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Recent advances in the use of clomipramine in urine marking in cats

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Introduction

Elimination disorders are the leading cause of feline behavioural complaints, often leading to relinquishment of the animal or euthanasia, and are therefore a welfare concern (Scarlett et al., 2002; Blackshaw, 1992). The use of pharmacological agents to treat behavioural disorders is on the increase (Neilson 2004) and a recent trend towards the belief that one drug can "cure" a wide range of unwanted behaviours may be unrealistic and may lead to relinquishment or euthanasia when owners are disappointed with results (Seksel, 2000; Overall, 2004). This review will examine recent advances in the most widely used behavioural modifying drug, clomipramine, on urine spraying in cats.

Discussion

When a cat is presented with an elimination problem, a thorough history and a full medical examination should initially be performed to rule out medical causes. Only after this should a behavioural diagnosis be considered (Overall, 2004). As the possible causes and treatments for elimination disorders are varied, it is important to diagnose the cause of the behaviour correctly (Seksel, 2000). Inappropriate urination, in which the cat may void large quantities of urine on horizontal surfaces, often responds to environmental modifications (Seksel, 2000). These include cleaning soiled areas with enzymatic cleaners, providing additional litter boxes that are cleaned daily and changing boxes weekly (Pryor et el., 2001a). Spraying may be more difficult to control if it is due to a problem that cannot be resolved, such as a territorial threat by the presence of a stray cat (Landsberg and Wilson 2005). In this case pharmacological therapy may need to be considered.

Treating urine marking with clomipramine
The most widely used psychotropic drugs are the tricyclic antidepressants, such as clomipramine (Overall, 2004), although selective serotonin reuptake inhibitors (SSRI), tranquillisers and antihistamines are still commonly used (Overall, 2004). After its initial use to treat separation anxiety in dogs, clomipramine has become widely used to treat many other behavioural problems, including feline spraying (Overall, 2004). A study by Dehasse (1997) showed that cats given 5 mg of clomipramine once a day showed an 80% decrease in marking behaviour over the 7-day trial, while 33% of cats in this study showed a total cessation of marking while undergoing treatment. These results have contributed to the widespread use of clomipramine, but further studies on long-term effects, dosing rates and comparisons with other drugs still need to be performed before the full efficacy is appreciated.

Landsberg and Wilson (2005) have built on the study by Dehasse (1997) examining clomipramine over a longer trial (4 weeks). They chose 25 cats using a detailed set of criteria designed to minimise any extraneous environmental or medical effects and administered clomipramine at an average dose of 0.54 mg/kg per day. No behavioural or environmental alterations were given during treatment and 20 of the cats showed a 75% reduction in marking behaviour. Although some cats were maintained on clomipramine for longer, no data were collected outside the four-week period. Although this advances our knowledge of the success of treatment with clomipramine for marking behaviour, it may not reflect the clinical norm, which involves cats being maintained for long periods (many months) on the drug. A longer-term study involving more animals should be conducted to reflect this.

Clomipramine dosage rates to treat urine marking
King et al. (2004) recently published a study to determine the optimal dosage rates of clomipramine when treating urine spraying. This is particularly important because of clomipramine's anticholinergic effects, including urine retention, constipation and sedation

(Landsberg, 2001). The study examined 67 neutered cats with a history (greater than one month) of spraying on vertical surfaces. Cats were given either a placebo or a specified dose of clomipramine. Three different dose rates were administered, varying from 0.125 mg/kg to 1 mg/kg, and marking events were recorded. At all dose rates, marking was significantly reduced but sedation effects in more than 50% of cats led the authors to recommend the dose rate that had minimal side effects with highest efficacy (0.25 to 0.5 mg/kg per day). The cat owners were given information on environmental modifications and behavioural treatments, thereby casting some doubt on the effect of clomipramine alone. As Pryor et el., (2001a) have shown, environmental modifications alone can significantly reduce marking behaviours. Any further studies should prevent any such manipulations to examine the drug effect in isolation.

Comparisons with other psychotropic drugs
SSRIs, such as fluoxetine, have also been shown to significantly reduce marking (Pryor et al., 2001b). In a recent trial, fluoxetine and clomipramine were compared to determine differences in efficacy in reducing feline marking behaviour (Hart et al., 2005). This study involved a double-blind clinical trial administering either clomipramine (0.5 mg/kg) or fluoxetine (1mg/kg) to 22 neutered cats (2 females, 20 males) exhibiting long-term marking behaviour. They found that both drugs had equivalent efficiency in treating marking, but after abrupt withdrawal, cats usually returned to marking. Cats that continued marking were placed back on treatment, resulting in another reduction in marking behaviour. Other recent studies suggest therapy should be maintained for two to four months before the cat is slowly weaned off medication over two to four weeks via dose reduction (Neilson 2004). Further studies may indicate whether abrupt withdrawal or a gradual weaning off the drug alters marking behaviour once drug therapy has ceased.

Conclusion

It is hoped that psychotherapeutic drugs, such as clomipramine, can help to reduce the numbers of cats that are relinquished or euthanased because of marking behaviour. Clomipramine, given at dose rates that minimise side effects, is showing promising results in reducing marking behaviours over the short to medium term and has equivalent efficiency to fluoxetine. It should be noted that when given in isolation of behavioural or environmental therapy, recidivism may be high at the cessation of treatment. Studies show that psychotherapeutic agents, in conjunction with behavioural modifications result in better, faster treatment outcomes (Overall and Dunham, 2002). For this reason it is recommended that clinicians use both behavioural and pharmacological therapies to treat marking behaviour. Further studies into long-term treatments should be performed to adequately reflect use of clomipramine in clinics.

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