antiarrhythmic drug response. Although overall group response rates to these three drugs were not different, their antiarrhythmic effects were discordant within individuals. Figures 2 and 3 show the individual concordance and discordance of effect on ventricular tachycardia/fibrillation inducibility. A total of 11 patients became noninducible on at least one drug (Fig. 2). Six responded to only a single drug (four to quinidine, two to disopyramide) and five responded to two or more (one to procainamide/quinidine, four to procainamide/disopyramide/quinidine). Thus, the concordance of drug response for complete responders may be stated: a response to any one drug was associated with a response to any of the others in 45% and to both of the others in 36%.

Inducibility of ventricular tachyarrhythmias: concordance of antiarrhythmic drug resistance. Because only 4 patients responded to all three drugs the remaining 28 patients will show the frequency of concordance of drug resistance. Twenty-one patients were resistant to all three drugs, 6 patients to two drugs and 1 patient to a single drug. Thus, the concordance of drug resistance may be stated:

Figure 2. Concordance of antiarrhythmic effects of procainamide (P), disopyramide (D) and quinidine (Q) in 11 responders. Vertical axes represent the number of patients. Letters below each bar indicate whether the response was to one, two or all three drugs.

Resistibility to any one drug was associated with resistibility to any of the others in 79% and to all the others in 75%.

Inducibility of ventricular tachyarrhythmias: discordance of number of extrastimuli used. In the preceding analysis of concordance of drug resistance, no allowance is made for the three subcategories of drug resistance repre
presented by continued ventricular tachycardia/fibrillation inducibility with the same number, with fewer and with more extrastimuli compared with baseline. These subcategory concordance data are shown in Figure 3. Inducibility with fewer extrastimuli on any one drug was associated with inducibility with fewer extrastimuli on either of the others in 25% and on both of the others in 0%. Unchanged inducibility on any one drug was associated with unchanged inducibility on either of the others in 59% and on both of the others in 14%. Inducibility with more extrastimuli on any one drug was associated with inducibility with more extrastimuli on either of the others in 29% and on both of the others in 0%. These subcategory concordances are clearly lower than the overall concordance of drug resistance. Although the latter may be of clinical utility, the subcategory concordances more directly address drug similarities and differences.

In contrast with these results, when one compares the number of extrastimuli needed to induce ventricular tachycardia/fibrillation in the baseline drug-free studies done in each patient, the same number of extrastimuli was used for all three baseline studies in 16 patients; the same number of extrastimuli was used for two of three baseline studies in 15 additional patients; and in only 1 patient was a different number of extrastimuli used at each baseline study. Thus the concordance of drug-free study results may be stated to be 97% for any two of three drug-free studies and 50% for all three drug-free studies.

**Serum drug levels.** For each drug the average serum concentration (μmol/liter) at the higher dosage was significantly greater than at the lower dosage: procainamide = 28.6 ± 12.1 versus 20.2 ± 6.9 (p = 0.002); disopyramide = 13.9 ± 3.7 versus 12.4 ± 2.8 (p = 0.001); and quinidine = 13.6 ± 6.5 versus 11.1 ± 6.1 (p < 0.001). Serum drug concentrations in those patients who became noninducible were not significantly different from those of patients whose ventricular tachycardia remained inducible: procainamide = 24.4 ± 18.3 versus 27.1 ± 10.5 (p = 0.60); disopyramide = 10.9 ± 0.6 versus 13.5 ± 3.5 (p = 0.09); and quinidine 10.2 ± 5.3 versus 12.9 ± 7.4 (p = 0.29). The average variation in serum drug levels from the beginning to the end of programmed stimulation ranged from −5.2 to +4.4%. The details of our pharmacokinetically designed quinidine infusion have been previously reported (11).

**Effects on other electrophysiologic measurements.** The effects of these three drugs on surface electrocardiographic measurements are presented in Figure 4. Each drug affected each of the surface electrocardiographic intervals equally, with one exception. The increase in QTc interval caused by the higher dosage of quinidine was significantly greater than that caused by the higher dosage of procainamide. The effects of these three drugs on ventricular tachyarrhythmia cycle length and ventricular refractoriness are presented in Figure 5. Each drug prolonged ventricular tachyarrhythmia cycle length. The effect of quinidine and disopyramide exceeded that of procainamide at low concentrations. Effects on ventricular effective and functional refractory periods were similar to those on ventricular tachyarrhythmia cycle length. Quinidine effects on refractoriness exceeded those of procainamide at both concentrations.

There was significantly greater prolongation of the QRS interval in responders to disopyramide compared with that in nonresponders (16 ± 8 versus 6 ± 19 ms). Conversely, there was significantly less prolongation of QRS interval in responders to quinidine compared with that in nonresponders (1 ± 14 versus 10 ± 12 ms). Procainamide had an equal effect on the QRS interval of responders and nonresponders (4 ± 9 versus 9 ± 16 ms). There was significantly greater prolongation of QTc interval in responders to quinidine compared with that of nonresponders (86 ± 67 versus 32 ± 54 ms), but this effect was not seen with either of the other two drugs. No other significant differences were
**Figure 5.** Effects of procainamide (P), disopyramide (D) and quinidine (Q) on ventricular tachycardia (VT) cycle length, and ventricular effective (VERP) and functional (VFRP) refractory periods of $S_2$ at ventricular paced cycle length of 500 ms. All axes are in ms and vertical bars indicate ± 1 SD (omitted when there is overlap). Each point is the mean of values obtained at the baseline drug-free study each day or the mean of those obtained at either the low or high concentrations of each drug. Significant (p < 0.05) differences are indicated as follows: *different from baseline, §high concentration different from low concentration, ‗quinidine different from procainamide, ‗‘disopyramide and quinidine different from procainamide.

noted among effects of the three drugs on the remaining electrophysiologic measurements in responders and nonresponders. Thus, when patients were categorized into those with and those without an antiarrhythmic response, there was also discordance among the effects of each drug on other electrophysiologic measurements.

**Relations between serum drug levels and changes in electrophysiologic measurement.** Relations between serum drug concentrations and electrophysiologic measurements were analyzed by linear regression. Over the wide range of concentrations tested in this study, all significant concentration-effect relations were linear according to analysis of residuals. For each drug, statistically significant correlations were found between serum concentrations and one or more ventricular refractory periods. For procainamide and quinidine there was also a significant correlation between serum concentration and ventricular tachycardia cycle length. The strength ($r$) and statistical significance (p) of the nonsignificant correlations was enhanced by considering only those individuals with a drug-induced decrease in sinus cycle length of ≥50 ms. For example, the linear relations between serum procainamide concentration and increased ventricular effective refractory period of $S_1$ had a slope of 1.1 ± 0.8 and an intercept of 0.4 ± 15.6 (N = 19, r = 0.31, p = 0.19) when all patients were included, but when only those with a drug-induced decrease in sinus cycle length were analyzed, the slope was 2.4 ± 1.0 and the intercept was −30.2 ± 21.0 (N = 12, r = 0.58, p = 0.04). Serum drug concentrations did not correlate significantly with changes in any of the surface electrocardiographic intervals.

The changes in ventricular tachyarrhythmia cycle length and refractoriness were concentration-related and these relations may therefore be used to estimate "electrophysiologically equivalent" ranges of serum levels for the three drugs. Setting an arbitrary "therapeutic range" of quinidine of 7.0 to 15.0 μmol/liter, linear regression indicates "equivalent ranges" of procainamide and disopyramide of 32.8 to 84.0 and 8.2 to 23.0 μmol/liter, respectively.

**Discussion**

Previous studies have retrospectively compared the antiarrhythmic efficacy of procainamide, disopyramide and quinidine. Our study is unique in that all patients received all three drugs, all three drugs were administered using the same route, concentration-response relations for both antiarrhythmic efficacy and other electrophysiologic effects were evaluated, and baseline measurements, including ventricular tachycardia/fibrillation inducibility, were repeated before the administration of each drug. This last point is particularly important as even negligible lingering blood levels of the previous drug may have some trivial residual effects when the next drug is tested.

**Antiarrhythmic response rates.** Although there were no significant differences in overall complete response rates among the three drugs, the response rates to disopyramide and procainamide tended to be lower than those to quinidine. This apparent trend may be related to a number of factors, the most obvious of which is the observation that the achieved serum concentrations of the three drugs did not produce precisely equivalent electrophysiologic effects. The quinidine levels achieved were higher than those usually reported. Although the procainamide levels achieved are within the generally accepted therapeutic range, they are lower than is sometimes required in patients with chronic ventricular arrhythmias (17,18). These considerations suggest that the trend in response rates in our study is not only statistically nonsignificant but also clinically unimportant. Complete response rates to the three drugs in our study are similar to those in previous reports (19) using definitions of response the same as those used here. Our definition of complete response is more rigorous than that of other investigators.
(5,6) reporting higher response rates. These higher response rates are achieved in our study with inclusion of what we have chosen to term partial responses.

**Discordance of antiarrhythmic drug response.** Despite the apparent similarity of these drugs implied by overall response rates, there is substantive discordance of individual responses. The positive concordance rate observed in this study was 36%. That is, complete responders to any one drug have a 36% chance of responding to the other two drugs. This probability is not significantly different from the probability of an untested patient responding to any one of these drugs (11 [34%] of 32). Therefore, at least with respect to individual antiarrhythmic response, these drugs are dissimilar. The clinical implication of this observation is that when it is necessary to change to another drug after successful antiarrhythmic control with one of the three drugs, efficacy must be tested on the new drug because the chance of success after empiric change to either of the other two is low. This low positive concordance rate could not have been improved by either higher procaainamide dosages or giving high-dose disopyramide to the patients with marked left ventricular dysfunction. As seen in Figure 2, only five patients responded to one or two drugs and could have improved concordance by responding to both procaainamide or disopyramide in higher dosages. However, four of these five did indeed receive the higher dosage of disopyramide. Therefore, although higher dosages of procaainamide may have increased the proportion of patients responding to that drug, the overall positive concordance rate could only have improved by a maximum of one patient (up to 45%).

**Concordance of antiarrhythmic drug resistance.** The overall negative concordance in this study was 79% (22 of 28). That is, nonresponders to any one drug have a 79% chance of not responding to one of the other two. Therefore, on average, the use of one drug to screen for nonresponse to the other two would deny 21% of these patients the opportunity for potentially effective therapy. However, resistance to a specific drug as a predictor of resistance to the other two ranged from 77 to 91%. The trend in this study was that high concentrations of quinidine have the greatest negative predictive capability (91%). This predictive capability was similar to that (87%) reported by Waxman et al. (6) with higher concentrations of procaainamide and that (73%) reported by Rae et al. (7), who also used higher concentration of procaainamide. The present data interpreted in the context of these earlier studies suggest the general principle that the screening capability of nonresponse to a class 1A antiarrhythmic agent is concentration-dependent rather than drug specific. Thus the negative concordance rates observed with high concentrations of class 1A agents may be clinically relevant.

**Discordance of number of extrastimuli used.** These high negative concordance rates contrast with the low positive concordance rates noted earlier from noninducibility. However, antiarrhythmic efficacy is not a dichotomy. The overall negative concordance rates, represented by persistent inducibility of ventricular tachycardia, fail to recognize the continuum of grades of inducibility. Therefore, assessment of the similarity or dissimilarity of these three drugs could be improved by analyzing grades of inducibility separated into 1) easier to induce, 2) inducibility unchanged, and 3) harder to induce. The definitions used in our study to explore this notion are arbitrary but the concept of grades of inducibility is supported by the observation that an increase in the number of extrastimuli needed to induce a ventricular tachyarrhythmia indicates an antiarrhythmic effect (20). We have previously shown (11) that site of stimulation can be an important factor for inducibility of ventricular tachycardia in the drug-free state. A second stimulation site was not examined during drug therapy in our study and its importance to these definitions is unknown. The concordance of each of these possible negative results ranged from 0 to 14% for all three drugs in our study and from 25 to 59% for any two of the three drugs. These values are less than are the chances that the same number of extrastimuli would be used to induce ventricular tachycardia/fibrillation on all three of three successive drug-free studies (50%) or any two of three successive drug-free studies (97%). Thus the high overall negative concordance rate reported here and elsewhere (6,7) likely overestimates similarities in antiarrhythmic inefficacy of these three drugs.

**Other electrophysiologic effects.** When data from all the patients were averaged, there were only minor quantitative differences in the effects of the three drugs on other electrophysiologic measurements. These differences are probably explained by the observation that equally effective serum concentrations of all three drugs were not achieved in each case. Nevertheless, when patients were categorized into responders (noninducible) and nonresponders (remain inducible), at least quantitative discordance among some of the other electrophysiologic effects was noted. These data imply that there is a complex and incompletely understood relation between antiarrhythmic response and other electrophysiologic effects.

**Conclusion**

Continued ventricular tachycardia inducibility with high concentrations of any one of these three class 1A drugs is highly predictive of continued inducibility on either of the other two. Nevertheless, the clinical utility of this result should not obscure the observation that antiarrhythmic efficacies of procaainamide, disopyramide and quinidine are discordant, even though the three drugs have the same general effects on other electrophysiologic measurements. Furthermore, the effects on other electrophysiologic measurements also become quantitatively discordant when patients are classified into responders and nonresponders.
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