CORRESPONDENCE


4-AMINOPYRIDINE FAILS TO INDUCE PORCINE MALIGNANT HYPERTHERMIA

Sir,—4-Aminopyridine (4-AP) has been introduced recently to clinical practice for the antagonism of neuromuscular blockade produced either by curare-like agents (Stoyanov et al., 1976), or antibiotics (Booij, Miller and Crul, 1978), and for the treatment of myasthenia gravis (Lundh, Nilsson and Rosen, 1979), and the Eaton–Lambert syndrome (Lundh, Nilsson and Rosen, 1977). 4-AP facilitates neuromuscular transmission by a pre-synaptic effect on the motor nerve terminal in which both the spontaneous and the evoked output of acetylcholine is increased, and also by a direct effect on muscle to increase contractility (Bowman, Khan and Savage, 1977). The mode of action of 4-AP is thought to be an increase in the intracellular Ca\(^{2+}\) concentration either as a result of blockade of the potassium channel in the cell membrane with prolongation of the action potential (Molgo, Lemeignan and Lechat, 1977), or by a direct effect on the calcium channel in the membrane (Lundh and Thesleff, 1977). There are, therefore, good grounds for suggesting that 4-AP may trigger porcine malignant hyperthermia (MH), since this syndrome is caused by an increase in the Ca\(^{2+}\) concentration within the striated muscle cell. This contention is supported by studies which have shown that the effects of 4-AP on striated muscle are antagonized by dantrolene (Bowman, Khan and Savage, 1977) and Mg\(^{2+}\) (Marshall, Lambert and Durant, 1979), both of which have been used successfully to treat porcine MH (Hall, Lucke and Lister, 1980).

We have investigated the effects of the administration of 4-AP in four MH-susceptible Pietrain pigs, anaesthetized with increments of thiopentone, the lungs being ventilated artificially with nitrous oxide in oxygen. 4-AP was administered i.v. in a total dose of 3–4 mg kg\(^{-1}\) body weight. In a preliminary experiment we demonstrated that 4-AP had a marked direct effect on the muscle at this dose as it was possible to reduce only partially the coarse muscle twitching by the administration of large doses of pancuronium. The ability of 4-AP to trigger MH was assessed by frequent estimations of arterial blood-gas tensions, muscle temperature, plasma potassium and blood lactate concentrations for 1–2 h. 4-AP failed to induce MH in all the pigs studied and their susceptibility was proven at the end of the experiment by ventilating with 1% halothane.

The inability of 4-AP to trigger porcine MH suggests that this compound is unlikely to induce MH in susceptible patients. The dose of 4-AP used in this study was 10 times greater than the 0.35 mg kg\(^{-1}\) body weight recommended for use with neostigmine for the antagonism of neuromuscular blockade in man (Miller, 1979). Furthermore, the results indicate that porcine MH cannot be induced by a compound the effect of which is mediated, at least partly, by a direct action on the muscle membrane to increase the intracellular Ca\(^{2+}\) concentration. This suggests that the recent emphasis on the sarcolemma or sarcolemma–sarcoplasmic reticulum junction as the site of the primary defect in MH may not be valid.

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REFERENCES


did not correlate with the degree of spread. Incidentally, Nishimura, Kitahara and Kusakabe (1959) reached the same conclusion using yet another technique employing radioisotope tracers.

The lack of correlation between the rates of injection and the injection pressures reported by Husemeyer and White is surely because the subjects were all young people and relatively small volumes were used. As the authors rightly say “Injection pressures may therefore depend as much on the rate of leakage as on the rate of injection.” In our series, volumes of 20 and 40 ml were used with an age range 21–69 yr; our experience confirmed the findings of Erdemir, Soper and Sweet (1965) and Usubiaga, Wikinski and Usubiaga (1967) that, under such circumstances, rapid injections (1–2 ml s⁻¹) can produce high pressures resulting in unpleasant and possibly even hazardous effects.

Our conclusion was that, as rapid injections appeared to confer no clinical benefit, they should not be used.

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REFERENCES


EFFECTS OF INTRAOPERATIVE NEFOPAM (ACUPAN)

Sīr,—Nefopam is a novel analgesic which appears to have no respiratory depressant effects. It does, however, cause an increase in heart rate and arterial pressure, and also sweating and flushing. A simple study was carried out to ascertain whether these effects would also be seen when nefopam is given to patients anaesthetized with halothane. Thirty-one patients were studied, most of whom were undergoing minor general surgical procedures, hysterectomy or tubal ligation. Nefopam was given at a time when effects of surgical stimulation on heart rate and arterial pressure would be minimal.

In 17 patients, breathing was spontaneous; 15 of these showed an increase in heart rate (range 4–32 beat min⁻¹) and 14 showed an increase in arterial pressure (range 5.1–35.2 mm Hg). In the 14 artificially ventilated patients, seven showed an increase in heart rate (range 8–72 beat min⁻¹) and 12 an increase in arterial pressure (range 5.1–35.2 mm Hg). Two patients sweated and six were flushed. In three of these patients, these effects were not observed until the patient was in the recovery room. One patient showed an increase in heart rate from 88 to 160 beat min⁻¹ during operation and after operation her arterial pressure readings were 160/110 and 145/155 mm Hg. She was not hypertensive before her operation.

Insufficient patients were studied to ascertain whether there was any association between particular anaesthetic drugs and these changes of heart rate and arterial pressure. It is suggested that caution should be exercised in the use of nefopam during the course of an anaesthetic.

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ARRHYTHMIAS AND THE CAROTID ARTERY

Sir,—I have read with interest two letters in the past year in which the authors describe severe cardiac arrhythmia as a result of carotid artery palpation. Amaranath, Kirilcuk and Leon-Ruiz (1978) described multiple deformed QRS complexes which occurred while routinely palpating the carotid artery during hip replacement. Sprigge and Oakley (1979) recorded a case of ventricular fibrillation following palpation of the carotid artery before cannulation of the internal jugular vein.

These reports were of concern in a department which undertakes a considerable number of general anaesthetics for carotid angiography. At Atkinson Morley’s Hospital, carotid angiography is carried out following direct puncture of the carotid artery and this procedure necessitates handling of the carotid vessels both during cannulation and after de-cannulation to ensure haemostasis. It was decided, therefore, to monitor these patients continuously with an electrocardiograph and to record any abnormality produced.

The patients were in a wide age group, from young adults to the very elderly. They were being investigated for a variety of neurological conditions, but most commonly following subarachnoid haemorrhage. Patients less than 65 years of age were premedicated with hyoscine 0.3 mg, those older than 65 with atropine 0.4 mg i.m. Anaesthesia was induced with thiopentone, tracheal intubation followed relaxation with succinamethion and IPPV continued using tubocurarine as the muscle relaxant. Anaesthesia was maintained with nitrous oxide, oxygen and either small doses of fentanyl or halothane 0.25–0.5%.

More than 100 patients have now been monitored and no cardiac arrhythmia has occurred. Thus, it would seem that prolonged manipulation and handling of the carotid artery is not usually accompanied by cardiac arrhythmia. This does not detract from the finding that, in an occasional patient, perhaps especially those with pre-existing cardiovascular disease, a serious abnormality of cardiac rhythm may occur. However, it would seem unnecessary, for example, to monitor the e.g.c. routinely in every patient requiring cannulation of the internal jugular vein.

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REFERENCES
