Comparison of clomipramine and fluoxetine treatment of dogs with tail chasing

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Key words
Tail chasing, dog, clomipramine, fluoxetine, compulsive disorder

Summary
Objective: The aim of the study was to determine the response to treatment with clomipramine and fluoxetine in dogs with tail chasing. Material and methods: Twenty-five client owned dogs with tail chasing were included in this study. Diagnosis of tail chasing was made on the basis of the dog’s behavioral history, clinical signs, and results of laboratory parameters. The study had a randomized, placebo-controlled, double-blind design. Dogs were allocated to three groups. During 12 weeks, dogs of one group were given 2 mg/kg clomipramine hydrochloride orally, dogs of the second group received 1 mg/kg fluoxetine orally and placebo was administered to control dogs. Changes in signs of tail chasing were weekly reported by the owners. Treatment was assessed in four intervals: weeks 1–3, 4–6, 7–9, and weeks 10–12, respectively. Results: German shepherd dogs and Anatolian sheepdogs were overrepresented. In all four intervals improvement of tail chasing did not differ significantly between clomipramine and fluoxetine (p > 0.05). Improvement of behavior in the clomipramine group was significantly better than in the placebo group between weeks 1–3 and 4–6 and between weeks 7–9 and 10–12 (p < 0.05). Furthermore, there was a significantly better improvement in the fluoxetine group between weeks 7–9 and weeks 10–12 when compared to the placebo group (p < 0.05). Conclusion and clinical relevance: Clomipramine and fluoxetine seem to be equally effective in the treatment of tail chasing. Treated dogs responded well to the drugs and both drugs did not show superiority over each other.
Introduction

Canine compulsive disorder (canine CD) is a syndrome of abnormal behaviors that are believed to result from conflict or frustration (5). Examples are persistent tail-chasing and self-mutilation (10). Compulsive tail chasing in dogs is a stereotypic or obsessive-compulsive disorder (OCD). It occurs most frequently in Bull Terriers and German shepherd dogs and may be seen subsequently to physical trauma, surgery, or medical illness. It may represent an epileptic episode or a biochemical disturbance at the level of neurotransmitter systems (3). Recently, similarities in the clinical signs, development, and response to pharmacological treatment of compulsive behavior patterns in companion animals and humans have been recognized (15). Similar to treatment of human OCD, drugs inhibiting serotonin re-uptake have been found to be effective in the treatment of CD in dog, although it may take 4 weeks of treatment or longer to see an effect (4, 10).

Clomipramine has been successful in the treatment of human and canine obsessive compulsive disorders (4, 12, 13). There are few reports of research on treatments for canine CD, but there is evidence that the antidepressant clomipramine may be of use (2, 4, 13, 15). Clomipramine appears to be safe when used in dogs but it has been associated with sedation, anorexia and excessive swallowing, restlessness, lip-licking associated with nausea (2, 15). Abrupt withdrawal of clomipramine might lead to acute worsening of the dog’s condition, analogous to the “acute withdrawal syndrome” described in humans when therapy with selective serotonin re-uptake inhibitor (SSRI), tricyclic antidepressant (TCA) or monoamine oxidase inhibitor (MAOI) drugs is stopped suddenly (4, 9). Return of signs of stereotypies has also been reported in dogs after cessation of treatment with clomipramine (11, 12).

Fluoxetine, a selective serotonin re-uptake inhibitor widely used in human medicine has proven efficacy in treating anxiety disorders in people (18) and this drug is efficacious in the treatment of aggressions (1), obsessive-compulsive disorders (15, 21), generalized anxiety (16) and separation anxiety in companion animals (8).

There are few reports (12, 19) of research on treatments for tail chasing. Therefore, the objective of the present study was to compare the effectiveness of clomipramine and fluoxetine in the treatment of dogs with tail chasing.

Material and methods

Dogs

Twenty-five dogs were referred to the Small Animal Clinic, Department of Internal Medicine of the Veterinary Faculty of Uludag University. A behavioral diagnosis was made for each dog on the basis of the dog’s behavioral history, clinical signs and results of laboratory parameters. Behavioral history included age at onset, frequency and duration of bouts since onset, general history, and current or previous medical conditions. Affected dogs of different age, sex and breed (Table 1) had to have tail chasing bouts for a minimum of 60 s/bout to be included in the study.

Study design

The study had a randomized, placebo-controlled, double-blind design. Dogs were allocated to three groups. Clomipramine hydrochloride and fluoxetine hydrochloride were supplied as tablets and capsules, respectively. Clomipramine hydrochloride tablets, fluoxetine capsules and placebo were administered in opaque gelatin capsules to allow for the blind design. Dosages of drugs were 2 mg/kg BID and 1 mg/kg SID for clomipramine and fluoxetine, respectively. As placebo 2.5 mg dextrose was administered SID. Treatment was given 10 minutes before feeding. Dogs received drugs for 12 weeks. Owners were advised to exercise their dogs 30 minutes per day and feed a low-protein diet (16 to 20% protein on a dry matter basis).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Breeds, gender and age of dogs in the three groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clomipramine (n = 8)</td>
<td>Fluoxetine (n = 9)</td>
</tr>
<tr>
<td>Breeds</td>
<td>ASD (n = 2) GS (n = 2) Terrier (n = 2) Husky (n = 1) Pointer (n = 1)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male (n = 7) Female (n = 1)</td>
</tr>
<tr>
<td>Median of age [months] (25%–75%)</td>
<td>24 (15–60)</td>
</tr>
</tbody>
</table>

ASD: Anatolian sheepdog, GS: German shepherd
Sampling

After a fasting period of 12–16 h venous blood samples were collected from the cephalic vein into vacutainer tubes with and without EDTA for complete blood count and serum concentrations of urea, creatinine, total protein, albumin, globulin, and glucose, and activities of alanine amino-transferase. Results of the laboratory and physical examination were used to exclude dogs with seizure disorders, diabetes mellitus, liver disease, glaucoma, cardiac disease, local vasculitis, neuritis, anal sac diseases and pruritus.

Scoring of treatment

In all dogs, response to treatment was monitored and evaluated weekly by phone conversation or personal contacts using score sheets. Score sheets included whether the owner had observed any adverse effects and, if so, what kind of effects had been seen, how many hours the owner had spent with the dog that day, the number of episodes of compulsive behavior the owner had witnessed that day, the duration of the longest observed episode, and whether the behavior ended on its own or because it was interrupted. Similar as in the study of Moon-Fanelli and Dodman (12) owners were asked to assign a score on the basis of the following scale for improvement in behavior: 0 = no change was observed, 1 = minimal improvement, 2 = moderate improvement, 3 = marked improvement and 4 = substantial improvement. Response to treatment was evaluated for the following four intervals: weeks 1 to 3, weeks 4 to 6, weeks 7 to 9, and weeks 10 to 12.

Statistical analyses

Data were analyzed by Friedman test followed by Wilcoxon signed rank test in each group. The Kruskal Wallis test followed by Mann Whitney U Test was used to compare score differences between the three groups (SPSS for Windows version 13.0). For comparison of scores between each treatment section in each group, results were analyzed using the Friedman test for statistical differences between mean duration of treatment. In case of a significant difference the Wilcoxon signed rank test was used to compare sections two by two. Improvement in behavior for sequential weeks computed as score differences was analyzed between all groups by using the Kruskal Wallis test. When groups were significantly different the Mann Whitney U test was used to compare groups with one another.

Results

Male dogs (n = 19) were more often affected than female dogs (n = 6). Concerning the breed German shepherd dogs (n = 7) and Anatolian sheepdogs (n = 5) were overrepresented. In 10 out of 25 dogs tails were bandaged because of injury. Five dogs chased their tails in presence of their owners and only stopped this behavior when their attention was focused on another object or person. The other dogs did not stop. Drugs affecting gastrointestinal motility including anti-emetics, anti-diarrhoea medication or drugs affecting urinary function including diuretics were not administered during the trial. Adverse effects or worsening of behavior was not noted in any case.

Table 2
Response to treatment groups according to weeks

<table>
<thead>
<tr>
<th>Interval</th>
<th>Treatment groups</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks 1–3</td>
<td>Clomipramine (n = 8)</td>
<td>2</td>
<td>6</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine (n = 9)</td>
<td>1</td>
<td>8</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 8)</td>
<td>8</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Weeks 4–6</td>
<td>Clomipramine (n = 8)</td>
<td>–</td>
<td>2</td>
<td>6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine (n = 9)</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 8)</td>
<td>5</td>
<td>3</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Weeks 7–9</td>
<td>Clomipramine (n = 8)</td>
<td>–</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine (n = 9)</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 8)</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Weeks 10–12</td>
<td>Clomipramine (n = 8)</td>
<td>–</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Fluoxetine (n = 9)</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo (n = 8)</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*Treatment scores: 0 = no change, 1 = minimal improvement, 2 = moderate improvement, 3 = marked improvement, 4 = substantial improvement
Repeated score measures of treatment sections were significantly different for all three groups (p < 0.001) but clomipramine and fluoxetine were more effective and well-tolerated in controlling signs of tail chasing. The effect of clomipramine did not differ significantly compared to fluoxetine between weeks 4–6 and 7–9. Response to treatment in the three groups according to weeks are shown in Table 2. After computing differences of scores between sequential treatment sections we compared these values among groups to determine difference of improvement in behavior. It was found that clomipramine and fluoxetine groups were not significantly different for the improvement in all treatment intervals (p > 0.05). Improvement of behavior in the clomipramine group was significantly better than in the placebo group in all treatment intervals (p < 0.05) (Fig. 1).

Discussion

The result of our study that 76% of tail-chasing dogs were male shows parallelism with the literature (14). It was remarkable that 32% of these dogs were under 1 year old with a median age of about 36 months. It is likely that young dogs have a lower threshold against environmental or psychologic pressures (12). Onset of tail chasing between 3 and 12 months of age in eight sexually intact dogs suggested that hormonal changes associated with puberty could have been involved in triggering this condition similar as in human beings (13). The most affected breeds in our study were German shepherd dogs, Anatolian sheepdogs, and Terriers. Although tail chasing can be observed in several breeds of dogs, there are reports in the literature (12) that it predominantly occurs in terriers and breeds selected for herding. The association of identifiable environmental, physiologic, or psychological experiences with onset of tail chasing in dogs suggested that anxiety resulting from stress, conflict, boredom or environmental changes may have been a contributing factor.

Comparison of treatment scores shows that there are significant differences between treatment groups and placebo group, while no statistical difference between the two treatment groups can be found. Therefore we conclude that the two drugs are successful in the treatment of tail chasing and that they do not have superiority over each other.

A limited number of studies concerning clomipramine and fluoxetine for treatment of tail-chasing in dogs are available. Clomipramine is effective and well-tolerated in controlling signs of obsessive-compulsive disorders. Moon-Fanelli and Dodman (12) reported 75% or greater improvement in tail chasing when clomipramine was given in a total daily dose between 1 and 5 mg/kg. In a retrospective study of 103 dogs with various manifestations of compulsive disorder, clomipramine was found to be significantly more effective than amitriptyline (14). Stein et al. (20) used fluoxetine in a dosage of 1–2 mg/kg daily for an 8-week open trial on five dogs with acral lick dermatitis (ALD), and three dogs showed substantial improvement. In another study using fluoxetine in cases of OCD manifested as canine ALD a 50% success rate was reported (7). Wynchank and Berk (21) conducted a double-blind, randomized, placebo-controlled trial on the use of fluoxetine and demonstrated the efficacy of fluoxetine in the treatment of ALD in dogs. Rapoport et al. (15) compared fluoxetine to fenfluramine in 14 dogs with ALD and found that improvement on fluoxetine was significantly greater than on fenfluramine.
Conclusion for practice
As a result of the study, it was concluded that clomipramine or fluoxetine can be safely used in the treatment of dogs displaying tail chasing, that treatment with these drugs has positive effect and the two drugs do not have superiority over each other.

Conflict of interest
The authors confirm that they do not have any conflict of interest.

References