Antinociceptive effects of low dose ketamine infusions in conscious cats

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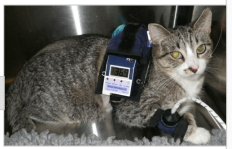
INTRODUCTION

In veterinary medicine ketamine is commonly used for induction and maintenance of anaesthesia. Subanaesthetic concentrations of ketamine have gained acceptance for acute and chronic pain management in dogs, horses and humans and are recommended for balanced anaesthesia and post-operative analgesia in clinical veterinary patients. Ketamine hydrochloride produces antinociceptive effects via inhibition of N-methyl-D-aspartate receptors in the spinal cord. It also has effects on opioid, monoaminergic, and muscarinic receptors, as well as voltage-sensitive Ca^{2+} channels.[1] In experimental studies ketamine however has been shown to produce variable anti-nociceptive effects in humans, dogs and ponies.[2,3,4] In cats there is limited published evidence of the anti-nociceptive efficacy of ketamine when given alone.[5]

OBJECTIVE

•To study the antinociceptive effects of two low dose ketamine infusions in cats using mechanical and thermal threshold models

•To record and describe side effects (sedative and psychosomatic)



MATERIALS and METHODS

Study design

Randomized, blinded crossover design with minimum 8 days between treatments

Animals

Eight healthy adult cats (six castrated males, two females, 3.7-6.7 kg)

Thermal and Mechanical nociceptive threshold testing

•Thermal thresholds (TT):
Wireless TT testing system (WWT1, Topcat Metrology Ltd)
A heater element and a temperature sensor housed in a small probe were held against the thorax of the cat with an elastic band and a pressure bladder to assure consistent contact.

•Mechanical threshold (MT):
A hand held MT testing system (ProD-Plus, Topcat Metrology Ltd) connected to an actuator was used. The actuator was secured on the anterolateral aspect of the cat's thoracic limb and was used to apply force using 3 round-ended pins.

When the cat responded by flinching, turning, jumping or limb movement, the stimulus was terminated and the threshold was recorded. Both systems contain safety cutouts at a pre-set temperature or force to avoid tissue injury.

On the day of the study thorax and lower thoracic limbs of each cat were shaved for TT and MT testing respectively, and a cephalic catheter was placed for drug administration.

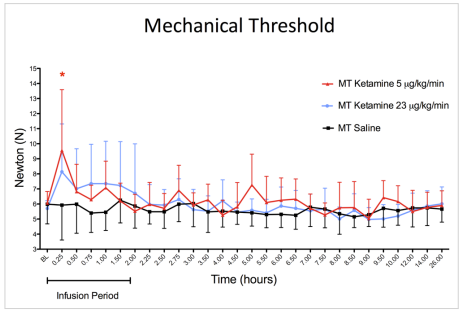


Figure 1: Mechanical threshold (mean ± SD) in eight cats
Significant changes from BL (baseline): (*) in K5

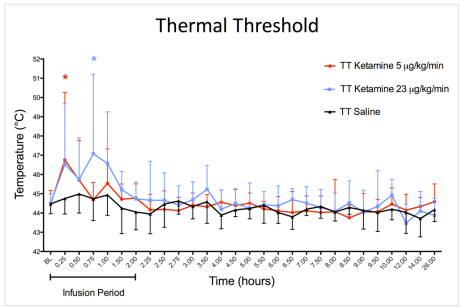


Figure 2: Thermal threshold (mean ± SD) in eight cats
Significant changes from BL (baseline): (*) in K5
Significant changes from BL and between treatments: (*) in K23

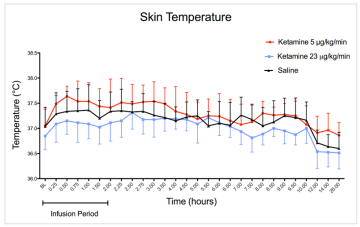
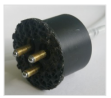


Figure 3: Skin temperature (mean ± SD) in eight cats



Actuator for Mechanical Threshold

Thermal Probe for Thermal Threshold

MATERIALS and METHODS

Treatments

•Ketamine 5:
0.5 mg kg^{-1} ketamine followed by an infusion of 5 µg kg^{-1} $minute^{-1}$ for 2 hours

•Ketamine 23:
0.5 mg kg^{-1} ketamine followed by an infusion of 23 µg kg^{-1} $minute^{-1}$ for 2 hours

•Saline:
Equivalent volume of 0.9% saline solution given as loading dose and infusion

The investigator was blinded to the treatment.

Sedation scores, skin temperature, MT and TT were obtained:
•Prior to drug treatment (baseline)
•During infusion: 0.25, 0.5, 0.75, 1, 1.5, 2 hours after the loading dose (LD)
•Post infusion: 2.25, 2.5, 2.75, 3 hours, then every 0.5 hours for 7 hours, and at 10, 12, 14 and 26 hours after administration of the loading dose

Data were analyzed by repeated measures ANOVA with correction for multiple comparisons. All data are reported as mean ± SD. $P < 0.05$ was deemed significant.

RESULTS

Most cats became sedated after the LD (sedation score 1 out of 4) and 4 cats in the K23 group remained sedated during the infusion period. Three cats in each group displayed minimal head weaving after the LD, no other behavioral effects were observed.

CONCLUSION

Results indicate that low dose ketamine infusions minimally affect thermal and mechanical antinociception in cats. This might be due the fact that the acute analgesiometric methods used in this study are inappropriate to investigate ketamine induced antinocieption. Further studies with different nociceptive testing methods are needed and at the moment these low-dose ketamine infusion regimes cannot be recommended as a sole analgesic.

References

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3. Bergadano A et al. (2009) Vet Journal 182, 252-260.
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