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REVERSAL OF TILETAMINE -ZOLAZEPAM - XYLAZINE ANAESTHESIA WITH AMINOPHYLLINE IN DOGS*

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Tiletamine-zolazepam** a parenteral anaesthetic agent composed of a 1:1 combination of tiletamine hydrochloride and zolazepam hydrochloride has been reported to be useful for diagnostic and surgical procedures in a number of species of animals (Booth and Mc Donald, 1988). But at low dose levels (less than 5 mg/kg body weight) the combination did not induce muscle relaxation and analgesia sufficient for surgery in dogs (Donaldson *et al.*, 1989). Xylazine at the rate of 1 mg/kg and zoletil at the rate of 1.25 mg/kg was found to produce satisfactory short-term surgical anaesthesia in dogs (Mini *et al.*, 1995). Aminophylline has been reported to reverse anaesthesia induced by tiletamine-zolazepam combination in dogs (Hatch *et al.*, 1988). The present study was conducted to study the effect of aminophylline on zoletil xylazine anaesthesia in dogs.

Materials and methods

The study was conducted in eighteen, apparently healthy, adult mongrel dogs of either sex, randomly assigned to three treatment groups of six each. Xylazine at the rate of 1 mg/kg bodyweight was administered i/m along with atropine at the rate of 0.05 mg/kg s/c. and Zoletil was administered intravenously at the rate of 1.25 mg/kg bodyweight, 15 minute later. The time of disappearance of skin clamp reflex was noted. After 8 min., aminophylline was administered at the rate of 20 mg/kg and 40 mg/kg bodyweight intravenously to T_2 and T_3 groups respectively.

Two nociceptive stimuli as described below were used to test the depth of analgesia viz. (1) skin clamping: a fold of skin and subcutis posterior to the mid-point of last rib was clamped using an Allis forceps and the response was studied. (2) Tail clamping: a segment of tail including vertebra was clamped using an Allis forceps.

The stimuli were applied at 3 min. intervals. When the animals became recumbent, the ear-twitch reflex and pedal reflex were also tested at 3 minutes interval. Time of onset of recumbency, disappearance of response to skin-clamp and tail-clamp, pedal reflex, ear-twitch reflex and the time for regaining of sternal recumbency were recorded. The time of re-appearance of the reflexes, standing and walking were also recorded.

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** Zoletil-(Tiletamine-zolazepam), Virbac Pharmaceuticals, France.

The pulse rate, respiration rate and rectal temperature were recorded before administration and at 5, 10, 20, 30, 45, 60, 90 and 120 min. after the administration of Zoletil. Blood samples were collected before, at the middle (ie. 8 min. after the disappearance of skin clamp reflex) and after recovery from anaesthesia for haematological examination. The data were analysed statistically using one way analysis of variance.

Results and discussion

The data are presented in the Table 1.

The time of reappearance of response to tail-clamp for the 3 groups were 18.6 ± 1.2, 14.2 ± 1.2 and 15.7 ± 1.2 min. respectively for which significant difference was found to exist between T_1 and T_2. The reappearance of response to skin clamp was noticed at 22.7 ± 1.3, 14.8 ± 1.3 and 16.7 ± 1.3 min. respectively which also showed significant difference between T_1 T_2.

The mean time of regain of righting reflex for the groups T_1, T_2 and T_3 were 35.8 ± 2.2, 24.0 ± 2.2 and 24.8 ± 2.2 min. respectively. The mean time for attaining sternal recumbency were 43.3 ± 2.0, 28.5 ± 2.0 and 29.8 ± 2.0 min. respectively. Significant difference was found to exist between T_1 and T_2 groups in these parameters also.

All these suggest that aminophylline shortens tiletaminezolazepam-xylazine anaesthesia significantly.

The duration of absence of response to skin clamp and the recovery time for the group T_1 were 15.2 and 20.7 min. for the group T_2 were 10.1 and 13.7 min. and for T_3 were 11.9 and 13.1 min. respectively. These values were also significantly shorter for T_2 and T_3 when compared to T_1. These also suggest that aminophylline both at 20 mg/kg and 40 mg/kg rates can be used as a reversing agent for tiletamine-zolazepam-xylazine anaesthesia and that there is no added advantage by increasing the dose of aminophylline from 20 to 40 mg/kg bodyweight.

The mean time for standing and walking did not show any significant changes between the 3 groups. The time of reappearance of ear twitch reflex and pedal reflex did not show any significant difference between the groups.

Recovery was smooth, satisfactory and without any side effects in all the 3 groups. The body temperature variation showed a similar pattern for the 3 groups during the entire period of monitoring except at 10 minutes time. At 10 min. following administration of zoletil, the decrease in body temperature was found to be significantly higher for T_2 and T_3 when compared to T_1. The adenosine receptor blocking property of aminophylline can be attributed to this effect (Gilman *et al.*, 1991).

The pulse rate, the respiration rate and the haemogram did not show any significant difference between the groups.

The study thus pointed out that aminophylline at the dose of 20 mg/kg can adequately reverse the anesthesia produced by tiletamine-zolazepam-xylazine combination.

Table 1 Effect of Tiletamine-Zolazepam-Xylazine administration on duration of reflexes in dogs

Group	Disappearance of tail clamp reflex (Min.)	Disappearance of skin clamp reflex (Min.)	Time of regain of righting (Min.)	Reappearance of tail clamp reflex (Min.)	Reappearance of skin colamp reflex (Min.)	Regain of sternal recumbency (Min.)	Time for standing (Min.)	Time for walking (Min.)	Duration of skin clamp anaesthesia (Min.)	Duration of tail clamp anaesthesia (Min.)
T_1	4.0±0.6	7.5±0.8	35.3±2.2	18.6±1.2	22.7±1.3	43.3±2.0	47.5±3.9	48.3±4.4	15.2	14.7
T_2	2.7±0.6	4.7±0.8	24.0±2.2	14.2±1.2	14.8±1.3	28.5±2.0	41.3±3.9	42.2±4.4	10.1	11.5
T_3	2.8±0.6	4.8±0.8	24.8±2.2	15.7±1.2	16.7±1.3	29.8±2.0	39.5±3.9	40.8±4.4	11.9	12.8

T_1 - Tiletamine - zolazepam (1.25 mg/kg) + xylazine (1 mg/kg)
T_2 - Tiletamine - zolazepam (1.25 mg/kg) + xylazine (1 mg/kg) + aminophylline (20 mg/kg)
T_3 - Tiletamine - zolazepam (1.25 mg/kg) + xylazine (1 mg/kg) + aminophylline (40 mg/kg)

Summary

The efficacy of aminophylline as a reversing agent in tiletamine-zolazepam-xylazine anaesthesia was studied in 3 groups of dogs. Xylazine (1 mg/kg, i/m) followed by tiletamine-zolazepam (1.25 mg/kg, i/v) was administered to all three groups of animals. In the 2nd and 3rd groups of animals in the middle of anaesthesia, aminophylline at the rate of 20 mg/kg and 40 mg/kg respectively. Aminophylline significantly shortened the time (i) of reappearance of response to tail clamp and skin clamp, (ii) for sternal recumbency, (iii) regaining of righting and (iv) the duration of absence of response to skin clamp and tail clamp and the recovery time. It could be concluded that aminophylline at the dose of 20 mg/kg i/v could be used effectively to reverse anaesthesia produced by tiletamine-zolazepam-xylazine combination in dogs.

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