EDITORIAL

Should Lidocaine be Administered Routinely to All Patients After Acute Myocardial Infarction?

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SUMMARY For more than 10 years, coronary care units have used electrocardiographic monitoring for detecting and treating life-threatening arrhythmias in patients who have had acute myocardial infarction. With this experience as background, it is opportune to reassess some of the principles that are used in many coronary care units for treating these patients. Some investigators question whether all patients with acute infarction should receive antiarrhythmic drugs routinely to prevent primary ventricular fibrillation. The purpose of this editorial is to review this concept.

ONE OF THE ORIGINAL descriptions of the coronary care unit suggested that all patients who experience ventricular fibrillation or life-threatening ventricular tachycardia had "warning arrhythmias," such as frequent premature ventricular contractions (PVCs), R-on-T PVCs, couplets, multiform beats or short runs. It was further suggested that these so-called warning arrhythmias could be suppressed, when detected, with complete prevention of primary ventricular fibrillation. Treatment programs utilizing lidocaine were developed and used widely in coronary care units. Subsequently, the concept of warning arrhythmias has been investigated in a number of medical centers. Although many episodes of ventricular fibrillation may be preceded by such arrhythmias, between 25–50% of patients in the coronary care unit have no clearly defined warning arrhythmias before their first episode of ventricular fibrillation. During the first 12 hours after myocardial infarction, fewer episodes of warning arrhythmias occur and the time recorded from the first of such arrhythmias to ventricular fibrillation is much shorter, in many instances only a matter of minutes. It has also been suggested by Julian et al. and Lie et al. that ventricular fibrillation occurs less commonly in patients over 70 years old who experience myocardial infarction. No physiologic basis exists to explain this observation, and before being accepted, it should be confirmed by other investigators. Thus, the concept of warning arrhythmias for primary ventricular fibrillation has not stood the test of time, and in many instances of acute myocardial infarction, there is no prior warning.

Is Lidocaine Effective Early After Infarction?

This is an important question in coronary care and precorony care, since it is soon after infarction when most primary ventricular fibrillation occurs.

Review of the available data indicates a major controversy. In some studies it has been suggested that although lidocaine successfully suppresses late coupled PVCs, it prevents neither early PVCs nor ventricular fibrillation. On the contrary, several studies suggest that lidocaine may prevent primary ventricular fibrillation, even though it does not suppress all ectopic PVCs. The bulk of the evidence does suggest that lidocaine is less effective in the first few hours after myocardial infarction, as illustrated in the studies from the Mobile Coronary Ambulance Program in Belfast, and by others, that most lidocaine failures in the coronary care unit occur in the first 12 hours after infarction. However, in none of these studies was lidocaine administered in a program designed to achieve optimal arrhythmia-suppressing plasma levels, and the possibility of a "therapeutic hiatus" during the first few hours certainly seems possible. Lie suggested that ventricular fibrillation occurring in his prophylaxis study was not time-dependent after acute infarction.

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Arrhythmia Detection in the Coronary Care Unit?

If warning arrhythmias are to be used as indicators to commence antiarrhythmic drug therapy, as is commonly thought in many coronary care units, it is pertinent to examine the reliability of the average coronary care unit in detecting these arrhythmias. Romhilt et al.,13 in 1973, compared the real-time detection of arrhythmias by the nursing staff in the coronary care unit with those recorded on tape and analyzed with a computer system and validated by physician review. The real-time detection by the coronary care unit staff for any PVC was only 45%, that of serious ventricular arrhythmias only 16%, of multiformal beats only 7%, and of couplets 13%. The computer detected 97% of any PVC, 93% of serious ventricular arrhythmias, 87% of multiformal beats, and 78% of couplets. The failure by the coronary care unit staff to detect arrhythmias delayed antiarrhythmic drug therapy for an average of 10 hours in some patients with serious arrhythmias.

More recently, Homberg examined this same problem.14 The coronary care unit staff detected 86% of so-called warning arrhythmias when they occurred in three 1-minute episodes over a 30-minute period, 48% when they occurred in one 1-minute episode over a 30-minute period, and only 42% of all ventricular tachycardias that were detected. He stated that the delay in starting treatment was not more than 30 minutes in his coronary care unit. In another study by Vetter and Julian,15 computer analysis was compared with analysis by the staff of the coronary care unit. Real-time detection in the coronary care unit for any ventricular premature beat was 36%, for ventricular tachycardia only 18%, and, if the concept of warning arrhythmias was used, 52% of all patients who would have required treatment never received therapy. It appears that between 95–100% of patients who experience myocardial infarction have some evidence of ventricular arrhythmias during the first 48 hours after infarction. Fifty to 75% of such patients have “warning arrhythmias,” less than half of which are detected by the staff of a coronary care unit. Failure to detect such arrhythmias and delay in treatment are common.

Thus, it is questionable whether warning arrhythmias really warn, and even if they do they are frequently not detected.

Does Suppression of Less Serious Ventricular Arrhythmias Prevent Ventricular Fibrillation?

A number of early studies using warning arrhythmias as a criterion for instituting therapy demonstrated a reduction in ventricular tachycardia and PVCs when lidocaine was used.4–10 However, it remained for Lie and associates8 to demonstrate in a randomized study that the prophylactic administration of lidocaine would reduce the incidence of ventricular arrhythmias and primary ventricular fibrillation. Two hundred twelve patients under the age of 70 years who were treated within 6 hours of the onset of myocardial infarction received lidocaine as a 100 mg bolus followed by an infusion of 3 mg/min for 48 hours. Ventricular fibrillation occurred in nine patients receiving placebo infusion and in none of the patients receiving lidocaine. Eight of the patients who had ventricular fibrillation were resuscitated, and there were mild side effects in 15% of the patients receiving lidocaine.

It is well-documented that lidocaine can reduce the incidence of primary ventricular fibrillation, even without suppressing all PVCs.8–16 However, coronary care units are equipped to resuscitate patients with primary ventricular fibrillation, and this raises the following question.

Is There Evidence that Preventing Episodes of Fibrillation Reduces Mortality in the CCU?

Ventricular fibrillation is a serious complication of myocardial infarction and occurs in 5–11% of patients admitted with proven infarction.17–19 In one recent report it occurred even in 9% of those patients who did not have signs or symptoms of heart failure on admission to the CCU.17 In this study only 59% of 102 patients experiencing cardiac arrest survived hospitalization, emphasizing the dire consequence of this complication. Furthermore, it was demonstrated that those patients having ventricular fibrillation had a poorer long-term prognosis than those who did not. This report is in contrast to the results of other published data,18–21 where long-term prognosis was not influenced by primary ventricular fibrillation occurring early after infarction, but it agrees with the report of Sioman and Pina.22

From these studies it is clear that ventricular fibrillation is a major problem even in well-run coronary care units, and should be avoided if a safe, effective therapy can be used.

Using lidocaine prophylactically in all patients admitted to the CCU for infarction means that it will be administered to many patients who are later found not to have infarction. Since many of these patients do have unstable angina and are at high risk for arrhythmias, this does not become a significant problem. The drug can be withdrawn when the diagnosis is clarified.

Ample evidence supports the hypothesis that lidocaine is effective, so safe administration programs should be studied.

Recommendations for Lidocaine Administration

Many investigators have suggested that the administration of lidocaine to all patients will result in a high incidence of toxicity. Since the pharmacokinetics of lidocaine are now well understood, it is possible to recommend a program of primary prophylaxis (table 1).2, 3, 23–26 It must be understood that the drug is distributed rapidly throughout a central pharmacologic compartment after its intravenous administration.26 It then is transferred rapidly into a peripheral or outer
tissue compartment after a single bolus injection, and effective plasma concentrations which correlate with effect persist for only a short time (8–15 minutes). Therefore, a loading dose followed by an infusion must be administered to raise the plasma concentration to a level high enough to suppress arrhythmias.

There are several safe and effective ways to administer the loading dose, which probably should total 200 mg in patients not in heart failure or shock. The lidocaine may be administered as two 1-minute 100 mg injections 10 minutes apart, four 50 mg injections at 5-minute intervals, or an infusion of 20 mg/min for 10 minutes.24 27 An infusion of 2–3 mg/min should be started simultaneously with the loading dose. In order to control the infusion carefully, infusion pumps or other infusion controlling instrumentation should be used. With this technique there will be no “therapeutic hiatus,” and adequate plasma levels of greater than 1.5 µg/ml, which is the minimal level necessary to suppress arrhythmias, will be achieved at all times (table 1). Steady-state conditions will not be achieved for approximately 400 minutes, or four half-lives for the metabolic degradation of lidocaine, with this therapeutic regime.24 If, during the course of the infusion it is necessary to suppress other ventricular arrhythmias, another bolus loading dose of 50–100 mg given over 1–2 minutes should be administered, simultaneously raising the infusion rate.26 28 When the drug is discontinued, it can be stopped abruptly without having to taper it, since the drug will diffuse back from the outer tissue compartment into the central volume of distribution and not drop to subtherapeutic levels for 2–3 hours.

Because lidocaine’s effect is dose and plasma concentration-related,25 a few simple rules for administration will enhance its effectiveness and reduce the likelihood of severe toxic reactions such as convulsion and coma. In congestive heart failure, shock and liver disease, and in patients over 70 years old, the loading doses should be reduced by 50% and lower infusion rates of 2 mg/min are desirable.29 30 Lidocaine is metabolized primarily by the liver, and may accumulate to very high levels when hepatic blood or hepatocellular function is decreased.30 Proper application of the pharmacokinetic principles outlined in table 1 will generally prevent such side effects.

### Current Philosophy for Antiarrhythmic Prophylaxis

Routine administration of lidocaine to all patients in the coronary care unit seems indicated. This should exclude all patients with known sensitivity to lidocaine or its analogs. The drug’s administration program should be reduced by 50% in those patients with congestive heart failure, shock and liver disease. It should be administered for 24–36 hours after infarction, or until the diagnosis of infarction is excluded in those patients who are taking the drug because of chest pain. The rationale for these recommendations are: 1) routine prophylaxis prevents primary ventricular fibrillation; 2) warning arrhythmias are absent or are missed in a high percentage of patients in the coronary care unit; and 3) rational programs for administration minimize the likelihood of toxicity.

By administering lidocaine to all patients entering the coronary care unit, many patients who do not have subsequent documentation of infarction will be treated. Even though this may be 50% of all CCU admissions, this does negate these recommendations. Many of these patients have unstable angina and a high incidence of arrhythmic deaths.31 Treatment can be discontinued once infarction has been excluded.

These recommendations may prove controversial, since only one acceptable study utilizing lidocaine in the prevention of primary ventricular fibrillation has been performed. A carefully designed clinical trial of routine lidocaine administration should be carried out to provide definitive information for the physician treating patients who have had myocardial infarction. Such trials should begin immediately, in view of the magnitude of the problem and the fact that routine prophylaxis of arrhythmias after myocardial infarction is not common policy. Such a study, if well designed, can answer the questions of the need to monitor patients if they are all receiving prophylaxis and the safety of administering lidocaine to larger patient groups, and will define more completely the natural history and survival of ventricular arrhythmias occurring after myocardial infarction.

### References


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