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 μmol litre⁻¹ and clodanolene sodium 3 μmol 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 μmol 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 μmol litre⁻¹ (P < 0.01, n = 5), 15 μmol litre⁻¹ (P < 0.01, n = 5) and 30 μmol litre⁻¹ (P < 0.05, n = 5). The difference between the effects of the two drugs at a concentration of 6 μmol 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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REFERENCE


SUPRAVENTRICAL 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 evidence of complete right bundle right bundle branch block and was operated on for closure of bronchopleural fistula. He had bilateral pneumonias 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.c.g. was recorded and the patient was given lignocaine hydrochloride 200 mg in two divided doses i.v. and digoxin 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.c.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 twitchings in his extremities developed. The concentra-
tion of free morphine in serum and cerebrospinal fluid (c.s.f.) was at this time 62 nmol litre⁻¹ and 10 9 nmol litre⁻¹ respectively, measured by a radioimmunoassay technique (Abuscreen).

Concentrations in serum and in c.s.f. present considerable interindividual variations some hours after extradural morphine injections (Jørgensen, Andersen and Engquist, 1981; Weddel and Ritter, 1981). The concentrations of morphine in our patient were within the limits of variations and had probably been larger before the concentrations had been determined, as maximum values for both probably will be reached earlier than 4 h after the injection (Magora et al., 1980; Weddel and Ritter, 1981; Möller et al., 1982).

Tolerance is probably developed in long-term treatment with extradural morphine, so that even large doses of morphine can be tolerated without adverse side-effects. However, extradural morphine administration by unskilled persons might prove hazardous.

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REFERENCES

NITROUS OXIDE IN OXYGEN AND TRACHEAL TUBE CUFF VOLUMES

Sir,—In this very interesting article, Mehta (1981) demonstrates that the increase of cuff pressure because of nitrous oxide diffusion is a phenomenon that has to be considered even during brief anaesthesia. He showed that the volume in low pressure-cuffs had almost doubled after 3 h. These results correspond with our own investigations when we found the main increase in cuff pressure to be during the first hours of anaesthesia (Brandt, Pokar and Renz, 1980; Brandt, Beck et al., 1981).

It seems to be important to make some remarks on the following point: Dr Mehta cites Stanley (1975), who asserted that there was a smaller increase in cuff volume and cuff pressure in vivo than in vitro. He explained this by the smaller diffusion area in vivo. In our own studies, pressure and volume were increased in vitro just as in vitro (Brandt, Pokar and Renz, 1980).

Therefore we questioned the theory of Stanley that only the distal portion of the cuff, that is, the portion not in contact with the tracheal wall, should be the area of diffusion. Our experience indicates that, in vivo, the contact area with the tracheal wall is a diffusion area also. This theory can be proved by analysing the cuff pressure curve during operations with extracorporeal circulation (ECC). An example is shown in figure 1.

Immediately after intubation (A) the cuff pressure was 24 mm Hg. Until the onset of ECC (B) it increased to 98 mm Hg within 95 mm. During the whole time of ECC the pressure decreased discontinuously by 54 mm Hg (D—end of ECC). This pressure reduction occurred in spite of continuing the tracheal ventilation during ECC with 1 litre min⁻¹ of the same anaesthetic gas mixture as before ECC (FIN2O 0.66). This ensured that partial pressure relations of the gases were kept constant at the cuff area. Nevertheless, the cuff pressure decreased. This pressure decrease during ECC can only occur if nitrous oxide diffuses out of the cuff through the contact area with the tracheal wall additionally. Partial pressure relations changed in this area only: the tracheal tissue becomes free of nitrous oxide during ECC. After termination of ECC (D) the conditions become the same as before ECC. Cuff pressure increases again to nearly the same value of 90 mm Hg until the end of anaesthesia (E).

Therefore, in our opinion, the whole cuff wall constitutes a diffusion area for nitrous oxide in vivo (Brandt, Gumrukcu et al., 1981). Moreover, as the size of the contact area is about 10 times the cuff area not in contact with the tracheal wall, the main part of diffusion takes place from tracheal tissue through the contact area into the tracheal cuff, and vice versa.

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REFERENCES