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Behavioural Changes in Dogs with Acral Lick Dermatitis During a 2 Month Extension Phase of Fluoxetine Treatment

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Acral lick dermatitis (ALD) is a condition described in dogs that is believed to be an animal model of obsessive–compulsive disorder (OCD) in humans. In both conditions, serotonergic neural dysfunction is believed to be responsible for aberrant grooming behaviour. ALD is the first animal model proposed for a psychiatric condition. Serotonergic antidepressants are recommended as first line treatment in OCD. However, many patients have been discouraged from using these by reports of aggression and suicide-inducing effects of these drugs. This study examined behavioural effects of a 2 month extension phase of fluoxetine treatment in dogs previously diagnosed with ALD. A 2 month extension phase on fluoxetine 20 mg daily, immediately followed on a 6 week double blind, randomised, placebo-controlled trial of fluoxetine in 63 dogs with ALD, diagnosed for at least 6 months. The Dodman scales measured excitability, fearfulness, dominance and territorial aggression at the start and end of the 2 month extension phase. Excitability was rated in four settings, referred to as questions 1 to 4. Fifty-four dogs completed the extension phase. Three subjects were withdrawn with no reason given, one for vomiting on fluoxetine. At the end of the extension phase, the analysis of variance showed no significant difference between dogs who received placebo or fluoxetine during the original trial, for scores of fearfulness ($p = 0{\cdot}127$), dominance ($p = 0{\cdot}274$) or territorial aggression ($p = 0{\cdot}172$). Excitability also caused no significant difference on the four questions ($p_1 = 0{\cdot}822$, $p_2 = 0{\cdot}607$, $p_3 = 0{\cdot}975$, $p_4 = 0{\cdot}820$). After the extension phase, owners assessed dogs as being neither more aggressive nor anxious. Particularly, there was no difference in levels of dominance aggression ($p = 1$). Using the paired *t*-test there was no statistically significant difference between scores obtained both at the end of the 6 week trial and the extension phase for fearfulness ($p = 0{\cdot}128$), dominance aggression ($p = 1{\cdot}0$), territorial aggression ($p = 0{\cdot}422$) and excitability ($p_1 = 0{\cdot}487$, $p_2 = 0{\cdot}571$, $p_3 = 0{\cdot}711$, $p_4 = 0{\cdot}086$). These results may serve to refute further the reports of the emergence of impulsive aggression in human subjects on fluoxetine treatment as no significant behavioural changes were noted in the dogs treated with fluoxetine for ALD. © 1998 John Wiley & Sons, Ltd.

KEY WORDS — acral lick dermatitis; fluoxetine; aggression

INTRODUCTION

Controversy regarding the potential of the selective serotonin reuptake inhibitors (SSRIs) to induce aggression followed the report of Teicher *et al.* (1990), who described six depressed patients who developed intense, violent, suicidal preoccupation after 2–7 weeks of fluoxetine treatment.

In contrast to these case reports, Beasley *et al.* (1991) performed a meta-analysis of controlled trials of treatment for depression and found that fluoxetine was not associated with an increased risk of suicidal acts or the emergence of suicidal ideation among depressed patients. In 1·2 per cent of fluoxetine treated patients, suicidal ideation emerged during treatment. This was significantly lower than in those patients receiving placebo (2·6 per cent, $p = 0{\cdot}042$) or tricyclic antidepressants, (3·65 per cent, $p = 0{\cdot}001$). Significantly more patients who were treated with fluoxetine showed an improvement in suicidal ideation than those treated with placebo (72·0 per cent versus 54·8 per cent, $p = 0{\cdot}001$). There was no significant difference between the fluoxetine and tricyclic treated patients.

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Similarly, Fava and Rosenblum (1991) did not replicate Teicher's findings in a survey of 27 psychiatrists treating 1017 depressed outpatients with antidepressants during 1989. This study found no significant difference in the incidence of suicidal ideation in patients treated with fluoxetine and other antidepressants.

Acral lick dermatitis (ALD) is a condition described in dogs that is believed to be an animal model of obsessive–compulsive disorder (OCD) in humans. In both conditions, an underlying malfunction of serotonergic neural mechanisms is purported to give rise to aberrant grooming behaviour (Winslow and Insel, 1990). Fluoxetine has been reported as an effective treatment of ALD (Rapoport *et al*., 1992).

The aim of this study was to measure behavioural changes in dogs, particularly dominance and territorial aggression, excitability and fearfulness, during the follow up phase of a double blind, randomised, placebo-controlled trial of fluoxetine in the treatment of ALD. It is hypothesized that any behavioural change in the ALD dogs may serve as an animal model of human behavioural changes associated with fluoxetine treatment.

METHODS

This study comprised a 2 month open label extension phase of fluoxetine treatment, which followed a 6 week double blind, randomised, placebo-controlled trial of fluoxetine (in press). In the initial phase, subjects included 63 domestic dogs suffering from ALD on no concurrent treatment, diagnosed by a veterinarian at least 6 months previously. Other causes of licking behaviour were excluded by examining the dogs' clinical history, typical lesion appearance and past history of treatment response. The minimum weight of dogs was 5 kg. The dogs' age range and male to female ratio were 1–13 years and 62:38 per cent, respectively. The dose used was 20 mg daily, resulting from data of Rapoport *et al*. (1992). The outcome measure used to assess improvement in the first limb of the study was photographs of the ALD lesions rated by independent veterinarians, blind to treatment randomisation. Modified Clinical Global Impression scores were also used.

In the current study, the Dodman scales were used to assess excitability, fearfulness, dominance and territorial aggression on a score of 0–10 at the start of the open label extension phase and at its completion after 2 months. The scale uses owner rated descriptions of the dog's behaviour in a range of situations. Excitability was rated in four settings; referred to as questions 1–4 (Dodman *et al*., 1996).

Every owner gave informed consent, received an information booklet and was able to withdraw at any point. Weekly phone calls discussed side effects. The study was approved by the Animal Ethics Committee of the University of the Witwatersrand. Analysis was performed using the ANOVA and paired *t*-tests with $p < 0{\cdot}05$ defined as significant.

RESULTS

Of the 63 dogs who entered the 6 week double blind phase, 58 completed it. Four dogs were prematurely withdrawn by their owners and one dog underwent euthanasia for an unrelated reason before completion. Fifty-four dogs entered the extension phase and owners of three subjects withdrew consent without giving any reason. One dog was withdrawn because of vomiting on fluoxetine. All four dogs withdrawn from the extension phase had been on placebo during the 6 week phase.

In order to control for the fact that half the dogs received fluoxetine for a total of 14 weeks and half for 8 weeks (since half had received placebo for the initial phase), we compared the Dodman scores in the two groups at the end of the extension phase. There were no significant differences between dogs who initially received placebo or fluoxetine for scores of fearfulness ($F = 2{\cdot}40$, $df = 1{\cdot}0$, $p = 0{\cdot}127$), dominance aggression ($F = 1{\cdot}22$, $df = 1{\cdot}0$, $p = 0{\cdot}274$) and territorial aggression ($F = 1{\cdot}92$, $df = 1{\cdot}0$, $p = 0{\cdot}172$, ANOVA). There were no differences on scores of excitability on any of the four subscales ($F = 0{\cdot}05$, $df = 1{\cdot}0$, $p_1 = 0{\cdot}822$; $F = 0{\cdot}27$, $df = 1{\cdot}0$, $p_2 = 0{\cdot}607$; $F = 0{\cdot}00$, $df = 1{\cdot}0$, $p_3 = 0{\cdot}975$; $F = 0{\cdot}05$, $df = 1{\cdot}0$, $p_4 = 0{\cdot}820$, respectively). This suggests that the length of fluoxetine treatment did not affect the dogs' behaviour.

Comparing the owners' ratings on the Dodman scales at the start and end of the extension phase, owners assessed the dogs as being neither more fearful ($T = 1{\cdot}56$, $p = 0{\cdot}128$) nor territorially aggressive ($T = 0{\cdot}812$, $p = 0{\cdot}422$). There was no difference at all in levels of dominance aggression ($T = 0$, $p = 1$, paired *t*-test). Excitability ratings showed no significant difference after the extension phase ($T = 0{\cdot}702$, $p_1 = 0{\cdot}487$; $T = 0{\cdot}571$, $p_2 = 0{\cdot}571$; $T = 0{\cdot}373$, $p_3 = 0{\cdot}071$; $T = 1{\cdot}76$, $p_4 = 0{\cdot}086$, paired *t*-test).

DISCUSSION

SSRIs are recommended as an effective treatment for OCD (Rasmussen *et al*., 1993). However, many patients have been discouraged from using these drugs by reports of aggression and suicide inducing effects (Teicher *et al*., 1990).

ALD is the first animal model proposed for a psychiatric condition. Since treatment response in both ALD and OCD appear similar (Rapoport *et al*., 1992), it was hypothesized that behavioural responses to SSRIs in domestic dogs might parallel those in humans. This study failed to show any change in the behaviour of domestic dogs after fluoxetine treatment. The absence of emerging irritability or aggression in the dogs on fluoxetine treatment supports the findings of Beasley *et al*. (1992) and Fava and Rosenblum (1991) who did not find an increase in impulsivity and aggression in clinical studies.

Limitations of the study include that the extension phase was open label, and the rating scales were done by the owners. Furthermore, the extent to which inferences regarding human behaviour can be drawn from animal models is debatable. Nevertheless, these results do not support the emergence of impulsive aggression associated with fluoxetine treatment.

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