CORRESPONDENCE

CLODANOLENE SODIUM AND MALIGNANT HYPERPYREXIA

Sir,—We wish to report the results of in vitro experiments which examined the effects of clodanolene sodium on muscle contracture in swine which were susceptible to malignant hyperpyrexia (MH). Clodanolene sodium is a skeletal muscle contraction antagonist, closely related to dantrolene sodium.

Susceptibility to MH was identified in seven swine by demonstrating increased sensitivity of their muscle to 3% halothane, caffeine 2 mmol litre\(^{-1}\), suxamethonium chloride (Wellcome) 1 mmol litre\(^{-1}\) and potassium chloride 80 mmol litre\(^{-1}\). The effectiveness of dantrolene sodium 3 \(\mu\)mol litre\(^{-1}\) and clodanolene sodium 3 \(\mu\)mol litre\(^{-1}\) in inhibiting or reversing the drug-induced contractures was assessed. The effects of dantrolene sodium and clodanolene sodium on isometric twitch were also examined in a range of concentrations from 3 to 30 \(\mu\)mol litre\(^{-1}\).

Dantrolene sodium and clodanolene sodium were equally effective in inhibiting and reversing contractures induced by 3% halothane, caffeine 2 mmol litre\(^{-1}\) and suxamethonium chloride 1 mmol litre\(^{-1}\). Dantrolene sodium had a significantly greater inhibitory effect on contractures induced by potassium chloride 80 mmol litre\(^{-1}\) than clodanolene sodium (\(P<0.025\), \(n=7\), Student’s \(t\) test). Dantrolene sodium also had a significantly greater effect than clodanolene sodium on isometric twitch at concentrations of 3 \(\mu\)mol litre\(^{-1}\) (\(P<0.01\), \(n=5\)), 15 \(\mu\)mol litre\(^{-1}\) (\(P<0.01\), \(n=5\)) and 30 \(\mu\)mol litre\(^{-1}\) (\(P<0.05\), \(n=5\)). The difference between the effects of the two drugs at a concentration of 6 \(\mu\)mol litre\(^{-1}\) was not statistically significant.

Both dantrolene sodium and clodanolene sodium act at the level of excitation–contraction coupling in muscle (Ellis and Wessels, 1978). The differences reported here between the effect of dantrolene sodium and clodanolene sodium on potassium-induced contractures and isometric twitch in MH muscle, show that subtle differences in drug structure may have significant effects on the ability of skeletal muscle contraction antagonist drugs to inhibit the increased muscle contractility in MH. The results also suggest that clodanolene sodium has no advantage over dantrolene sodium in the treatment or prevention of MH.

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ACKNOWLEDGEMENT

We are indebted to Dr K. O. Ellis of Norwich–Eaton Pharmaceuticals for supplying us with dantrolene sodium and clodanolene sodium.

REFERENCE


SUPRAVENTRICULAR TACHYCARDIA FOLLOWING PANCRURONIUM

Sir,—We read with interest the correspondence by Saemund and Dalenius (1981) on Pancuronium and nodal rhythm. We report here a patient who developed supraventricular tachycardia following pancuronium. This male patient, aged 50 yr, was hypertensive and diabetic, with e.g. evidence of complete right bundle right bundle branch block and was operated on for closure of bronchopleural fistula. He had bilateral pneumonitis leading to postoperative ventilatory insufficiency on the 3rd day after operation. He was given dazepam 10 mg i.v. and put on Bird Ventilator and was given pancuronium 4 mg i.v. to control the ventilation. Immediately after i.v. administration of pancuronium the patient developed tachycardia with a heart rate of 180 beat \(\min^{-1}\) and arterial pressure 200/100 mm Hg. The oscilloscope showed evidence of supraventricular tachycardia which persisted. An e.g. was recorded and the patient was given lidocaine hydrochloride 200 mg in two divided doses 1 i.v. and doxigou 0.25 mg i.v. without any change in rhythm. After 10 min verapamil 4 mg i.v. reverted the rhythm to sinus tachycardia with heart rate of 140 beat \(\min^{-1}\). Repeat e.g. after control of arrhythmia failed to show any evidence of myocardial ischaemia, thus ruling out the possibility of ischaemia-induced arrhythmia.

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REFERENCE


ACCIDENTAL HIGH-DOSE EXTRADURAL MORPHINE

Sir,—Long-term use of extradural morphine in reducing chronic pain has been used for home care (Zenz et al., 1981). The possibility of misadministration and the risks of side-effects will increase under these circumstances. During a 6-month period, home treatment with extradural morphine was performed on a 61-year-old man suffering from painful metastases secondary to hypernephroma. During the period of treatment the dose of morphine was increased gradually to 6 mg diluted in 15 ml of isotonic saline given extradurally in the lumbar region four times daily. The extradural injections were given by the patient’s wife.

Because of still insufficient pain relief a small increase in the daily dose was intended, but by mistake the wife injected morphine chloride 16 mg extradurally five times daily on 2 days (that is 160 mg within 48 h).

Four hours after the last morphine dose the patient was in his usual bad general condition; respiration was unaffected, but catatonic twichings in his extremities developed. The concentra-