THE EFFECT OF CENTRAL SYMPATHECTOMY BY 6-HYDROXYDOPAMINE (6-OHDA) ON THE RESPONSE TO MORPHINE IN CONSCIOUS SHEEP

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ABSTRACT


When morphine, an opioid μ-agonist, was administered in vivo into the third cerebral ventricle (ICV) of conscious sheep at 20 and 40 μg/kg body weight, it caused psychomotor excitability for 2-3 h and a significant decrease in the retieuloruminal frequency for 45 min and in the mean amplitude of the primary contractions for 65 min. From 60 min after infusion, the same doses of morphine caused a significant increase in the average amplitude of the contractions for 45 min. This suggests that an inhibitory μ-opioid acceptor is involved in the central control of forestomach motility and general behaviour in sheep. All the effects of morphine were completely prevented by pretreatment with 18.2 μg/kg body weight 6-OHDA ICV. These results suggest that both morphine-induced inhibition of rumen motility and psychomotor excitability are due to central noradrenergic descending system activation. The exact location of the noradrenergic system remains to be determined.

Keywords: 6-hydroxydopamine, behaviour, morphine, ruminal contractions, sheep

INTRODUCTION

Exogenous opioids (morphine, normorphine, loperamide, etorphine and fentanyl) have an inhibitory effect on gastric motor function in rats, rabbits, dogs and humans (Buénó et al., 1985; Fioramonti et al., 1985; Porreca et al., 1986; Buénó and Fioramonti, 1988) and to some extent in ruminants (van Mier and Maas, 1984; Maas and Leek, 1985) and a stimulatory effect on the duodenum (Ruckebusch et al., 1984). Different behaviour by different species was observed after administration of morphine subcutaneously, intravenously or into the cerebral ventricles. After infusion of small amounts, psychomotor excitability was noted in mice, sheep, goats (Maas, 1982), cattle, pigs and horses, and psychosedative effects only in rats (Davis et al., 1972), dogs and humans. In ruminants, IM or IV injection of etorphine, fentanyl and morphine in a large dose – or with neuroleptic drugs – caused only slight excitomotor action for a short time, but it caused general catatony and immobilization (Kania, 1985a,b,c).

Morphine is a stereospecific agonist of the central μ-opioid receptor and naloxone is a stereospecific antagonist of the central μ, δ and κ opioid receptor. It is well known that naloxone prevents and/or abolishes all the responses to morphine (Maas, 1982). These observations suggest that an inhibitory μ-opioid receptor may be involved in the control of forestomach motility and general behaviour in conscious sheep (Maas and Leek, 1985).
The behaviour of animals after treatment with morphine may depend on the phyllogenetic development of the cerebral cortex, the dose, mode of administration, general condition and the extent of central adrenergic system participation (Maynert, 1967). It was decided to evaluate both the extent of central adrenergic system participation in morphine-induced inhibition of forestomach motility and the paradoxical excitomotor influence on the general behaviour of sheep. In order to do so, central chemical sympathectomy was done by ICV infusion of 6-hydroxydopamine (6-OHDA). This causes degeneration of the dopaminergic and noradrenergic neural endings in the adrenergic structures of the CNS in rats, cats and sheep (Thoenen and Tränzer, 1968; Thoenen et al., 1973; Domański et al., 1980). Reader and Gauthier (1984) showed that 6-OHDA infused into the third cerebral ventricle in rats reduced the concentration of dopamine (DA) in the hypothalamus by 63% and the concentration of noradrenaline (NA) by 75%.

MATERIALS AND METHODS

Animals

The experiment was carried out on 12 Polish Merino ewes aged 3.5–4.5 years in the anoestrus phase. They were housed individually in 2 × 2 m boxes under natural light conditions. They were fed hay *ad libitum* and a commercial concentrate feed (600 g/day per animal). All the sheep had free access to water.

Animal preparation (surgery)

Stainless steel cannulae of 0.5 mm diameter were implanted into the third cerebral ventricle of all the animals using a stereotactic technique (Welento et al., 1969). Six to seven days after the surgical procedure, the animals in the experimental group (group II) received 18.2 μg/kg of 6-OHDA (2,4,5-trihydroxyphenylethylamine hydrochloride) dissolved in 300 μl of 5% glucose containing 1% ascorbic acid (POLFA, Warsaw), infused into the third cerebral ventricle at 12 μl/min (Domański et al., 1985). The animals in the control group (group I) were treated in a similar way with the vehicle only. Fourteen days after the infusion of 6-OHDA, the animals showed complete recovery and were suitable for further experimentation. We observed fewer side-effects after 6-OHDA infusion than were reported by Domański et al. (1985) in sheep and Ungerstedt (1971) in rats.

Experimental procedure

The animals were randomly divided into two equal groups. During the first part of the experiment, the animals in group I received an ICV infusion of morphine (Morphinum hydrochloricum – POLFA, Warsaw) at 40.0 μg/kg body weight (BW) (Maas, 1982) in 200 μl saline, and during the second stage of the experiment, 2 weeks later, they received the vehicle for 6-OHDA (5% glucose with 1% ascorbic acid) in the same volume. This experiment was repeated 2 weeks later again using morphine.