MASSIVE LIGNOCaine OVERDOSE DURING CARDIOPULMONARY BYPASS
Successful treatment with cardiac pacing


SUMMARY
A case of accidental massive overdose of lignocaine while a patient was on cardiopulmonary bypass is described. The benefits of cardiopulmonary bypass and cardiac pacing in the management of the patient are discussed.

The widespread use of lignocaine in the treatment of cardiac arrhythmias, and in local analgesia (especially intravenous regional blockade) has led inevitably to a significant incidence of serious toxic reactions following inadvertent overdosage (Kew and Lowe, 1978; Burlington and Freed, 1980; Badui, Garcia-Rubi and Estanol, 1981). Central nervous system depression followed rapidly by convulsions and respiratory arrest are often the first manifestations (Kew and Lowe, 1978). However, once adequate oxygenation has been achieved, successful resuscitation depends on the adequacy of cardiovascular support. Depression of autorhythmicity and conduction occurs, leading to bradycardia, bundle branch block and asystole. These disturbances are associated with a decrease in myocardial contractility which may be profound (Lieberman et al., 1968). Treatment in reported cases has been principally pharmacological. Cardiac pacing has been attempted only rarely, often after considerable delay and with poor results (Burlington and Freed, 1980; Antonelli and Bloch, 1982; Freedman, Gal and Freed, 1982). Extracorporeal support has been considered in one case of etidocaine overdosage (Prentiss, 1979), and has been advocated, following uniformly successful resuscitation in dogs receiving lignocaine overdoses which were lethal to 75% of animals treated more conventionally (Freedman, Gal and Freed, 1982).

We report the case of a patient who received a massive dose of lignocaine whilst on cardiopulmonary bypass.

CASE HISTORY
Presentation
Five months after triple coronary artery bypass grafting, a 58-year-old man (weight 76 kg) was readmitted to hospital with recurrent effort-induced angina which severely limited his activities and prevented his return to work. Examination and investigations were within normal limits except for an ischaemic electrocardiogram, hyperlipidaemia and coronary angiography which revealed occlusion of two of the grafts with slight ventricular impairment. Treatment of the patient with nifedipine 10 mg 8 hourly and isosorbide dinitrate 10 mg 12 hourly was started; his dose of propranolol was doubled and he was referred for further coronary artery bypass grafting.

Anaesthetic management and operative course
Papaveretum and hyoscine were given as premedication with the patient’s normal dose of propranolol. Anaesthesia was induced with nitrous oxide and trichloroethylene in oxygen. The electrocardiogram and arterial pressure were monitored continuously. Neuromuscular blockade was achieved with pancuronium, the trachea was intubated and ventilation controlled artificially. The patient was established on cardiopulmonary bypass. Double coronary artery bypass grafting was carried out, but the procedure was prolonged greatly as a result of the massive lignocaine overdose.
result of the presence of adhesions and lack of suitable grafting material. Eventually, a composite graft was fashioned and attached to one of the original vein grafts, the aorta being markedly atheromatous.

After the patient had been rewarmed, and on removal of the aortic cross-clamp, the heart began to fibrillate vigorously. This was treated by defibrillation, but when fibrillation recurred, a bolus of lignocaine 200 mg was requested. Two concentrations of “Xylocard” were available, supplied in pre-packed sterile 5-ml syringes containing lignocaine 100 mg or 1 g, respectively. Despite several warnings on the packaging, lignocaine 2 g was administered accidentally into the cardiopulmonary bypass circuit and almost immediately the heart became completely flaccid in asystole. Calcium chloride 3 mmol was given immediately and an isoprenaline infusion started, but cardiopulmonary bypass support had to be re-started as no satisfactory output could be obtained. It was decided that sequential atrioventricular cardiac pacing would offer the best hope of acceptable postoperative cardiac output and atrial leads were sutured into place. At this point, some 45 min after the administration of the lignocaine, it was found that atrial pacing alone provided a good cardiac rhythm in the presence of isoprenaline. Cardiac output was sufficient to allow discontinuation of cardiopulmonary bypass, the operation was completed and the patient transferred to the intensive care unit.

Postoperative course

Sinus rhythm returned about 4 h after the lignocaine had been given; the isoprenaline infusion and demand pacing were continued overnight. Sodium nitroprusside and adrenaline infusions were added to improve the circulation. Fresh frozen plasma, fresh and stored blood were given to replace blood loss. By morning the patient was stable haemodynamically and was responding to verbal commands and moving all limbs. No further pacing was required, but inotropic support was necessary for a further 36 h to maintain an adequate circulation and urine production. The trachea was extubated on the 2nd day after operation.

At no time during surgery or recovery was there any clinical evidence of seizure activity. Cerebral function monitoring was commenced at the time of overdosage and no abnormal electrical activity was detected. There was, however, intermittent confusion for several days following the operation, but despite this, the patient made a full recovery and was discharged home 14 days following surgery. When seen in the Outpatient Clinic at 12 months, he had remained completely well.

DISCUSSION

Clearance of lignocaine from the plasma is related to hepatic blood flow, and under normal circumstances this is related linearly to cardiac output. Less than 5% is excreted in the urine (Stenson, Constantino and Harrison, 1971). In the patient with poor cardiac output there may be greatly diminished hepatic perfusion and drug elimination may be prolonged, leading, in many circumstances, to effectively irreversible drug intoxication. This is probably compounded by a pathological decrease in the apparent volume of distribution (V) of the drug maintaining high plasma concentrations (Freedman, Gal and Freed, 1982).

In the presence of an extracorporeal circulation, it has been shown in man that the apparent steady state (V<sub>ss</sub>) and beta phase (V<sub>beta</sub>) distribution volumes for lignocaine are approximately doubled (Morrell and Harrison, 1983), an effect thought to be caused predominantly by albumin dilution rather than by the increase in circulating volume. Plasma clearance (CL<sub>p</sub>) is unchanged. This is supported by evidence from animal studies (Freedman, Gal and Freed, 1982). Thus, by maintaining cardiopulmonary bypass for long enough to allow the plasma lignocaine concentrations to decrease sufficiently, full recovery could be anticipated.

The immediate problem of cardiac flaccidity and asystole has been well described previously. In this patient, this was treated successfully with cardiopulmonary bypass, followed by atrial pacing combined with inotropic support. It is perhaps a little surprising that atrioventricular conduction was not a problem; however, many factors which might influence the pharmacokinetics and pharmacodynamics are present, including local tissue acidosis and dilution of tissue proteins. Further in their study, Freedman, Gal and Freed (1982) found that sinus rhythm could be returned in all dogs within 90 min of extracorporeal support, the animals having received a dose of lignocaine comparable to that received by our patient (30 mg·kg<sup>-1</sup>). Indeed, three of eight animals remained in sinus rhythm throughout. Finally, in most reported cases where lignocaine has been administered, there has been some preceding hypoxic insult to the heart which is likely to increase
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the incidence of conduction disturbances. During cardiopulmonary bypass, the myocardium is carefully protected (Wheeldon et al., 1976).

Little evidence of central nervous system toxicity was seen in the case of lignocaine overdosage described, although the peak plasma concentrations of lignocaine may have been decreased by the mechanisms outlined above. Oxygenation of the brain was, of course, unaffected.

The importance of prolonged resuscitative efforts, especially where the newer, highly protein bound compounds are used, has been emphasized (Prentiss, 1979). The plasma concentrations of drug do decrease, even during prolonged cardiac massage. Extracorporeal support, whilst of theoretical value in the treatment of local anaesthetic overdosage as illustrated by this case, is unlikely to be available in most clinical situations. In these circumstances, it would seem that cardiac pacing, transvenously or via the oesophagus, may have a role in the treatment of local anaesthetic overdosage and should form a part of immediate resuscitative efforts where indicated.

The responsibility of the anaesthetist to check drug identity and dosage carefully before administration must be emphasized. However, in this case, although warnings appear prominently on the packaging, the markings on the syringe containing the concentrated solution are obscured by the plunger and printing on the opposite side visible through the glass. A similar accident involving the inappropriate administration of a concentrated dextrose solution resulting in two deaths drew attention to the need for clarity in labelling (Bethune and Wheeldon, 1980).

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REFERENCES


