ELECTROENCEPHALOGRAM OF THE CAT AFTER INTRAVENOUS INJECTION OF LIDOCAINE AND SUCCINYLCHOLINE

Fiona Acheson, Arthur B. Bull, Paul Glees

Although the peripheral effects of local anaesthetics have been widely studied, relatively little work has been done to illustrate their impact upon the central nervous system. The present paper describes, first, the electroencephalographic changes occurring with varying doses of lidocaine given intravenously and second, the effect on the tracings of simultaneous intravenous succinylcholine.

Method

The experiments were carried out on cats, a total of 30 animals being used, many being subjected to the tests again and again. All the tracings described were typical of those elicited from several animals on different occasions.

Only nitrous oxide and oxygen were used as anaesthetics. No other anaesthetic agent was employed at any time, nor any form of pre-medication, as it was felt that such drugs per se might produce electroencephalographic changes and so confuse the picture. The cats were subjected to an atmosphere of 80 per cent nitrous oxide and 20 per cent oxygen which was found to produce unconsciousness and yet to contain an ample supply of oxygen. Anaesthesia was also maintained with the same mixture, and this was administered from a continuous flow anaesthetic apparatus via a specially constructed face piece. A permanently patent intravenous channel was obtained by means of a Mitchell (1) self-sealing intravenous needle in the saphenous vein (fig. 1).

Six steel gramophone needles were used as electrodes. The scalp was shaven and the needles were hammered into the skull of the anaesthetised animal in three symmetrically placed pairs, one pair over the frontal lobes, the second pair over the parietal lobes and the third over the occipital lobes (fig. 1). Care was taken to ensure that the needles did not penetrate the meninges, and thus no trauma was inflicted upon the cerebral cortex. They were then connected to an Ediswan electroencephalogram in the manner illustrated in figure 2.

Received from the Department of Physiology, University of Oxford, England, and accepted for publication June 12, 1956. Dr. Acheson’s work was supported by a personal grant from the Nuffield Foundation, London. Dr. Acheson is now Senior Instructor, Department of Anesthesia, Western Reserve University, Cleveland, Ohio. Dr. Bull is a Nuffield Travelling Fellow in Anesthesia. Dr. Glees is Lecturer in Physiology, University of Oxford, England.
FIG. 1. A cat while electroencephalographic tracings are being taken. Note the Mitchell needle in the right saphenous vein, the specially designed face piece, and the six electrodes in position in the shaven scalp.

RESULTS

Electroencephalogram of the Cat Anaesthetised with 80 per cent Nitrous Oxide and 20 per cent Oxygen.—The typical tracing of the cat under N₂O–O₂ anaesthesia was one showing predominant 15–20 cycle/sec. waves of low voltage in all leads. There were occasional short

FIG. 2. Detailed representation of the cortical areas from which the tracings were taken. Note the connections used for the leads.
bursts of slower waves in the 4–6 cycle/sec. range of higher amplitude with signs of superimposed fast activity. This was seen consistently and was accepted as a baseline.

Electroencephalogram After the Rapid Intravenous Injection of Lidocaine in Doses of 2 mg./kg.—The most notable feature in the tracing following the rapid injection of 2 mg./kg. of lidocaine was that the 15–20 cycle/sec. waves were disrupted 5–10 seconds after injection. The appearance of 8–10 cycle/sec. waves, which tended to be grouped in runs of up to 20, was most characteristic of lidocaine in this dosage

---

Fig. 3. Electroencephalographic tracing after intravenous injection of 2 mg./kg. lidocaine.

(fig. 3). This pattern did not persist for more than five minutes after injection.

Electroencephalogram After the Rapid Intravenous Injection of 5 mg./kg. Lidocaine.—The rapid injection of 5 mg./kg. of the drug was followed in 5–10 seconds by very large slow waves of 2–3 cycle/sec. and these often had faster waves superimposed upon them (fig. 4). This picture persisted for 2–3 minutes, following which the tracing again became as described after lidocaine doses of 2 mg./kg. with subsequent reversion to the basic pattern.
Intravenous Injection of 10 mg./kg. Lidocaine.—When the dose of lidocaine was raised to 10 mg./kg. the tracing passed rapidly through the stages already described, before the appearance of spike and wave complexes of very high voltage. Then 10–12 seconds after injection the animal suffered a clinical convulsion and the tracing showed a typical grand mal discharge picture. The duration of the grand mal discharge was usually from 2–3 seconds and alternated with a completely flat record lasting 2–3 seconds (fig. 5) for up to eight minutes after injection. Then, after a period when isolated spike discharges

rose from a flat record, there was a gradual reversion of the tracing to the basic pattern described.

Intravenous Injection of Succinylcholine Chloride 1 mg./kg.—When 1 mg./kg. succinylcholine was given intravenously there was an over-all increase by about one third in the amplitude of the basic nitrous oxide-oxygen tracing. Otherwise no change in the baseline pattern was ever seen.

Simultaneous Intravenous Injection of Lidocaine 5 mg./kg. and Succinylcholine 1 mg./kg.—The combination of lidocaine, 5 mg./kg.,
with succinylcholine, 1 mg./kg., usually produced a tracing similar to that described after the injection of 10 mg./kg. of lidocaine alone. The amplitude and duration of each epileptic discharge was the same as before, and so was the interval between the fits (fig. 6). The total duration of the repeated fits was, however, shorter. Owing to the peripheral action of the succinylcholine, no clinical convulsions were observed after the initial muscular fibrillation induced by the relaxant had ceased. Artificial ventilation was carried out during the stage of paralysis from succinylcholine.

Fig. 6. Electroencephalographic tracing after intravenous injection of 5 mg./kg. lidocaine in combination with 1 mg./kg. succinylcholine. Note the marked similarity between this record and that shown in figure 5, and its difference from that shown in figure 4.
DISCUSSION

The combined effect of lidocaine and succinylcholine is worthy of some discussion. It will be seen that succinylcholine doubles the epileptogenic effect of lidocaine. Although 10 mg./kg. of lidocaine were required to cause a convulsion when given alone, 5 mg./kg. had the same effect when combined with a therapeutic dose of succinylcholine. Among others, Foldes and his coworkers (2) have shown that the destruction of succinylcholine and of lidocaine in the body probably depends on the same enzyme, pseudocholinesterase. Thus it may be postulated that succinylcholine in some way fixes part of the pseudocholinesterase in the central nervous system allowing the lower dosage of lidocaine to produce its convulsive effect.

Bernhard and Bohn (3) have demonstrated anticonvulsive properties of lidocaine when injected intravenously in doses of 2 mg./kg. It was at this dose level in our experiments that the first notable change in electroencephalographic record appeared—changes in frequency which could be interpreted as signs of cortical depression. The same authors found that if they increased the intravenous dosage to 14–16 mg./kg., convulsions occurred in cats. This is a higher dose than we used to the same effect, but an important difference between the two experiments was the greater speed of injection in our series.

Central effects of other neuromuscular blocking agents have been described by Feldberg and Sherwood (4) and by Chang (5). The former showed that when decamethonium was introduced directly into the lateral ventricle of the cat a condition of spasticity with twitching and trembling ensued. D-tubocurarine, given by the same route, caused convulsive seizures resembling the grand mal of epilepsy. Chang (5) concluded that the central effect of curare was similar to that of strychnine. He showed that these two drugs both depress the general excitability of nervous tissue, but that they improve the efficiency of the synchronization of nerve impulses. None of these investigators describe the central action of succinylcholine.

The effect of succinylcholine in facilitating lidocaine convulsions might be explained in one of two ways. First, it may be the result of competition by the two drugs for pseudocholinesterase, or second, the succinylcholine may act as a blocking agent upon an inhibitory system.

A further point of interest is the relatively rapid return to normal of the electroencephalographic tracing. This would appear to be out of keeping with the long duration of action of lidocaine seen on peripheral nerves. Here again, pseudocholinesterase may be responsible. Cavanagh, Thomson and Webster (6) have shown that neuroglial tissue is particularly rich in this enzyme, in sharp contrast to the peripheral conductive fibers, where it is scanty.

Clinically, Lowe, Gray and North (7) have used combined lidocaine and succinylcholine intravenously in a large series of cases and it is
interesting to note that they have found that a relatively low dosage of succinylcholine is required to maintain relaxation in these circumstances. This again can be ascribed to the fact that both drugs depend for their breakdown on the cholinesterase system, but here the lidocaine is potentiating the action of the relaxant. These authors have consistently used a lidocaine dosage below that which we found to produce convulsion in cats when combined with succinylcholine. In addition, a barbiturate was used in their series during induction of anesthesia which would have an anticonvulsive effect.

SUMMARY

A series of experiments is described in which the electroencephalographic tracings after intravenous lidocaine, succinylcholine and the two drugs in combination were studied. Thirty cats were used as experimental animals, and anesthesia was induced and maintained with a mixture of 20 per cent O₂ and 80 per cent N₂O. It was found that 1 mg./kg. succinylcholine had no significant effect upon the electroencephalogram and that 10 mg./kg. lidocaine was strongly epileptogenic. However, when the drugs were combined, succinylcholine doubled the epileptogenic effect of lidocaine. The convulsions never lasted more than ten minutes.

It is suggested that this synergy between the drugs may be due to the fact that they both depend upon pseudocholinesterase for their destruction. It is further argued that the relatively transient effect of lidocaine upon the central nervous system, as compared with its long lasting effect peripherally, is that pseudocholinesterase is rich in the neuroglia.

ACKNOWLEDGMENTS

We should like to express our thanks to Sir Robert Macintosh and Professor E. G. T. Liddell for providing facilities for this work. We are also grateful to Dr. Epstein and Mr. Richard Salt who gave constant technical advice and to Miss Clare Pearson and Mr. R. C. Hutchinson who assisted with the experiments.

REFERENCES

3. Bernhard and Bohn: Local Anesthetics as Anticonvulsants (in preparation), Personal communication to the authors.