Does lignocaine increase the chance of survival from massive heart attack?

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Introduction: Lignocaine (lidocaine) blocks voltage-activated sodium channels and has been used extensively since the 1960s in patients presenting with suspected acute myocardial infarction (AMI). In a review of many clinical trials and publications, Yadav & Zipes (2004) concluded that although prophylactic lignocaine administered after a suspected AMI appeared to reduce the incidence of primary ventricular fibrillation (VF, the fastest and most lethal tachyarrhythmia) by as much as 33%, lignocaine was also associated with an increased incidence of bradycardia (slow heart rate), asystole (no heart beat), and subsequent mortality. Because of this, Yadav & Zipes recommended that on the basis of contemporary information, prophylactic lidocaine should not be used in the management of patients with proved or suspected AMI.

Aim: To determine in an animal model of AMI whether lignocaine reduces the incidence of tachyarrhythmias (VF and/or haemodynamically compromising ventricular tachycardia (VT)) when administered prior to a coronary artery occlusion sufficient to produce an AMI.

Methods: 21 pigs (M+F, 20-35 kg) were sedated with stresnil (1-2 mg/kg im), anaesthetised with thiopentone sodium (10-15 mg/kg iv) and maintained under general anaesthesia with a mixture of isoflurane (0.5 – 2%) in oxygen. Artificial ventilation was maintained at a volume of 15 ml/kg and a rate of 12 breaths per minute. An intravenous saline drip was maintained for intra-operative hydration or lignocaine administration. Blood pressure (BP) and a lead II electrocardiogram (ECG) were monitored, digitised and recorded. Lignocaine (2.5 – 12 mg/kg bolus plus 0.05 – 0.24 mg/kg/min iv continuous infusion) was administered to 11 of the pigs. Following a mid-sternotomy and dissection of the pericardium, the left anterior descending coronary artery (LAD) was ligated 40 min (39 +/- 13 min sd) after the commencement of lignocaine or saline administration mid-way along its length.

Results: The results in Table column 1 refer to the number of animals; the remaining columns refer to all animals. Sustained is defined as lasting longer than 15s and likely to be fatal if not externally reverted.

	animals developing sustained arrhythmia	sustained VTs in 1st 2 h	sustained VFs in 1st 2 h	non-sustained arrhythmias between 1 and 15s in 1st 2 h	total arrhythmias in 3rd hour
Control (n=10)	10	13	43	91	88
Lignocaine (n=11)	6	3	10	70	2

Discussion and Conclusion: The results clearly showed that when lignocaine was administered prior to a coronary artery occlusion it significantly reduced the number of animals which developed a haemodynamically compromising tachyarrhythmia and the number of sustained and non-sustained tachyarrhythmias for all animals.So why then do Yadav & Zipes recommend that lignocaine not be used? Consider the following 2 points: a) After a coronary artery occlusion, the distal tissue becomes ischaemic, hypoxic, and ultimately infarcted. Between the ischaemic region and the surrounding perfused region there is a border zone which receives limited perfusion. Clearly then, iv lignocaine administered after a coronary artery occlusion can not have a pharmaceutical effect on the ischaemic region other than at the border zone. b) Tachyarrhythmias can develop from AMIs in which the occlusion remains intact as well as from AMIs in which the occlusion dissipates and the tissue becomes reperfused. From these 2 points, we can develop 3 scenarios: 1) that an ischaemic region can become reperfused subsequent to an occlusion if the occlusion dissipates, 2) that an occlusion can remain intact but the ischaemic region can be small either because the occlusion is in a small artery or because the border zone is wide as a result of extensive collateral circulation, and 3) that an occlusion can remain intact and produce a large ischaemic region with a narrow border zone. In light of our results and the reduction in incidence in arrhythmias quoted by Yadav & Zipes, we suggest that lignocaine would likely reduce the incidence of arrhythmias in the first 2 scenarios wherein iv lignocaine could perfuse a large portion of the ischaemic region. In contrast, we suggest that in the 3rd scenario, iv lignocaine would never reach the ischaemic region and subsequently it would have no effect on that tissue, irrespective of the dose administered. Finally, we suggest that the lignocaine-related bradycardic and asystolic deaths referred to by Yadav & Zipes may have resulted from overdosing of lignocaine in a setting where it was showing no effect as in scenario 3. In this instance lignocaine, being a sodium channel blocker, would be shutting-down cell conduction. Because of these considerations, we argue with Yadav & Zipes' recommendation and suggest that lignocaine is beneficial in reducing the incidence of tachyarrhythmia in those AMIs where it can be delivered to the ischaemic tissue but the serum levels need.to be kept low so action potentials are not blocked.

Yadav, A.V. & Zipes, D.P. (2004) *The Americal Journal of Cardiology* **94**, 606-608.