THE EFFECTS OF OTHER DRUGS ON THE STIMULATION OF LARYNGOSPASM IN THE CAT: ATROPINE; THIOPENTONE; SUXAMETHONIUM; LOCAL ANALGESICS

BY
M. A. E. REX

SUMMARY
The effects of atropine, thiopentone, suxamethonium and local analgesics on the stimulation of laryngospasm were studied in anaesthetized and decerebrate cats. Atropine and thiopentone had no significant effect on the laryngeal reflex in these preparations. Suxamethonium prevented laryngospasm by paralyzing the intrinsic laryngeal muscles. The use of local analgesic sprays in the pharynx and larynx caused a considerable reduction in the effects of stimulation of the respiratory tract by volatile anaesthetic agents.

METHODS

Preparations.
The preparations used were two cats anaesthetized with chloralose (65 mg/kg) and nine decerebrate cats. The techniques of anaesthesia and decerebration have been described previously (Rex, 1970a, 1971). The experiments described here were carried out in an attempt to determine whether the laryngeal reflex is modified by the administration of atropine, thiopentone, suxamethonium, and local analgesic drugs.

Recording.
Needle electrodes placed in the cricothyroid muscle and the diaphragm were used to obtain electromyograms. The techniques of electromyography have been described in a previous paper (Rex, 1970a).

Experimental manipulations.
Exposure of the respiratory tract to an ether spray or to 10–20 per cent ether vapour in oxygen stimulated laryngospasm and apnoea or changes in respiratory rhythm. Atropine sulphate, thiopentone sodium and suxamethonium chloride were administered intravenously through an indwelling polyethylene catheter to five decerebrate cats to determine their effects on the stimulation of laryngospasm by ether vapour. In four decerebrate cats and two cats under chloralose anaesthesia a local analgesic solution was sprayed on to the pharynx and anterior larynx. The respiratory tract was then exposed to ether vapour or spray to determine whether laryngospasm was still stimulated.

RESULTS

Atropine.
Atropine was administered intravenously to each of five decerebrate cats. In four of the cats a dose rate of 0.1 mg/kg was given. Atropine at this dose rate, which is commonly used in clinical pre-anaesthetic medication in cats, had no effect on the stimulation of apnoea and laryngospasm when ether vapour was passed through the isolated nasopharynx and larynx.

In one cat, a dose of atropine over thirty times that used in clinical anaesthetic practice was administered, but it failed to modify the effect of ether vapour administered by mask or tracheal cannula. By mask, ether stimulated laryngospasm and an interruption of the regular rhythm of the respiratory tract was prevented.

M. A. E. REX, M.A., VET.M.B., PH.D., M.R.C.V.S., Department of Veterinary Clinical Sciences, Massey University, Palmerston North, New Zealand.

Present address: Veterinary Clinical Centre, University of Melbourne, Werribee, Victoria 3030, Australia.
diaphragm. Ether inhaled into the trachea and lungs stimulated laryngospasm and apnoea. Atropine appeared to have no direct effect on the stimulation of laryngospasm under these conditions.

**Thiopentone.**

Figure 1a shows the records obtained from the cricothyroid muscle and diaphragm of a decerebrate cat during administration of ether and oxygen by mask. Laryngospasm and apnoea were stimulated. Resting activity was considerable in the cricothyroid muscle and diaphragm in this cat. After intravenous administration of thiopentone sodium (2 mg/kg) the respiratory rate slowed and the frequency of the discharge from the cricothyroid muscle was diminished. Administration of ether by mask (figure 1b) still caused laryngospasm and apnoea, but the cricothyroid discharge was no greater than it had been before thiopentone.

In four other decerebrate cats thiopentone was administered at the same dose rate. No increase in sensitivity to the administration of ether vapour by mask or tracheal cannula was observed. Under these circumstances, thiopentone does not appear to enhance the laryngeal reflex. It is possible, however, that a different effect may be produced in the cat with an intact neuraxis under light thiopentone anaesthesia.

**Suxamethonium.**

Suxamethonium was administered intravenously at a dose rate of 1 mg/kg to five decerebrate cats. Each cat had previously exhibited laryngospasm when exposed to ether vapour administered by mask or tracheal cannula. The effect of suxamethonium was to stimulate an initial period of increased muscle activity which was followed by paralysis. Increased activity of both the cricothyroid muscle and the diaphragm was stimulated 6.5 sec after the depolarising relaxant was given. Activity in the cricothyroid muscle stopped 18 sec after the injection of suxamethonium, whereas the diaphragm remained in a state of apnoea for 30 sec followed by 30 sec of reduced activity, before action potentials from it stopped. The lungs were then ventilated rhythmically. During the period of paralysis of the cricothyroid muscle and the diaphragm, laryngospasm could not be stimulated by the administration of ether by mask or tracheal cannula. Fifteen minutes after the suxamethonium had been given, spontaneous respiration started again, and laryngospasm could be stimulated by the administration of ether.

**Local analgesics.**

It was demonstrated in a previous paper (Rex, 1971) that by spraying the pharynx and larynx with lignocaine hydrochloride and lubricating the endotracheal tube with a local analgesic cream, the reaction of the larynx and trachea to mechanical stimulation during intubation could be abolished or reduced. The spray also reduced the effects of the inhalation of volatile anaesthetics.

In a cat anaesthetized with chloralose, whose respiratory tract was kept intact, spraying the pharynx and larynx with lignocaine hydrochloride and lubricating the endotracheal tube with a local analgesic cream, the reaction of the larynx and trachea to mechanical stimulation during intubation could be abolished or reduced. The spray also reduced the effects of the inhalation of volatile anaesthetics.
EFFECTS OF OTHER DRUGS ON STIMULATION OF LARYNGOSPASM

Decerebrate cat prepared under halothane/ether anaesthesia. From above down traces show time marker 0.2 sec (interruptions of the time trace and arrows indicate the start of ether administration), (i) electromyogram from cricothyroid muscle, (ii) electromyogram from diaphragm. (Spikes retouched.)

(a) Effects of ether administered by mask. Laryngospasm and apnoea are stimulated and the start of a period of apneusis can be seen at the end of the diaphragm trace.

(b) Effects of ether administered by tracheal cannula. A short period of laryngospasm was stimulated and the interval between periods of inspiratory activity of the diaphragm increased.

(c) Effects of ether administered by tracheal cannula after analgesic spray of pharynx and larynx. The effect was almost identical with b. No protection was afforded.

(d) Effects of ether administered by mask after analgesic spray of pharynx and larynx. Laryngospasm, as indicated by increased cricothyroid activity was almost abolished.

in decerebrate cats. Reaction to the stimulus was not entirely abolished, however, and the fact that in some cases there was still both an increase in activity of the cricothyroid muscle and some change in the respiratory rhythm suggested that the stimulation of receptors lower down the respiratory tract should be considered.

Figure 2a, recorded from a decerebrate cat with a tracheal cannula inserted, shows the effects of ether administered by mask. There was a high frequency discharge of a large number of motor units from the cricothyroid, and the diaphragm showed apnoea followed by apneusis. Ether administered into the trachea and lungs stimulated a short period of laryngospasm (2 sec) and an increase in the interval between diaphragm activity from 2 to 6.5 sec (fig. 2b). The pharynx and anterior larynx were then sprayed with 2 per cent lignocaine. Figure 2c shows the effects of administration of ether to the trachea and lungs after spraying with the local analgesic solution. The record is almost identical in duration of cricothyroid activity and change in respiratory rhythm to that in figure 2b. Administration of ether by mask (fig. 2d), however, now produced only a small increase in cricothyroid activity of short duration. There was no initial stimulation of the diaphragm, but there was a period of apnoea followed by apneusis.

In another decerebrate cat, with no tracheal cannula inserted, the technique of spraying local analgesic solution currently used for intubation of cats in clinical anaesthesia was investigated. In this cat ether spray stimulated laryngospasm and apnoea (fig. 3a). After spraying the pharynx and larynx with a 10 per cent lignocaine solution from an aerosol pack, an ether spray stimulated a very slight increase in cricothyroid activity after 4.5 sec. The interval between periods of activity of the diaphragm was increased from 1.5 to 3.75 sec for one respiratory cycle and then returned to normal (fig. 3b). In the same cat reaction to
mechanical stimulation and intubation was greatly diminished.

**DISCUSSION**

Burstein and Rovenstine (1938) suggested that drugs of the atropine group should be administered before using short-acting barbiturates. Their experiments were carried out on cats and were inconclusive, although excessively high doses of atropine were given. Rail, Gilbert and Trump (1945), using decerebrate dogs, reported that in ten of eleven animals neither vagotomy nor doses of atropine of 10 mg per dog entirely abolished reflex bronchoconstriction, which they produced by mechanical stimulation of the nasopharynx, electrical stimulation of the peripheral end of the cut vagus nerve, or injection of drugs such as acetylcholine and histamine. Rosen (1960) stressed that there is no evidence that the laryngeal muscles and their motor nerves differ from other striated muscles and motor nerves in the body. Therefore, atropine should not be expected to relieve laryngeal spasm. He pointed out that the doses of atropine used by Burstein and Rovenstine in cats would be considered poisonous in man. Harrison (1962) reported that atropine, at a dose rate of 1.2 mg per cat in animals anaesthetized with cyclopropane or thiopentone failed to modify responses such as coughing, breath-holding or laryngospasm to the inhalation of cigarette smoke. Subsequently Harrison and Vanik (1963) recorded a slight decrease in severity of laryngeal spasm in cats anaesthetized with cyclopropane which were subjected to bursts of high concentrations of ether vapour. The dose rates of atropine used were 6.6–18.2 mg/kg (60–180 times the clinical dose rate in cats). They suggested that the antisialogogue action of atropine is the only one likely to have any effect on the incidence and severity of laryngospasm.

In the five cats which were given atropine intravenously, no change was observed in the effects of ether administered by mask or tracheal cannula, although one cat received over thirty times the dose rate used in clinical anaesthesia. This confirmed the results of previous workers.

In five experiments in this study, the effect of intravenous thiopentone sodium on the incidence of laryngospasm was recorded. Ether still stimulated laryngospasm after the administration of thiopentone but it was no more intense than it had been before the barbiturate was given. This result supports Dundee's suggestion that the supposed stimulation of laryngospasm by barbiturates in man may in fact be a failure of depression of laryngeal reflexes (Dundee, 1965). Murtagh and Campbell (1954) were also unable to demonstrate any evidence of increased activity of the intrinsic laryngeal muscles in goats in response to thiopentone sodium. Harrison (1962), however, concluded that in man reflex responses to respiratory irritation were more prolonged with thiopentone and cyclopropane than with nitrous oxide alone or halothane with nitrous oxide. The effect of barbiturates on the laryngeal reflex remains to be determined unequivocally, but the evidence appears to point to a failure to suppress the reflex rather than to an active stimulation or sensitization.

The administration of suxamethonium 2–3 mg intravenously immediately after induction of anaesthesia has been used for many years to facilitate endotracheal intubation in the cat (Hall, 1966), and is used in human anaesthesia (Evans and Gray, 1965). The duration of action of suxamethonium is longer (usually 10–15 min) in the cat than in man (up to 5 min) and therefore it has the disadvantage that a longer period of controlled or assisted respiration is necessary after its use. Murtagh and Campbell (1954) gave doses of the order of 5 mg of suxamethonium to several goats of unspecified weights, which were anaesthetized with intraperitoneal pentobarbitone sodium. Respiration stopped within 1 minute, but the action potentials of the intrinsic laryngeal muscles continued. Their experiment provides an indication that the activity of suxamethonium on the intrinsic laryngeal muscles may be different for cats and goats. In the five experiments in the cat reported here, paralysis of the diaphragm was accompanied by paralysis of the laryngeal muscles, during which it was impossible to stimulate laryngospasm by exposing the cats' respiratory tracts to ether.

The fact that abolition or a reduction of the response to mechanical stimulation of the pharynx and larynx occurred after spraying these structures with a local analgesic solution suggests that many of the mechanoreceptors for the laryngeal reflex are situated in these areas. However, in
many preparations some laryngeal adductor activity was still stimulated, suggesting the existence of receptors further down the respiratory tract and in the nasopharynx which the local analgesic spray had not reached.

When a 10 per cent aerosol spray of lignocaine had been applied to the pharynx and larynx, administration of ether by mask stimulated a very slight increase in cricothyroid activity in cats with an intact respiratory tract. Reaction to mechanical stimulation of the epiglottis and vocal cords at this stage was greatly reduced and endotracheal intubation was achieved with ease. This fact has been applied in clinical anaesthesia in cats with the result that what was at one time regarded as a hazardous and difficult procedure may now be carried out with little danger. Experiments on nerve cutting and stimulation which were described in a previous paper (Rex, 1970b) provide a logical basis for the results of the application of local analgesics.

These experiments confirm and amplify earlier work by Larsell and Burget (1924), who described the effects of cocaine on the trachea in the rabbit and dog, and Teitelbaum, Ries and Lisansky (1936), who reported that cocaine desensitized the cat's pharyngopalatine mucosa to mechanical stimulation.

Walds and Kassity (1965) used methylene blue to study the spread of a local analgesic solution. They administered the solution through the cricothyroid membrane or between the first and second tracheal rings in conscious men. They found that the degree of spread of the agent was not necessarily related to the site of injection and that extensive spread above the vocal cords could result from both techniques. Their techniques may prove useful for future work in animals, for instance as a method of providing analgesia of the larynx for endotracheal intubation in the pig.

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REFERENCES


