Hemodynamic Effects of Lidocaine in Patients with Heart Disease

By Richard R. Schumacher, M.D., Alan D. Lieberson, M.D., Richard H. Childress, M.D., and John F. Williams, Jr., M.D.

SUMMARY

The intravenous administration of 50 mg of lidocaine as a single bolus to four patients with heart disease did not result in a significant change in cardiac output or left ventricular end-diastolic pressure (LVEDP). Two patients had moderate decrease in systemic arterial pressure which was not accompanied by symptoms, was of short duration, and did not require therapeutic intervention. Left ventricular function, as assessed by the relationship of changes in stroke volume index (SVI) and stroke work index (SWI) to changes in LVEDP, was not significantly affected nor was the maximum rate of rise of left ventricular pressure (dp/dt).

The intravenous injection of 100 mg of lidocaine into eight additional patients with heart disease did not produce a statistically significant change in any of these hemodynamic variables when compared to their respective control values. Examination of individual responses, however, revealed that some depression of left ventricular function occurred in at least three and probably four of these patients. Nevertheless, this depression of myocardial function was not of sufficient magnitude to produce symptoms or reduce the cardiac output and generally did not result in an inordinate increase in LVEDP.

It is concluded that 100 mg or less of lidocaine injected intravenously has remarkably few, if any, adverse hemodynamic effects of clinical significance in man.

Additional Indexing Words:
Cardiac output Ventricular function Systemic arterial pressure

THE DEVELOPMENT of cardiac arrhythmias in patients with heart disease occurs all too frequently and the serious consequences which may result are well known to all clinicians. Although several drugs are available which can abolish many of these arrhythmias, enthusiasm for their administration often is tempered by knowledge of the undesirable hemodynamic effects which they are capable of producing. The propensity for quinidine and procainamide, two of the more commonly used anti-arrhythmic agents, to produce systemic hypotension when administered intravenously is well known, and a depressant effect upon the myocardium has been observed by several investigators. The discovery that diphenylhydantoin also was effective in abolishing many cardiac arrhythmias and that significant systemic hypotension did not occur with intravenous administration appeared to offer promise that this was a more ideal anti-arrhythmic agent for intravenous use than either quinidine or procainamide. However, recently it has been demonstrated that diphenylhydantoin also is not totally devoid of adverse hemodynamic effects since it will depress myocardial function in patients with heart disease. Furthermore, fatalities have occurred after its intravenous use.

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Table 1

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<th>SVI</th>
<th>SWI</th>
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Key: BSA = body surface area in m²; ASHD = arteriosclerotic heart disease; PMD = primary myocardial disease.

Time = time in minutes after drug injection with 0 representing the control period; HR = heart rate in beats/min; Mean art pr = mean arterial pressure in mm Hg; CI = cardiac index in L/min/m²; LVEDP = left ventricular end-diastolic pressure in mm Hg; SVI = stroke volume index in ml/m²; SWI = left ventricular stroke work index in g-m/m²; dp/dt = maximum rate of rise of left ventricular pressure as per cent of control.

Lidocaine, best known as a local anesthetic, has been found to be effective in the treatment of many tachyarrhythmias, and initial studies on the hemodynamic effects of this agent indicated that it had distinct advantages over other commonly used anti-arrhythmic drugs when administered intravenously. In animals cardiac output has been found to increase, and in man arterial pressure generally is little affected by the administration of therapeutic doses of lidocaine. In addition, Harrison and associates reported that myocardial contractile force measured directly in patients at the time of corrective cardiac surgery was not affected significantly by this agent. However, more recently Nelson and Harrison observed that lidocaine does diminish the force of isometric contraction in the isolated papillary muscle preparation, and Austen and Moran have demonstrated a negative inotropic effect in dogs.

The following study was undertaken to provide information concerning the hemodynamic effects of lidocaine in unanesthetized humans and in particular to observe its effect on left ventricular function. Furthermore, it was proposed that these effects be examined in subjects who would most likely receive this agent therapeutically, for example, patients with heart disease, and that the doses used be those which are commonly used in the treatment of arrhythmias.

Methods

Twelve male patients, ranging in age from 33 to 73 years (average, 52 years), were the subjects of this study. Three patients had hypertensive cardiovascular disease, two had arteriosclerotic heart disease with angina pectoris, and the remainder were believed to have primary...
myocardial disease (tables 1 and 2). All patients but L. L. and G. G. had radiographic evidence of cardiomegaly, a history of congestive heart failure, and were receiving a digitalis glycoside at the time of the study. Patient G. G. (table 2) had electrocardiographic evidence of left ventricular hypertrophy. All patients were in sinus rhythm, and none had clinical evidence of congestive heart failure at the time of the study. All studies were performed in the postabsorptive state with the patient in the supine position. Secobarbital, 100 mg, was given orally 60 to 90 min before the procedure. Following diagnostic right and left heart catheterization, catheters

For abbreviations, see table 1. HCVD = hypertensive cardiovascular disease.
The effect of lidocaine on hemodynamic variables assessing left ventricular function. For abbreviations, see text. Values represent mean values ± standard error of the mean. Open circles connected by broken lines indicate values for patients receiving 50 mg of lidocaine; closed circles connected by solid lines, values for those receiving 100 mg. Abscissa represents control period (C) and time in minutes after drug injection.

Figure 1

were left in the main pulmonary artery for purposes of injection and in the left ventricle for the recording of pressure. Cardiac output was determined by the indicator-dilution method. Indocyanine-green dye was injected and rapidly flushed into the pulmonary artery while blood from the brachial artery was withdrawn through a Gilford densitometer. The maximum rate of rise of left ventricular pressure was measured using an R-C differentiating circuit with a 15-Hz filter. A standard limb lead of the electrocardiogram and the brachial arterial pressure were recorded with the hemodynamic variables on a multi-channel oscillograph. The midthoracic level was used as the zero reference point for intravascular pressure.

After systemic arterial pressure, heart rate, and left ventricular end-diastolic pressure (LVEDP) had remained constant for 15 to 20 min, 50 mg of lidocaine was injected as a single bolus into

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the pulmonary artery of four patients (group 1). All measurements were then repeated 5, 10, 15, and 30 min after drug injection. Since no adverse effects were noted with this dose of lidocaine, the next eight patients (group 2) received 100 mg of lidocaine injected as a single bolus; measurements were repeated as above.

Stroke work index (SWI) in g-m/m² was calculated from the following formula:

$$SWI = \frac{SVI \times (LVSP - LVEDP) \times 1.36}{100}$$

where SVI means the stroke volume index in milliliters per square meter, LVSP is the mean left ventricular pressure during ejection in mm Hg determined planimetrically, and LVEDP is the left ventricular end-diastolic pressure in mm Hg.

Results

Group 1

The individual hemodynamic data before and after injection of 50 mg of lidocaine are presented in table 1, while the mean values are illustrated in figure 1.

In three patients heart rate was essentially unchanged or demonstrated only a slight fall following drug administration, while a fall of 16 beats/min was observed at the 30-min period in the remaining patient. Mean arterial pressure remained relatively constant in two patients, but had decreased by 16 and 11 mm Hg at the 30-min period in the other two. Neither patient developed symptoms of arterial hypotension, and the arterial pressure gradually returned to the control values without therapeutic intervention. Cardiac index (CI) at rest was reduced to < 2.5 L/min/m² in two patients. After the injection, CI was relatively unchanged in all patients during the first 15 min, but a small decline from the control value was observed in four patients at the 30-min period, the maximum decrease being 0.52 L/min/m². Left ventricular end-diastolic pressure (LVEDP) at rest exceeded normal (> 12 mm Hg) in only one patient. Lidocaine did not result in a significant increase in LVEDP in any patient and, in fact, a significant fall occurred at the 30-min period in the patient with the highest resting LVEDP. In two patients small reductions in SVI of 2 and 4 ml/m² occurred at the 5-min period and thereafter returned to control values. In the remaining two patients maximum decreases in SVI of 5 and 8 ml/m² occurred at the 30-min period. SWI also decreased in each patient at some time after drug injection with the greatest decrease being 8.7 g-m/m². In two patients the maximum decrease in SWI occurred at the 5-min period whereas in the remaining two this was noted at 30 min. The maximum rate of rise of left ventricular pressure fell below the control value in three patients, the greatest decrease being 13% which occurred at the 30-min period. The reduction in dp/dt in the remaining two patients did not exceed 10% and, by the 30-min period, values exceeding the control were observed.

Group 2

The individual hemodynamic data before and after 100 mg of lidocaine are given in table 2 and the mean values are illustrated in figure 1. The mean values for LVEDP, SWI, and maximum dp/dt at the 10-min period include observations on only seven patients. However, recalculation of mean values for all the variables using data from only these seven patients did not appreciably alter the results.

Changes in heart rate were variable after lidocaine, the maximum increase observed being 12 beats/min and the maximum decrease 6 beats/min. The average heart rate at all periods after lidocaine was essentially unchanged from the control rate which averaged 98 ± 6 (se) beats/min. The response of mean arterial pressure to lidocaine also varied among the patients, although the average value at each period was quite similar to the control of 99 ± 8 mm Hg. The maximum decrease in mean arterial pressure observed in any patient was 11 mm Hg which occurred at the 5-min period and which had returned to essentially control values at the 15-min period in this patient. Cardiac index was reduced at rest in five patients and averaged 2.43 ± 0.25 L/min/m². After lidocaine the average cardiac index was essentially unchanged, and the maximum decrease observed in any patient was 0.56 L/min/m².
LVEDP at rest was elevated in five patients and averaged $17 \pm 3$ mm Hg. The response of LVEDP to lidocaine was quite variable. However, an elevation of LVEDP to abnormal levels occurred in only one of the patients in whom the resting value was normal. In the five patients with elevated LVEDP at rest a further rise after lidocaine occurred in four. In one of these latter patients an increase of 11 mm Hg was observed whereas in the others the increase did not exceed 4 mm Hg. Lidocaine produced a decrease in SVI in six of eight patients. However these changes generally were quite small averaging only 1 ml/m² below control through the 15-min period. In all but two of these patients SVI had returned to near control values by the 30-min period which averaged 1 ml/m² above control. Similarly, SWI decreased at some time during the first 15 min after lidocaine in the same six patients and in four returned toward their respective control values by 30 min. The maximum decrease in the average SWI occurred at the 10-min period, having decreased from the control average of 33.5 g-m/m² at rest to 28.9 g-m/m². This decrease however is somewhat magnified by the failure to obtain measurements at the 10-min period in one patient. Excluding this patient the average decrease in SWI between the control and 10-min periods was 3.0 g-m/m². The maximum rate of rise of left ventricular pressure decreased by more than 5% in five patients. In each of these patients the maximum decrease occurred at the 5-min period and in four of these patients maximum dp/dt had returned toward control values by 30 min. In the remaining one of these four patients, dp/dt had returned to near control values by the 15-min period but, in association with a marked fall in LVEDP, decreased again at the 30-min period. The average decrease in dp/dt for the group was small, averaging 4% at the 5-min period and thereafter exceeding control values.

**Discussion**

It was the purpose of the present investigation to determine the hemodynamic effects of lidocaine and in particular the effect of the drug on left ventricular function in man. Although changes in arterial pressure, heart rate, and cardiac output can be detected with relative ease and reliability in man, detection of alterations in left ventricular function presents significantly greater problems. Several investigators however have demonstrated that the relationship of the mechanical work performed by the ventricle, that is, SVI and SWI to the left ventricular end-diastolic volume as reflected in the LVEDP, is a useful measure of myocardial function. Thus, an increase in SVI and SWI, or both, from the same or diminished LVEDP indicates an increase in the contractile state of the myocardium whereas a decrease in SVI and SWI, or both, with the same or increased LVEDP indicates depressed myocardial function. Therefore, this relationship was used in the present study to assess the effects of lidocaine on left ventricular function. In addition the maximum rate of rise of left ventricular pressure also was measured since changes in the contractile state of the ventricle can occur which are reflected only in changes in the velocity of myocardial contraction.

Interpretation of the data from the patients given 50 mg of lidocaine is difficult because of the variable results obtained in this small number of patients. However, since it was not the purpose of this investigation to study dose response relationships of lidocaine and since no major untoward hemodynamic effects occurred in this group of patients, we elected not to include a larger number of patients. Two patients given 50 mg of lidocaine did develop decreases in mean arterial pressure of 16 and 11 mm Hg although this was not accompanied by symptoms, was relatively short-lived, and did not require therapeutic intervention. A relatively small decrease in cardiac index was observed in each patient, the maximum being 0.52 L/min/m², whereas a significant rise in LVEDP did not occur in any patient. Unequivocal evidence of a myocardial depressant action with this dose of the drug was not obtained in
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any patient. Changes in SVI and SWI generally paralleled the changes in LVEDP, and in the two patients in whom changes in these variables suggested a depression of myocardial function, an increase in maximum dp/dt occurred at that time. Furthermore in the two patients in whom maximum dp/dt fell after lidocaine, the decreases were small, 9 and 7%, and in one this could be attributed to a simultaneous reduction in heart rate and LVEDP.25, 26

The administration of 100 mg of lidocaine to eight patients also resulted in variable but generally small changes in all hemodynamic variables, none of which was significantly different statistically from its respective control at any time period. The maximum decrease in mean arterial pressure in any individual was 11 mm Hg which occurred in one patient at the 5-min period and which had returned to control values by the 15-min period. The maximum decrease in CI in any patient was 0.56 L/min/m² which occurred at the 10-min period and which had returned to control values by the 15-min period. In only one patient was a marked increase in LVEDP observed (11 mm Hg), and this also quickly returned toward control values. None of the patients developed symptoms following lidocaine injection.

These results are in agreement with previous reports concerning the effect of this drug on systemic arterial pressure.3, 9, 10, 13, 15 The observation that there was no statistically significant change in SVI, SWI, dp/dt, or LVEDP from their respective control values would indicate that this agent did not depress myocardial function. This would be in accord with the observation of Harrison and associates3 who measured right ventricular contractile force in man but at variance with studies using dogs17 or isolated muscle preparations.16

However examination of individual responses in the group 2 patients revealed that left ventricular function was depressed by lidocaine in some patients. Three patients (J. B., W. G., and H. M.) responded to the drug with an increase in LVEDP whereas maximum dp/dt and SWI fell in each and SVI declined in two. In an additional patient (L. H.), maximum dp/dt fell and SVI and SWI increased only slightly in spite of an increase of 11 mm Hg in LVEDP. Thus the effect of 100 mg of lidocaine on myocardial function in patients with heart disease is variable. Of equal or greater importance however is the observation that, even when impairment of left ventricular function did occur, it was not of sufficient magnitude to produce symptoms or reduce the cardiac output and the effect was short-lived.

It is of interest that the response to lidocaine was not influenced by the type of heart disease or its severity as judged by the resting CI and LVEDP. However the small number of patients studied would not permit a definitive conclusion in this regard. Certainly it must be appreciated that a more pronounced effect might occur in patients with more advanced heart disease or in those receiving larger doses of this drug. Nevertheless, it would appear from this study that the injection of lidocaine in amounts commonly used in the treatment of arrhythmias exerts remarkably few, if any, adverse hemodynamic effects of clinical significance in man.

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