

Efficacy of dog-appeasing pheromone (DAP) for ameliorating separation-related behavioral signs in hospitalized dogs

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Abstract — Dogs hospitalized in veterinary clinics are likely to show signs of separation-induced anxiety from hospitalization. The study assessed the effect of dog-appeasing pheromone (DAP) on 10 typical separation-related behavioral signs in hospitalized dogs. A DAP treated group ($n = 24$) was compared with a placebo control group ($n = 19$). There was overall amelioration of the signs without 'vigilance' and 'anorexia' in the DAP-treated dogs; marked decreases were noted in elimination ($P = 0.038$), excessive licking ($P = 0.005$), and pacing ($P = 0.017$). The results suggest that the use of DAP could decrease separation-induced anxiety, distress, and fear in inpatients, and possibly facilitate recovery in hospitalized dogs.

Résumé — Efficacité de la phéromone d'apaisement des chiens pour améliorer les signes comportementaux liés à l'anxiété de séparation chez les chiens hospitalisés. Les chiens hospitalisés dans les cliniques vétérinaires manifesteront probablement des signes d'anxiété causés par la séparation lors de l'hospitalisation. L'étude a évalué l'effet de la phéromone d'apaisement des chiens (PAC) sur 10 signes comportementaux types liés à la séparation chez les chiens hospitalisés. Un groupe traité à la PAC ($n = 24$) a été comparé à un groupe témoin traité au placebo ($n = 19$). Il s'est produit une amélioration générale des signes sans «vigilance» et «anorexie» chez les chiens traités au PAC; des baisses marquées ont été observées pour l'élimination ($P = 0,038$), le léchage excessif ($P = 0,005$) et le va-et-vient ($P = 0,017$). Les résultats suggèrent que l'usage du PAC pourrait réduire, chez les patients, l'anxiété, la détresse et la peur causées par la séparation et éventuellement faciliter le rétablissement des chiens hospitalisés.

(Traduit par Isabelle Vallières)

Can Vet J 2010;51:380–384

Introduction

Dogs are social animals which have a strong inherent desire to interact with their social group including human family members (1). Separation-related behavioral signs in dogs result from a strong social bond and hyper-attachment between dogs and their owners (2–6), and are likely to be shown if dogs are separated from and/or denied access to their owners. The behavior is likely due to a variety of factors including anxiety, fear, distress, frustration, and panic (7). Destructiveness, vocalization,

inappropriate elimination, attempt to escape, pacing, trembling, depression, and self-mutilation are commonly expressed as separation-related behavioral signs (8).

A natural form of dog-appeasing pheromone is secreted from the sebaceous glands between the mammary chains of lactating bitches directly after parturition. The pheromone is reported to be detected by Jacobson's organ or the vomero-nasal organ (VNO), and to have calming effects in both young and adult dogs under a wide variety of stressful situations (9). Dog-appeasing pheromone (DAP; Ceva Sante Animale, Libourne, France) is a synthetic congener of natural dog-appeasing pheromone (9). that has been promoted as an adjunct treatment to ameliorate conditions such as separation-related behavior problems, phobias, and hyper-attachment (10). Dog-appeasing pheromone has been reported to reduce separation-induced anxiety (11), fear in puppies in a new environment (12), and anxiety and stress during transportation (13,14). It can also diminish anxiety of aggressive dogs (15), stresses of dogs in public shelter (16), training-derived stresses of police dogs (17), and anxiety of puppies in learning and socialization (18). Also, DAP might be a potential treatment for dogs that are fearful of fireworks (19). Use of DAP in veterinary clinics was significantly associated with greater relaxation in dogs, but did not have an effect on aggression (20). There was no significant difference in effectiveness of DAP and clomipramine for ameliorating separation-related behavior problems in dogs (11). Furthermore,

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Table 1. Reference indicators to evaluate the state of separation-related behaviors in hospitalized dogs for baseline and final assessments

Behavioral signs	Four-point scale (score)	Frequency/severity in behavioral signs
Destructiveness (scratching/digging/chewing)	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing 1 to 2 times of the sign Showing 3 to 5 times of the sign Consistent destructiveness for escape
Vocalization (whining/barking/howling)	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing 1 to 2 times of the sign Showing 3 to 5 times of the sign Consistent or compulsive vocalization
Elimination (urination/defecation)	none (0) mild (1) moderate (2) severe (3)	Showing normal elimination in the view of the veterinarians Showing slightly increased in the volume or frequency from normal elimination in the view of the veterinarians Showing noticeably increased in the volume or frequency from normal elimination in the view of the veterinarians Showing seriously increased in the volume or frequency from normal elimination in the view of the veterinarians
Vigilance	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing mild vigilance in the view of the investigators Showing noticeable vigilance in the view of the investigators Showing serious vigilance in the view of the investigators
Excessive licking	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing 1 to 2 times of the sign Showing 3 to 5 times of the sign Consistent or compulsive licking or grooming
Anorexia	none (0) mild (1) moderate (2) severe (3)	Showing normal appetite in the view of the investigators Showing slightly reluctant taking food in the view of the investigators Showing noticeably reluctant taking food in the view of the investigators Completely refusing to take food
Gastrointestinal problems (vomit/diarrhea)	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing 1 time of the sign Showing 2 times of the sign Showing over 3 times of the sign
Hyper-salivation	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing slightly increased the sign in the view of the investigators Showing noticeably increased the sign in the view of the investigators Consistently showing the sign in the view of the investigators
Trembling	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing slightly increased the sign in the view of the investigators Showing noticeably increased the sign in the view of the investigators Consistently showing the sign in the view of the investigators
Pacing	none (0) mild (1) moderate (2) severe (3)	Absence of the sign Showing slightly increased the sign in the view of the investigators Showing noticeably increased the sign in the view of the investigators Consistently showing the sign in the view of the investigators

DAP has no toxicities or side effects and is particularly beneficial for sick and geriatric dogs (CEVA Sante Animale-Product instruction).

Anxiety or distress-related behavioral signs such as frequent barking and whining, vigilance, anorexia, trembling, and pacing are commonly observed in hospitalized dogs. These signs are associated with pain, cage confinement, sleep deprivation, and noise from other dogs in veterinary clinics (21–25). Consequently, it was hypothesized that the use of DAP might ameliorate separation-related behavioral signs in hospitalized dogs.

The purpose of this study was to evaluate the efficacy of DAP on 10 typical separation-related behavioral signs in hospitalized dogs by comparing DAP treated and placebo-control groups.

Materials and methods

Placebo-controlled and double-blinded study designs were used on 43 hospitalized dogs that were recruited to compare the effects of DAP ($n = 24$) and the placebo-control ($n = 19$). Dogs which had been hospitalized for more than 4 d were selected. Dogs with severe abnormal cognitive conditions such as stupor and coma, dogs that were being anesthetized for surgery, and dogs which were being treated with large amounts of analgesics and psychotropic drugs were excluded in order to appropriately evaluate changes in behavioral state. The sex, age, breed, sterilization status, medical diagnosis, and level of pain of each dog were not considered for recruitment, since it was difficult to secure enough dogs that simultaneously satisfied all of the requirements. The effects of medical diagnosis, level of pain,

cage confinement, and noise from other dogs in the sickroom were ignored.

Experimental environment

The study was undertaken at Lee Jong Kyung veterinary clinic in Seoul, South Korea. The sickroom was 4 m long × 2 m wide and held 10 cages. Each cage had the same design and layout with the base measuring 0.8 m² for small breeds, which is common in Korea (26). Most of the dogs (36, 83.7%) that participated in the study were small breeds. The medium-sized dogs (> 30 kg) were usually housed in a large pen. The hospitalized dogs were individually housed in a single cage or pen, except for a short period when they received medical treatment and the kennel was cleaned. All diffusers (dispensing DAP or a placebo) were installed at a height of 1.8 m on the wall of the sickroom and were changed once a month.

Treatment procedure

Concurrent evaluation of the DAP and placebo-control groups was avoided to prevent cross-contamination: the placebo-control group was evaluated first. The placebo diffusers were empty, whereas the dogs in DAP group were exposed to DAP (DAP; Ceva Santé Animale), and 2 diffusers were available to cover the sickroom.

The study was carried out using a double-blinded study design. The investigators (4 staff members including 2 veterinarians) were never informed which dogs were in the placebo or DAP groups, and all diffusers in both groups were covered with opaque tape to avoid visual identification by investigators. Also, all diffusers were installed and changed once a month by only 2 authors, not investigators.

Evaluation of behavioral state

Ten typical separation-related behavioral signs, namely, destructiveness (scratching or chewing bars to escape), vocalization (frequent whining, barking, and howling), elimination (frequent urination and defecation), vigilance, excessive licking, anorexia, gastrointestinal problems (vomiting and diarrhea), hyper-salivation, trembling, and pacing were selected for the study (6,8,20,27).

Each behavioral state of separation-related behavior signs shown by dogs was individually monitored by 4 investigators. They generated scores in accordance with the reference indicators (Table 1), and each score represented more than 3 observations made by the investigators.

The baseline assessment was usually made within 30 min directly after the owner's departure on the first day of hospitalization since separation-related behavioral signs are likely to be intense within 30 min after departure of the owner (28), and the final assessment on the same dog was monitored on the 4th day of hospitalization. The monitoring of baseline and final assessment each lasted for 8 h.

The observations by investigators in the baseline and final assessments generated scores based on a 4-point scale: 0 (none); 1 (mild); 2 (moderate); and 3 (severe) (Table 1). The change in behavioral state on each separation-related sign was calculated by subtracting the score in final assessment from the score in

Table 2. Demographic characteristics of the recruited dogs in the placebo-control and DAP groups

Variables	Placebo		DAP	
	<i>n</i>	%	<i>n</i>	%
	19	44.2	24	55.8
Sex				
Male	12	63.2	8	33.8
Female	7	36.8	16	66.7
Breed				
Pure	18	94.7	21	87.5
Mixed	1	5.3	3	12.5
Sterilization status				
Neutered	6	31.6	4	16.7
Intact	13	68.4	20	83.3
Age (year)				
Male (mean age)		4.6		6.3
Female (mean age)		6.1		5.6
Range (years)		1 to 13		1 to 17

n = number of dogs.

the baseline assessment. A 5-point scale was used to evaluate the changes in the behavioral state: -2 (much worse); -1 (slightly worse); 0 (same); 1 (slightly better); and > 2 (much better).

Statistical analysis

The Mann-Whitney *U*-test, a nonparametric statistic, was used to identify the efficacy of DAP by comparing the mean ranks of each separation-related behavioral sign between the placebo-controlled group and the DAP group. Also, the Pearson's chi-squared test was used for the influence of age and sex on the efficacy of DAP in the placebo-control and DAP groups. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences, version 12.0, USA), with *P* < 0.05 considered as statistically significant.

Results

Demographic characteristics

Forty-three dogs were recruited for the study: 19 (44.2%) were placed in the placebo group, and 24 (55.8%) in the DAP group. There were 23 female dogs (53.5%) and 20 males (46.5%). Most of the dogs were purebred (39, 90.7%) and included: Maltese (11, 25.6%), Shih-tzu (7, 16.3%), Yorkshire terrier (7, 16.3%), poodle (6, 14.0%), cocker spaniel (2, 4.7%), and 1 of each Chihuahua, Japanese spitz, Jindo, dachshund, Siberian husky, and beagle. There were more intact dogs (33, 76.7%) than neutered dogs (10, 23.3%). Dogs ranged in age from 1 to 17 y with a mean of 5.6 y.

There were more male dogs in the placebo-control group (12, 63.2%) than in the DAP group (8, 33.3%). Purebred dogs were similarly distributed in both the placebo-control (18, 94.7%) and the DAP group (21, 87.5%). There were few neutered dogs in both the placebo-control (6, 31.6%) and the DAP (4, 16.7%) groups. The mean age of dogs in the DAP group (5.9 y) was slightly higher than in the placebo-control group (5.3 y) (Table 2).

The recruited dogs were diagnosed as suffering from renal dysplasia, granulomatous meningoencephalitis, glaucoma, mitral valve insufficiency, esophageal foreign body, intervertebral disk

Table 3. Baseline assessment, final assessment, and change in the dogs' behavioral states for the 10 separation-related behavioral signs in placebo-control and DAP-treated groups

Separation-related behavioral signs	Placebo-control			DAP			<i>P</i> -value
	Baseline	Final	Change	Baseline	Final	Change	
Destructiveness	0.368	0.368	0.000	0.458	0.250	0.208	0.326
Vocalization	0.316	0.263	0.053	0.583	0.458	0.125	0.700
Elimination	0.053	0.211	-0.158	0.417	0.167	0.250	0.038*
Vigilance	1.053	0.790	0.263	0.500	0.083	0.417	0.673
Excessive licking	0.000	0.211	-0.211	0.417	0.167	0.250	0.005**
Anorexia	0.947	0.368	0.579	0.833	0.125	0.708	0.817
Gastrointestinal problems	0.000	0.105	-0.105	0.000	0.042	-0.042	0.422
Hyper-salivation	0.158	0.211	-0.053	0.042	0.000	0.042	0.159
Trembling	0.211	0.105	0.105	0.208	0.000	0.208	0.467
Pacing	0.947	0.579	0.368	1.000	0.125	0.875	0.017*

* Significant $P < 0.05$.** Significant $P < 0.01$.

disease, pancreatitis, mammary gland adenocarcinoma, inflammatory mammary gland carcinoma, haemophthalmia, chronic renal failure, fibrosarcoma, lymphoma, oestrogen toxicity (anemia), and hemivertebra.

Demonstration of separation-related behavioral signs

In total, 143 behavioral signs were manifested by the 43 dogs (3.3 signs per dog). The distribution of separation-related behavioral signs was well-balanced between the 2 groups. Pacing (34, 22.2%), anorexia (31, 20.3%), and vigilance (29, 18.9%) were commonly demonstrated in total. In the placebo-control group, vigilance (17, 26.6%) and anorexia (16, 25%) were common, but excessive licking and gastrointestinal problems were never exhibited. In the DAP group, the common behavioral signs were pacing (19, 21.3%), anorexia (15, 16.9%), vigilance (12, 13.5%), and vocalization (12, 13.5%). None of the dogs in either group had gastrointestinal problems.

Efficacy of exposure to DAP

In comparing the baseline and final assessments, there were aggravations of elimination (-0.158), excessive licking (-0.211), gastrointestinal problems (-0.105), and hyper-salivation (-0.053) in the placebo-control group. However, there were overall improvements of separation-related behavioral signs except gastrointestinal problems (-0.042) in the DAP group.

In comparing the mean ranks between the 2 groups, there was overall improvement except in vigilance (21.35) and anorexia (22.35) in the DAP group compared with the placebo control group; elimination ($P = 0.038$), excessive licking ($P = 0.005$), and pacing ($P = 0.017$) were significantly improved in the DAP group (Table 3).

Since the distribution of older and female dogs in the DAP group was higher than in the placebo group, the influence of age and sex on changes in the behavioral state was also evaluated in the DAP group. There was no age-related difference except in destructiveness ($P = 0.05$) and sex type never affected the changes in behavioral state in the DAP group.

Discussion

There was overall amelioration of separation-related behavioral signs in the DAP treated group. However, there were several methodological limitations to the study since it was difficult to secure a sufficient number of dogs to achieve homogeneity of sex, age, breed, sterilization status, medical diagnosis, duration of hospitalization, and level of pain in each group. Furthermore, dogs that are hospitalized in a veterinary clinic are likely to suffer from anxiety in general, due to cage confinement, pain, separation, and noise. Therefore, the abnormal behavior exhibited by hospitalized dogs does not result only from separation anxiety. The 10 typical behavioral signs used in the study, however, were selected by consideration of separation-related behavior problems. The effects of medical diagnosis, level of pain, effect of confinement, and noise from neighboring dogs in the sickroom were ignored in this study. Other potential factors that were not considered included the dog's temperament (hyper-attachment) and individual behavior history, including early traumatic experiences and environment (21,22). Consequently, the effects of potential factors and homogeneity of the groups of dogs upon separation-related behavioral signs should be considered in future studies.

The treatment duration was shorter than in previous studies on the efficacy of DAP (11,14). However, the effect of DAP has been shown in dogs that have been in public animal shelters for more than 7 d (16), and in dogs travelling in cars and given spray-type DAP 10 min before they travelled (13). Therefore, 4 d as treatment duration in this study was sufficient to evaluate behavioral changes in hospitalized dogs.

There was a decrease in several separation-related behavioral signs such as anorexia, pacing, vigilance, shaking, destructiveness, and vocalization in the placebo control group. It is suggested that protests, separation anxiety, and distress-related activities in dogs are intensified immediately after the owner departs (29,30), and the dogs gradually adapted and became habituated to the veterinary medical clinic, thereby diminishing some separation-related behavioral signs in the placebo group.

Behavioral signs, especially elimination, excessive licking, and pacing were significantly ameliorated in the DAP treated group.

Excessive licking and pacing are also commonly manifested as canine stereotypy and repetitive behaviors. It is considered that affected dogs exhibit these behaviors to cope with distress, conflict, and frustration (7,31). Consequently, it is suggested that DAP as an adjunct treatment could diminish distress and anxiety in canine stereotypy and compulsive disorders as well as separation-related behavioral signs. Therefore, further studies should also investigate the efficacy of DAP in ameliorating stereotypes and compulsive disorders in dogs.

Hormonal and immunological responses and healing in dogs are influenced by anxiety as a component of stress (23–25). Consequently, the use of DAP could decrease separation-induced anxiety and stress in hospitalized dogs and this would enhance their welfare and possibly facilitate recovery.

Acknowledgments

The authors thank the veterinary surgeons who provided technical assistance and cooperation in Lee Jong-Kyung veterinary clinic, and Seung-Yeol Nah, Department of Physiology, College of Veterinary Medicine, Konkuk University, who provided assistance in preparation of the manuscript. CVJ

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