COMPARISON OF ANALGESIC ACTIONS OF OXYMORPHONE AND MORPHINE IN RATS AND DOGS

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Summary: The analgesic effects in rats and dogs of different doses of oxymorphone have been compared with the standard analgesic dose of morphine. In both the species of animals oxymorphone in much smaller doses was found to be more potent as an analgesic than morphine. The side effects were less marked than with morphine.

Key words: analgesic action oxymorphone morphine

In human beings, oxymorphone hydrochloride is a more potent analgesic than morphine and pethidine (2,3,7). Its use in dog as an analgesic and preanaesthetic agent has been reported by Palminteri (6). The present study was undertaken with the object of comparing the analgesic effectiveness of oxymorphone with that of morphine in rats and dogs. The incidence of side effects of oxymorphone was also studied.

MATERIALS AND METHODS

Rats: Forty rats weighing 80-120 *g* and devided into four groups of 10 rats each were used. In the 1st group, morphine sulphate (10 *mg/kg*) was injected subcutaneously as recommended by Barnes and Eltherington (1). In the 2nd, 3rd and 4th groups, oxymorphone hydrochloride in doses of 0.125, 0.25 and 0.5 *mg/kg* respectively was injected subcutaneously. The analgesic effects were studied by red hot wire technique (4) with the help of Techno analgesiometer at an intensity of 4.5 amperes. The reaction time i.e., the time taken from the application of stimulus to the sudden lift of tail was recorded. In order to avoid any burn injury to the tail, the maximum duration allowed was never more than 30 sec.

Dogs: Twenty four mongrel dogs, 9 months to one year old weighing 6 to 10 *kg* and divided into four groups of 6 animals each were used. They were fasted overnight before the experiment. Animals of the first group received morphine sulphate in a dose of 4 *mg/kg* as recommended by Barnes and Eltherington(1). The 2nd, 3rd and 4th groups received oxymorphone subcutaneously in doses of 0.025, 0.1 and 0.2 *mg/kg* respectively. The analgesic effect was studied by applying the heat stimulus with the help of a red hot coil of the type usually employed as a cigarette lighter. The red hot coil was kept at a uniform distance of 1 cm from the clipped lateral side of the hind paw. The time taken (reaction time) from the application of stimulus to the sudden flinch of the paw was recorded. The stimulus was never applied for more than 90 sec to avoid any burn injury.

RESULTS

The data depicting the effect of morphine and oxymorphone on the reaction time is given in Table I.

Rats (Table Ia) : Five min after the administration of 0.25 and 0.5 *mg/kg* of oxymorphone, the reaction time increased by 83.1% and 76.2% respectively while with morphine it increased by 43%. The peak increase in reaction time with 0.25 and 0.5 *mg/kg* doses of oxymorphone (256.1 and 267·2 per cent respectively) and morphine (204.3 per cent) occurred 30 min following the administration. With 0.5 *mg/kg* of oxymorphone, the peak effect persisted upto 90 min and by 150 to 180 min the increase ranged between 218.2 and 39.5% respectively. This is quite significant when compared with the abrupt fall after 30 min with 0.25 *mg/kg* of oxymorphone and morphine. The tail became spastic with all doses of oxymorphone and morphine. The animals were sedated and the sedative effects persisted for the period of elevated reaction time.

Dogs (Table Ib) : The peak increase in reaction time with oxymorphone in doses of 0.1 and 0.2 *mg/kg* (538.30 to 539.1 per cent) persisted for 30 to 60 min. With 4 *mg/kg* of morphine (310.3 per cent) the peak effect occurred at 30 min. The increase in reaction time at 90 min with 0.1 and 0.2 *mg/kg* of oxymorphone was 194.7 and 219.1 per cent respectively in comparison with an increase of 54.5 per cent with morphine. At 120 min the increase in reaction with 0.2 *mg/kg* of oxymorphone was 162.2 per cent and with 0.1 *mg/kg* it was 50.8 per cent. With 0.1 and 0.2 *mg/kg* oxymorphone, the animals went to sleep within 5 to 15 min and though responsive, were reluctant to get up. On getting up they exhibited staggering of hind legs, which was not seen with morphine. With the higher dose of oxymorphone the side effects like salivation and defecation were similar to those seen with morphine. The animals given morphine were nauseated while those receiving oxymorphone were not. With 0.025 *mg/kg* of oxymorphone, there was only mild sedation.

DISCUSSION

In rats, the analgesic effects of oxymorphone (0.25 to 0.5 *mg/kg*) were more marked in comparison with those of morphine (*10 mg/kg*). In fact with the higher dose of oxymorphone the onset of analgesia was quicker and the degree of analgesia more pronounced. Furthermore, with this dose the maximal effects persisted much longer. There was no evidence of toxicity in rats with any of the doses of oxymorphone. This is contrary to the finding of Swerdlow and Brown (7). No side effects have been reported in human beings with the doses of oxymorphone equieffective with those of morphine (3).

In dogs, oxymorphone in the dose of 0.025 *mg/kg* which is 1/160th of the standard dose of morphine, produced less analgesic effect than morphine. However, by increasing

TABLE I: Analgesic effect of morphine and oxymorphone at various intervals after administration.

Drug and dose	*No. of animals*	Response time in seconds (mean ± S.E.)								
		Control	5 *min.*	15 *min.*	30 *min.*	1 *hr.*	1½ *hr.*	2 *hr.*	2½ *hr.*	3 *hr.*
(a) *Rats*										
Morphine sulphate 10 *mg/kg*	10	9.30 ±0.12	13.30 ± 1.10	24.50 ±1.80	28.30 ± 1.13	24.10 ± 2.63	12.40 ±2.04	9.65 ±0.44	—	—
Oxymorphone 0.125 *mg/kg*	10	8.65 ± 0.13	9.05 ±0.44	10.20 ±0.56	9.35 ±0.38	8.90 ± 0.17	—	—	—	—
0.25 *mg/kg*	10	7.92 ±0.3	14.50 ± 1.73	26.60 ±1.60	28.20 ± 1.58	20.90 ± 2.61	16.25 ±3.06	9.38 ±0.53	—	—
0.5 *mg/kg*	10	8.17 ±0.10	14.40 ± 2.15	28.30 ±0.27	30.0 ±0	30.0 ±0	30.00 ±0	28.50 ± 1.5	26.00 ± 2.47	11.40 ±0.68
(b) *Dogs*										
Morphine sulphate 14 *mg/kg*	6	11.65 ± 1.60	17.50 ± 0.99	24.0 ± 1.75	29.66 ± 2.46	47.8 ± 5.64	36.66 ± 7.36	18.00 ± 2.90	10.6 ± 0.21	—
Oxymorphone 0.025 *mg/kg*	6	11.91 ± 0.90	14.83 ± 2.33	23.16 ± 2.42	27.16 ± 1.94	30.80 ± 1.96	37.83 ± 2.08	18.00 ± 2.60	10.66 ±0.87	—
Oxymorphone 0.1 *mg/kg*	6	12.93 ± 1.06	30.83 ±6.55	52.16 ±9.35	70.66 ±9.58	82.50 ±4.78	82.66 ±7.33	38.1 ±4.40	19.50 ± 2.68	12.6 ±0.70
Oxymorphone 0.2 *mg/kg*	6	13.16 ± 1.38	31.30 ± 7.83	59.0 ± 13.3	67.1 ± 9.66	84.00 ±6.10	84.0 ± 4.53	42.0 ± 3.85	34.50 ± 3.25	11.3 ±0.71

the dose of oxymorphone to 0.1 *mg/kg* and 0.2 *mg/kg* i.e. 1/40th and 1/20th of the standard morphine dose respectively, the analgesic effects were more than doubled. The maximal analgesic effect was also manifested much earlier and persisted longer. There was nevertheless not much difference between the analgesic effects of these two doses of oxymorphone.

This observation of the greater potency of oxymorphone than that of morphine is in accord with those reported in literature for humans, dogs and mice (2,5,7). With higher doses of oxymorphone, the side effects like salivation and defaecation were similar to those of morphine. However, nausea was lacking in contrast to that observed with morphine. Panting reported by Nytch (5) was not observed in this study. Staggering to hind legs which was commonly observed in all the dogs administered 0.1 and 0.2 *mg/kg* of oxymorphone is similar to the findings of Nytch (5).

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