Effect of Epinephrine and Lidocaine Therapy on Outcome After Cardiac Arrest Due to Ventricular Fibrillation

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One hundred ninety-nine patients with out-of-hospital cardiac arrest persisted in ventricular fibrillation after the first defibrillation attempt and were then randomly assigned to receive either epinephrine or lidocaine before the next two shocks. The resulting electrocardiographic rhythms and outcomes for each group of patients were compared for each group and also compared with results during the prior 2 years, a period when similar patients primarily received sodium bicarbonate as initial adjunctive therapy. Asystole occurred after defibrillation with threefold higher frequency after repeated injection of lidocaine (15 of 59, 25%) compared with patients treated with epinephrine (four of 55, 7%) (p<0.02). There was no difference in the proportion of patients resuscitated after treatment with either lidocaine or epinephrine (51 of 106, 48% vs. 50 of 93, 54%) and in the proportion surviving (18, 19% vs. 21, 20%), respectively. Resuscitation (64% vs. 50%, p<0.005) but not survival rates (24% vs. 20%) were higher during the prior 2-year period in which initial adjunctive drug treatment for persistent ventricular fibrillation primarily consisted of a continuous infusion of sodium bicarbonate. The negative effect of lidocaine or epinephrine treatment was explained in part by their influence on delaying subsequent defibrillation attempts. Survival rates were highest (30%) in a subset of patients who received no drug therapy between shocks. We conclude that currently recommended doses of epinephrine and lidocaine are not useful for improving outcome in patients who persist in ventricular fibrillation. Lidocaine administration is commonly associated with asystole, and any possible attribute of initial adjunctive drug therapy is outweighed by its detrimental effect on delaying successive shocks for persistent ventricular fibrillation. (Circulation 1990;82:2027-2034)

The rationale for specific drugs administered during cardiac arrest is primarily based on observations made during experimental animal studies or from patients with ventricular arrhythmias complicating acute myocardial infarction. The American Heart Association Guidelines for Advanced Cardiac Life Support emphasize the use of both epinephrine and lidocaine for patients who persist in ventricular fibrillation after initial attempts at defibrillation.1 During experimental cardiac arrest, epinephrine administration results in higher rates of resuscitation, seemingly by augmenting myocardial blood flow during chest compression.2-8. Lidocaine is also often used to treat persistent ventricular fibrillation because the drug has been shown in some studies to prevent the emergence of ventricular fibrillation during the early hours of acute myocardial infarction.9-11 Other studies, however, have shown that lidocaine increases defibrillation energy level requirements and is relatively ineffective in terminating ventricular tachyarrhythmias after they have been established.12-17

Ventricular fibrillation persists after initial defibrillation attempts in 25–40% of patients discovered in cardiac arrest and may present a condition quite different from either acute myocardial infarction or experimental resuscitation, and thus may have different drug requirements.18,19 The purpose of this trial was to determine prospectively whether the initial administration of either epinephrine or lidocaine improved resuscitation results in patients discovered in ventricular fibrillation that was refractory to an initial defibrillation attempt.
Methods

The Seattle Emergency Medical System is a tiered response system. The first level of care is provided by firefighters. At the time of the study (mid-1980s), they, with rare exception, provided only cardiopulmonary resuscitation until paramedics arrived and took charge of the resuscitation effort. The second level of care is provided by paramedics, trained and equipped to provide endotracheal intubation, defibrillation, and intravenous drug therapy, practicing either under written standing orders or remote verbal prescription of a physician.

For several years before this study, the protocol for treatment of ventricular fibrillation was to deliver one countershock and then, if ventricular fibrillation persisted, place an endotracheal tube and intravenous catheter. A continuous infusion of sodium bicarbonate was administered and continued until further resuscitation efforts either resulted in an organized, perfusing rhythm or until 180 meq had been infused.

During this 2-year study ending in 1985, the treatment protocol was modified. Depending on the calendar day (odd number or even number), patients who persisted in ventricular fibrillation after the first 200-J shock were assigned to receive either a 100-mg bolus of lidocaine or a 0.5-mg bolus of epinephrine (open label) through a peripheral intravenous cannula before a second 200-J shock was given. If ventricular fibrillation persisted after the second shock, a second bolus of the assigned drug was authorized and was followed by a third 360-J shock. After this point, additional epinephrine or lidocaine (for those patients who had not previously received lidocaine) was authorized. The resuscitation attempt was continued until the patient either regained an organized rhythm or became refractory to all treatment and was declared dead.

During this 24-month study, a total of 471 patients were discovered in cardiac arrest and ventricular fibrillation by paramedics. Ninety-eight were excluded from the trial because each had received either intravenous drug therapy or defibrillation attempts given by specially staffed first-response units before paramedic arrival (advent of enhanced first-level services). Thus, 373 patients with cardiac arrest due to ventricular fibrillation were potential candidates for the lidocaine/epinephrine drug comparison.

The paramedics’ defibrillator monitors (Lifepak 5, Physio-Control Corporation, Redmond, Washington) were modified so that electrocardiographic (ECG) rhythm would be continuously recorded on magnetic tape. These tape recordings were reviewed to determine the times of drug administration and rhythms before and after each defibrillation attempt. Unfortunately, the miniature magnetic tape recording systems for this purpose are relatively unreliable (tape drive, cassettes, and limited battery capacity), and nearly one fourth of the resuscitations were not recorded. The rhythms were grouped as follows: ventricular fibrillation, asystole, supraventricular rhythms, and idioventricular rhythms (QRS complexes >110 msec and no discernible atrial activity). The patients’ prehospital and hospital records were reviewed to determine clinical and demographic factors, emergency response times, and hospital outcome for each patient.

To put the findings from this 2-year trial in overall perspective, we compared results with those in similar patients treated during the prior 24 months. In this control period, 630 comparable patients were discovered in ventricular fibrillation by Seattle Fire Department paramedics. Again, excluding those given drug therapy or early defibrillation by first responders before paramedic arrival, 500 (79%) patients provided a group for historical comparison. The protocol for resuscitation during this earlier 2-year period was the same as during the drug study, with the exception of the type of initial drug therapy prescribed. A continuous infusion of sodium bicarbonate was most often the only drug administered between the first two shocks. Treatment with epinephrine or lidocaine between shocks 1 and 2 was unusual.

Discrete variables were compared among patients in the lidocaine, epinephrine, and historical control groups by using \( \chi^2 \) analysis or Fisher’s exact test. Continuous variables were compared between treatment groups by using Student’s \( t \) test or analysis of variance. Multivariate analyses (logistic regression) were used to determine the effects of drug treatment and outcome. Where appropriate, the results were analyzed on the basis of intention to treat and actual treatment received.

Results

Patient Characteristics

During the 2-year period of epinephrine and lidocaine administration for treatment of persistent ventricular fibrillation, 373 patients were discovered by paramedics to be in cardiac arrest due to ventricular fibrillation; 199 (53%) persisted in ventricular fibrillation after the first 200-J shock. By odd/even calendar day, 106 of the 199 patients were allocated to receive lidocaine after shock 1, and 93 were allocated to epinephrine treatment. Of the total 199 patients with persistent ventricular fibrillation in both groups, 147 (74%) had adequate tape recordings for analysis of the ECG rhythm before and after shock 2; for the remainder, the recorder malfunctioned (battery or tape-drive problems) and no tape was available. The amplitude of ventricular fibrillation was greater than 200 \( \mu \)V in 129 (88%) and lower than 200 \( \mu \)V in 18 (12%) of the 147 patients in whom the resuscitation was recorded on tape.

Drug Assignment

Seventy (66%) of the 106 patients allocated to receive lidocaine received a bolus, per protocol, after shock 1. Thirty-four (49%) of the 70 patients treated
with lidocaine failed to defibrillate after a second 200-J shock; 29 of these 34 patients then received a second bolus of lidocaine and a third shock was given. Of the remaining five patients, one received both lidocaine and epinephrine and four received no drug between shocks 2 and 3.

Thirty-six (34%) of the 106 patients initially allocated to lidocaine treatment received either a sodium bicarbonate infusion alone \( (n=13) \) or no drug before shock 2 \( (n=15) \). A few others inadvertently received either epinephrine \( (n=6) \) or both study drugs \( (n=2) \). Seventeen patients in this subset of 36 failed to defibrillate after shock 2; 11 received a bolus of lidocaine (late treatment) before shock 3. Thus, in all, 83 (78%) of the 106 patients allocated to lidocaine received one or more boluses of lidocaine before shock 3 for treatment of persistent ventricular fibrillation; 53 patients (50%) received 100 mg, and 30 (28%) received 200 mg.

For the 93 patients allocated to receive epinephrine, 58 (62%) received a 0.5-mg bolus after shock 1. Thirty (32%) of these failed to defibrillate with the second shock; 27 of the 30 received a second bolus before a third defibrillation attempt. For the three remaining patients, one received sodium bicarbonate and two received no drug before shock 3.

Inadvertently, 35 (38%) of the 93 patients initially assigned to epinephrine treatment received either sodium bicarbonate alone \( (n=17) \), no drug \( (n=15) \), or lidocaine \( (n=3) \) before shock 2. Of the 24 patients in this subset who failed to defibrillate with the second shock, 15 received epinephrine before shock 3 (late treatment). In all, 70 (75%) of the 93 patients allocated to receive epinephrine for persistent ventricular fibrillation received one or more injections before the third shock, including 43 (46%) who received one injection and 27 (29%) who received two.

Considering the actual treatment received by patients with ventricular fibrillation persisting after either the first or second shocks, 86 (43%) were treated with lidocaine, 79 (40%) received epinephrine, five (2%) received both drugs, 15 (8%) received no drug treatment, and 14 (7%) received simply a continuous infusion of sodium bicarbonate during this initial phase of the resuscitation attempt.

Table 1 compares the age and emergency vehicle response times (surrogate measures of the delay from collapse to initiation of cardiopulmonary resuscitation and defibrillation) for the patients in the two drug treatment groups. The response times were similar for patients who received epinephrine treatment and patients who received lidocaine treatment. By chance, a greater proportion of the patients in the epinephrine group received cardiopulmonary resuscitation initiated by a bystander (46% vs. 29%, respectively; \( p<0.02 \)). From the taped recordings, the time of the first shock was 9 minutes after the emergency call. Approximately 4 minutes were required for intubation and intravenous cannulation after shock 1. The second shock was delivered an average of 14±4 minutes after the emergency call for patients in both treatment groups.

### ECG Findings After Treatment and Shocks 2 and 3

There were no significant differences in the resulting rhythms between the patients in the two treatment allocation groups after shock 2 (Table 2). One hundred thirty-nine (70%) of the 199 patients with cardiac arrest had taped resuscitations in which the rhythm was recorded from the time of attachment of the electrodes until cardioversion. The proportion of patients with each rhythm at the end of the protocol was as follows: supraventricular rhythm in 31 (22%), ventricular fibrillation in 44 (32%), idioventricular in 43 (31%), and asystole in 21 (15%). Approximately 20% of patients in both treatment allocation groups developed a supraventricular rhythm after the second shock. There was, however, a trend toward both shock 2 and 3 toward an increased incidence of asystole in patients who were randomized to receive lidocaine and a lesser trend toward more persistent ventricular fibrillation in those who received epinephrine.

Because some patients received the allocated drug late in the protocol (after the second shock) and there was a small proportion of crossover between groups, the resulting rhythm was analyzed.
Rhythms were tabulated for patients given either lidocaine or epinephrine for persistent ventricular fibrillation and a subsequent shock was delivered. Table 2 shows the distribution of rhythms after shock 2, shock 3, and at the end of the treatment protocol.

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Lidocaine group</th>
<th>Epinephrine Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After shock 2</td>
<td>After shock 3</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Supraventricular</td>
<td>14 (19)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>33 (44)</td>
<td>19 (59)</td>
</tr>
<tr>
<td>Idioventricular</td>
<td>19 (25)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Asystole</td>
<td>9 (12)</td>
<td>7 (22)</td>
</tr>
<tr>
<td></td>
<td>12 (18)</td>
<td>3 (8)</td>
</tr>
<tr>
<td></td>
<td>39 (59)</td>
<td>25 (66)</td>
</tr>
<tr>
<td></td>
<td>11 (17)</td>
<td>9 (24)</td>
</tr>
<tr>
<td></td>
<td>4 (6)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

Tape recordings of the resuscitation and rhythms were available in 141 of 199 patients who persisted in ventricular fibrillation after shock 1 and in 70 of 105 patients who persisted in ventricular fibrillation after shock 2.

Eighty-six patients received at least one bolus of lidocaine before the third shock and 79 received epinephrine before the third shock. Taped resuscitations were available in 59 (69%) of the patients treated with lidocaine and 55 (70%) of the patients treated with epinephrine. Asystole followed defibrillation threefold as frequently after treatment with lidocaine than with epinephrine, that is, 15 of 59 (25%) versus four of 55 (7%) (p<0.02) (Figure 1). The proportion of patients persisting in ventricular fibrillation at the end of the protocol was similar for both those receiving lidocaine and those receiving epinephrine, that is, 20 of 59 (34%) and 21 of 55 (38%), respectively. The proportion of patients treated with lidocaine who converted to a supraventricular rhythm, however, was half that observed in those who received epinephrine, or seven of 59 (12%) versus 13 of 55 (24%). Thus, the distribution of resulting rhythms (supraventricular, ventricular fibrillation, idioventricular, and asystole) was significantly different for the patients receiving the two treatments (p<0.05; test for trend, p=0.01), when the resulting rhythms were ordered and analyzed per drug given. This particular order was chosen because it is related to a descending likelihood of survival.

The total number of shocks delivered during resuscitation was greater for patients allocated to epinephrine than for those patients assigned to lidocaine (6.4±4.2 vs. 5.2±3.9, respectively; p=0.03), reflecting the association of persistent ventricular fibrillation with epinephrine treatment and asystole with lidocaine treatment.

**Patient Outcome for the Two Treatments**

Approximately one half of the patients were resuscitated and admitted to the hospital (Figure 2). The proportion of patients either fully awake or partially responsive at the time of admission (a finding consistent with rapid resuscitation) was similar for both treatment groups, that is, nine of 48 (19%) and seven of 46 (15%), respectively. Hospital mortality rates after admission were also comparable; 30 (59%) of the 51 patients assigned to lidocaine and 32 (64%) of the 50 patients assigned to epinephrine died after admission. Overall, 21 (20%) of the 106 patients assigned to lidocaine and 18 (19%) of the 93 patients in the epinephrine group were discharged from the hospital.

Outcomes were also similar when analyzed by drug treatment received. Thirty-six (42%) of the 86 patients treated with lidocaine and 40 (51%) of the 79 patients treated with epinephrine were admitted to hospital and discharged was similar for patients in both the epinephrine and lidocaine treatment groups during the study period.
the hospital. The rates for survival to hospital discharge were 13 of 86 (15%) versus 14 of 79 (18%), respectively.

The overall 16% survival rate (28 of 170) for patients who received either drug was significantly lower than the 38% survival rate (11 of 29) in the subset who either received no drugs (n=15) or simply a continuous infusion of sodium bicarbonate before the second shock (n=14) (p=0.01).

Survival (hospital discharge) was then analyzed by type of treatment given in a multivariate analysis that considered the previously stated clinical and emergency response factors. Longer times from the emergency dispatch to the arrival of the first emergency vehicle (odds, 0.25; 95% confidence interval [CI], 0.05–1.18; p=0.06), the time to first shock (odds, 0.57; 95% CI, 0.34–0.95; p=0.006), and treatment with lidocaine or epinephrine (odds, 0.24; 95% CI, 0.08–0.76; p=0.02) were each predictive of worsened survival.

**Lidocaine and Epinephrine Treatment Results Versus Results in Historical Controls (Sodium Bicarbonate)**

The outcome of patients treated with lidocaine and epinephrine was compared with the outcome in a similar group of consecutive patients treated during the prior 2 years. During that earlier time, 224 patients persisted in ventricular fibrillation after the first shock. Tape recordings were available in 149 (67%) of these 224 patients. The protocol for intubation and intravenous cannulation between shocks 1 and 2 was the same as during the epinephrine/lidocaine study years. The type of drug therapy delivered between the first two shocks could be ascertained in 214 of the 224 patients from review of the resuscitation tapes and prehospital medical records. Sodium bicarbonate was infused in 132 patients (62%), 33 (15%) received either lidocaine or epinephrine plus sodium bicarbonate, three received some other drug combination, and 43 (19%) received no drug between the first two shocks.

Patient age, the proportion of patients with witnessed collapse, as well as the response time of emergency vehicles were similar to those for the 199 patients treated with lidocaine or epinephrine with persistent ventricular fibrillation (Table 1). The overall proportion of patients who received bystander-initiated cardiopulmonary resuscitation tended to be higher during the later period than during the early period, that is, 41% versus 33%, which might bias toward higher survival rates for patients treated with epinephrine or lidocaine. The time delay between shocks 1 and 2 was significantly longer in patients treated with epinephrine and lidocaine (5.0±2.0 vs. 4.1±2.7 minutes; p=0.004). This probably reflects the additional time required to administer a bolus of these drugs compared with the continuous infusion of bicarbonate initiated at the time of intravenous cannulation in the earlier 2 years.

One hundred forty-five (64%) of the 224 historical control patients were resuscitated and admitted to the hospital compared with 101 (50%) of the 199 patients during the epinephrine/lidocaine period (χ²=7.92; df=1, p<0.005). The proportion of patients discharged, however, was similar for both periods, that is, 54 of 224 (24%) versus 39 of 199 (20%), respectively.

A stepwise logistic regression analysis of survival in all patients with persistent ventricular fibrillation after shock 1 who were treated during the 4-year period was performed. Survival was positively correlated with witnessed collapse, younger age, shorter paramedic response time, bystander-initiated cardiopulmonary resuscitation, and male sex (Table 3). Survival was adversely related to receipt of lidocaine, epinephrine, or both, before the second shock for persistent ventricular fibrillation.

**Time Between Shocks and Survival**

The possible relation between the adverse effect of treatment with epinephrine or lidocaine and the attendant delay in administering these treatments was then examined. The time between shocks 1 and 2 was known in a subset of 296 patients with taped resuscitation attempts, 147 patients from the epinephrine/lidocaine period and 149 from the earlier period. As a first step, the stepwise logistic regression shown in Table 3 was repeated. Paramedic unit response time was used as a surrogate measure of the time from the emergency call until the first defibrillation to provide known values in the greatest number of patients. Drug treatments were grouped as

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Witnessed collapse</td>
<td>2.4</td>
<td>1.24–4.80</td>
<td>9.07</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td>0.87</td>
<td>0.79–0.96</td>
<td>6.34</td>
<td>0.012</td>
</tr>
<tr>
<td>Paramedic response time†</td>
<td>0.73</td>
<td>0.56–0.95</td>
<td>6.49</td>
<td>0.011</td>
</tr>
<tr>
<td>Bystander-initiated CPR</td>
<td>1.78</td>
<td>1.06–2.97</td>
<td>4.73</td>
<td>0.030</td>
</tr>
<tr>
<td>Administration of lidocaine before shock 2</td>
<td>0.42</td>
<td>0.22–0.82</td>
<td>4.85</td>
<td>0.028</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.00</td>
<td>0.95–4.21</td>
<td>3.63</td>
<td>0.057</td>
</tr>
<tr>
<td>Administration of epinephrine before shock 2</td>
<td>0.56</td>
<td>0.28–1.10</td>
<td>3.02</td>
<td>0.082</td>
</tr>
</tbody>
</table>

CI, confidence interval; CPR, cardiopulmonary resuscitation.
† Evaluated in 5-year increments for odds ratio and confidence interval.
† Evaluated in 3-minute increments for odds ratio and confidence interval.
either 1) lidocaine, epinephrine, or both drugs versus 2) sodium bicarbonate or no drug administered.

Unlike the prior multivariate analyses, survival in the subset of patients with tapes of resuscitation (required to tabulate the time between shocks) is higher in the historical control versus the epinephrine/lidocaine periods and may possibly bias results. Survival was 29.5% for taped patients and 13% for untaped patients during the first 2 years. For the lidocaine/epinephrine years, no bias is apparent, that is, there was 19.7% survival in taped patients versus 19.2% in untaped patients, respectively.

Although our ability to conclusively evaluate the effect of drug treatment versus time to shock is possibly hampered by this problem, the stepwise logistic regression analysis was repeated with the significant predictors of patient outcome in the model at the outset (witnessed collapse, age, paramedic response time, and bystander-initiated cardiopulmonary resuscitation). Drug treatment and minutes between shock 1 and shock 2 were free to enter the analysis. Only the time delay between shocks (and not drug treatment) was a significant predictor of survival after adjustment for the previously noted covariates (odds ratio, 0.75; 95% CI, 0.57–0.97), thus suggesting that the major negative effect of drug treatment was the time required to give it.

Figure 3 shows the admission and discharge rates for 411 patients with persistent ventricular fibrillation (all patients, taped and not taped, in whom drug treatment could be determined) after shock 1 and treatment with either epinephrine or lidocaine (176), a simple continuous infusion of sodium bicarbonate (162), or no drug treatment (73). Both hospital admission and discharge rates differed by treatment delivered, being lowest in those patients who received either epinephrine or lidocaine and highest in those receiving no drug treatment between shocks.

**Discussion**

Two possible methods for improving outcome from cardiac arrest are to shorten the time to defibrillation as much as possible and to use a drug that can restore pulse and blood pressure when simple defibrillation does not. Rapid delivery of shocks to patients discovered in ventricular fibrillation is a significant predictor of successful outcome. In contrast, most patients are not defibrillated immediately, and adjunctive pharmacological treatments are commonly used.

Clinical studies of drug treatment and their influence on resuscitation outcome after cardiac arrest are complicated to conduct and interpret. First, patients discovered in out-of-hospital cardiac arrest rarely respond immediately to pharmacological treatment. The circulation and distribution of the drug during chest compression is altered, and thus, the onset of effect is delayed. Interpretation of the results is further complicated by the fact that if one drug fails to elicit a prompt response during the protocol, the clinician will often use any other drug available to resuscitate the victim although the full effects of the first drug may not yet be evident. Epinephrine is currently recommended as adjunctive treatment in resuscitation despite the fact that the drug may precipitate arrhythmias and increase myocardial metabolic demands. One recent trial showed epinephrine superior to methoxamine during resuscitation, suggesting that the choice of initial drug therapy can make a difference. An alternative approach for managing persistent ventricular fibrillation is to use an effective antiarrhythmic drug. One prior study failed to detect any benefit of lidocaine during resuscitation.

The current study was a prospective evaluation of the initial use of lidocaine or epinephrine for patients who persisted in ventricular fibrillation after the first 200-J defibrillation attempt. Parenthetically, an earlier study had shown that both 200-J and 360-J energy level shocks were equally effective for the first two defibrillation attempts. The purpose of this comparison was to determine which drug would prove more useful to treat persistent ventricular fibrillation, an antiarrhythmic drug or a drug aimed at augmenting perfusion during artificial circulation.

The interpretation of these results is complicated by the difficulty experienced by paramedics in adhering to a strict protocol during the highly charged and energetic effort of out-of-hospital resuscitation. When the first shock failed to cause defibrillation, only two thirds of the patients in each drug assignment group with persistent ventricular fibrillation initially received the assigned drug before the second shock, and three fourths of patients allocated to both lidocaine and epinephrine received the assigned drug before delivery of shock 3. On other occasions, shocks were delivered without intervening drug therapy, particularly if intravenous cannulation could not.
be rapidly accomplished. In the tape recordings of resulting rhythms, there were trends but no significant differences between the two drug treatments (intention-to-treat analysis). Results based on actual treatment received showed otherwise. The use of lidocaine was associated with a threefold higher occurrence of asystole in subsequent defibrillation attempts. Lidocaine treatment of ambient ventricular ectopy has also been reported to cause asystole.\textsuperscript{24,25}

The use of lidocaine, epinephrine, or both, between the initial two defibrillatory shocks was associated with poorer survival than in other patients with persistent ventricular fibrillation who received either only sodium bicarbonate or, instead, no drug treatment between shocks. Although the lack of tapes prevented an estimate of time between shocks in all cases, the adverse effect of epinephrine and lidocaine treatment for persistent fibrillation appeared related, at least in part, to the added time required to administer these drugs.

These results should not be interpreted to show that sodium bicarbonate, a drug with potentially adverse effects on cardiac resuscitation and hemodynamics, should be recommended for persistent ventricular fibrillation.\textsuperscript{20-29} It was the practice in the Seattle paramedic system during the early 1980s to start a continuous infusion of sodium bicarbonate in patients who remained pulseless after initial defibrillation attempts. The rate of infusion was slow so that several minutes were required to infuse no more than 180 meq to those patients who did not reestablish a pulse after initial countershocks. In contrast, these results failed to uncover any adverse effect of sodium bicarbonate use during resuscitation. The dosage of epinephrine used also may be criticized as being insufficient to maximize hemodynamic effects; that is, a dose several-fold higher may be required and could have yielded quite different results. There are several experimental studies and case reports purporting a benefit with higher than standardly recommended doses of epinephrine.\textsuperscript{30-35} This study, in fact, suggests that the current dose of 0.5–1.0 mg is ineffective, and the time required to give it is possibly detrimental. The clinical benefit and safety of higher epinephrine dosages is at present unclear, and the observations to date are inconsistent, some suggesting beneficial and others suggesting adverse effects with higher dosages.\textsuperscript{34,36}

The difficulties encountered in this study highlight the obstacles in performing studies during resuscitation. The management of out-of-hospital cardiac arrest requires intense effort with limited personnel. Unless there is a major and immediate salutary effect associated with a treatment, its benefit may go undetected. In spite of these obstacles, the importance of such investigation is obvious and the prehospital setting provides a less complicated clinical situation than the hospital, where cardiac arrest is often the end result of complex metabolic disorders.

The findings here provide a rationale for rapid repeated shocks for the patient who initially fails defibrillation. This is consistent with another report that showed the superiority of defibrillation compared with initial drug treatment for the initial management of cardiac arrest.\textsuperscript{37} It is unclear how many shocks should be repeated before drug therapy is initiated. Currently, three are recommended. The chance of defibrillation appears to be 50–60% with each attempt and is not influenced substantially by a prior failure. Perhaps, until an adjunctive pharmacological treatment is shown beneficial, even a greater number of shocks should be given, virtually assuring defibrillation (at least transiently) in all patients. The clinical importance of such an approach (lives saved), however, has yet to be shown.

**Summary**

In this study, there was no clinical evidence to support any form of drug therapy for initial treatment of persistent ventricular fibrillation. Drug treatment should be withheld until several repeated shocks have failed to restore an organized perfusing rhythm. The early use of lidocaine appears to cause asystole after countershocks. The present guidelines of three shocks for persistent ventricular fibrillation and then application of drug therapy need to be reexamined. Five successive shocks would achieve at least transient defibrillation in virtually all patients.

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