



SHORT COMMUNICATION

Oral supplementation with L-lysine did not prevent upper respiratory infection in a shelter population of cats

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Cats in animal shelters are highly susceptible to infection by feline herpesvirus (FHV) by virtue of their stress and close proximity to other cats. Animal shelters take several different approaches to prevent FHV-related upper respiratory infections (URIs), including empirically treating all cats with L-lysine, a supplement believed to prevent the replication of FHV and, therefore, manifestations of herpesvirus infections. In this study we tested oral supplementation of L-lysine as a means to prevent URIs. One hundred and forty-four cats were treated with L-lysine in a small amount of canned food once daily. A 'no treatment' group of 147 cats received no lysine during the course of the study. The development of conjunctivitis or URI was tracked between the two groups. In all measures, there was no effect between the two groups, suggesting that lysine was not able to prevent URI or conjunctivitis in our shelter situation. Cats entering shelters encounter stressors that may make them more susceptible to FHV reactivation or infection. Infection control and control of fomite transmission are also key to keeping cats healthy in a group housing situation. The finding that lysine did not prevent URI in this animal shelter suggests that shelters may better use their resources by finding ways to decrease stress among their feline population, focusing on proper infection control measures, and limiting fomite transmission of disease.

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Feline herpesvirus (FHV) is a common viral infection among cats causing conjunctivitis and signs of upper respiratory infection (URI), particularly those residing in animal shelters. One study showed that while only 4% of cats surrendered to animal shelters were shedding FHV at the time of surrender, after 1 week 52% were shedding virus (Pedersen et al 2004). Another study demonstrated that FHV was found in 31% of shelter cats with no signs of illness (Burgesser et al 1999). Illness resulting from FHV may prevent an animal from being placed for adoption if the shelter does not have the capacity to isolate and treat any secondary bacterial infections. FHV rapidly spreads through a captive population by direct contact and fomite transmission. In addition, many cats are latently

infected with FHV and periods of stress have the potential to reactivate the infection and induce shedding (Gaskell and Povey 1977). L-Lysine is an essential amino acid present in conventional feline diets that interferes with the replication of FHV in vitro (Maggs et al 2000). The mechanism of this effect is unknown but is thought to relate to competition with arginine, an amino acid necessary for the replication of the virus. A challenge with increased arginine is able to overcome the inhibition of replication due to lysine in vitro (Maggs et al 2000). There have been mixed results published with trials of lysine in FHV. Small studies have shown some success in preventing viral shedding (Maggs et al 2003) and clinical signs (Stiles et al 2002), but a more recent larger study has raised questions of efficacy among cats with unknown backgrounds and mixed presentations of URI

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(Maggs et al 2007). This study was designed to test the efficacy of oral supplementation of L-lysine in the prevention of URI among a group of felines surrendered to an open admission shelter.

During the months of February, March and April of 2007, all healthy incoming cats to the Humane Society of Indianapolis were randomly assigned on the basis of their computerized intake number to receive either no treatment or a daily supplement of 250 or 500 mg L-lysine (Viralys, Vet Solutions, Fort Worth, TX) in a small amount of canned food. Cats were defined as 'healthy' for the purposes of this study if they showed no signs of conjunctivitis or URI upon intake during an intake examination performed by veterinary assistants. Any cat with conjunctivitis, watery or purulent ocular or nasal discharge, or episodes of sneezing was excluded. Upon entry to the shelter all cats in the lysine group were given the lysine powder dissolved in water orally as a part of their vaccination protocol. Kittens under 5 months received 250 mg daily and cats 5 months and over received 500 mg. Cats surrendered with active URIs were excluded from the study as the study was intended to test the efficacy of lysine on prevention of URI. All cats were vaccinated with a modified live subcutaneous feline viral rhinotracheitis, calicivirus, panleukopenia vaccine (Felocell 3; Pfizer) on the day of intake. All kittens 8 months and under also received a modified live intranasal feline viral rhinotracheitis, calicivirus vaccine (Feline UltraNasal, Heska, Loveland, CO) during their physical examination on the day of intake. Each day every cat was evaluated for signs of conjunctivitis or URI (watery or purulent ocular or nasal discharge, with or without active sneezing) by veterinary assistants during their normal medical rounds at the shelter. The observers were not informed whether the cats were receiving lysine or no treatment. Healthy cats continued to receive lysine supplements every morning until their adoption. Cats and kittens with conjunctivitis or signs of URIs were treated according to standard shelter protocol and their lysine supplementation was discontinued. Standard treatment protocol includes removal of the cat from the general population into an isolation ward and antibiotics (doxycycline or triple antibiotic ophthalmic ointment) started for a 3-week course to prevent secondary bacterial infections. Close monitoring of their condition and supportive care is provided as necessary. Cats who are still showing signs at the conclusion of 3 weeks of doxycycline

(sneezing, watery or purulent nasal or ocular discharge) are continued on a second course of antibiotics for another 21 days (amoxicillin/clavulanic acid or terramycin ophthalmic ointment).

The cages at the shelter consist of stainless steel kennels (Shor-Line, Kansas City, KS) with variable measurements ranging from 22" × 22" × 28" up to 34" × 28" × 28". Cats remain in their assigned cages during cleaning to prevent cross contamination. They are moved to new cages only when they go to the adoption floor or are isolated due to URI. Cats with active URI are handled with gowns and gloves and the gowns/gloves are changed between cats to prevent fomite transmission. Other cats are handled minimally with handwashing between each animal, also to prevent fomite transmission. Cats are not housed or examined in proximity to dogs to prevent stress caused by dog noise. Although cats are housed in separate rooms from the time of surrender, it is possible that they hear some dog noise as it travels through the shelter. The density of the cats during this study varied from day to day, but averaged 76.2% of cages full in the evaluation area (ranging from 44.1 to 111%) and 85.9% cages full in the adoption area (ranging from 45.9 to 116%). More than 100% density represents all cages full with more than one cat (surrendered together) in some cages or corrals. The ventilation system brings 100% fresh air in 4–7 times per minute in all animal housing areas.

Statistical analyses were performed using either a Student's two tailed *t*-test to look for

Table 1. Descriptive information about each treatment group

	Lysine treated	Non-treated
Number of animals	144	147
Females (%) [*]	57.7	61.9
Previously altered (%) [*]	58.3	56.5
Average age at surrender (months ± SD) [†]	29.8 ± 30.2	36.2 ± 33.1
Median age at surrender (months)	24	24
Range of ages at surrender (months)	2–180	2–144

^{*}Distributions not significant between groups ($P > 0.1$) using the χ^2 test.

[†]Means not significantly different ($P = 0.08$) between groups using a Student's *t*-test.

differences between means, or a χ^2 test to test differences in distributions.

In total, 144 cats were enrolled in the lysine treated group and 147 cats in the untreated group. This represents all healthy cats who could receive a medical examination when entering the Humane Society of Indianapolis during the study time (February, March and April 2007). This number of study participants should offer sufficient power to see a small effect due to lysine administration. A sample size calculation suggests that a sample size of 138 per group should provide 80% power to see a 15% change in URI at a significance level of 0.05.

Table 1 shows the signalment information of the two groups. Figure 1 shows our findings. The percentage of cats from each group diagnosed with URI was not different between the two groups (Fig 1A; 37% in the lysine treated group versus 34% in the untreated group, $P > 0.5$). Of those cats diagnosed with URI, the percentage of animals who required a second round of treatment before being determined to be healthy did not differ between the treatment groups (Fig 1B; 19% in the lysine treated group versus 14% in the untreated group, $P > 0.5$). The mean number of days the cats remained healthy before signs of conjunctivitis or URI manifested was also not different between the two groups (Fig 1C; 13 days in each group). Finally, those animals that remained healthy during their entire stay spent the same average number of days in the shelter prior to adoption (Fig 1D; 10 days in each group).

All cats in the lysine group were given lysine via direct oral administration in conjunction with their vaccines and de-wormer upon entry, but otherwise were given the lysine in a small amount of canned food in a disposable bowl to prevent handling stress. This means of treatment also limits cage to cage fomite transmission of viruses through handling of numerous cats. The dose given upon entry was not thought to increase the stress over and above that of the normal vaccination procedure, and assured that

using the χ^2 test ($P > 0.5$). (C) Among the cats that were diagnosed with URIs or conjunctivitis, the number of days (mean \pm SD) they were at the shelter prior to diagnosis (healthy days). Not statistically significant between groups using two tailed Student's t -test ($P > 0.5$). (D) Among the cats that were not diagnosed with URIs or conjunctivitis, the number of days (mean \pm SD) they stayed in the shelter prior to outcome (healthy days). Not statistically significant between groups using two tailed Student's t -test ($P > 0.5$).

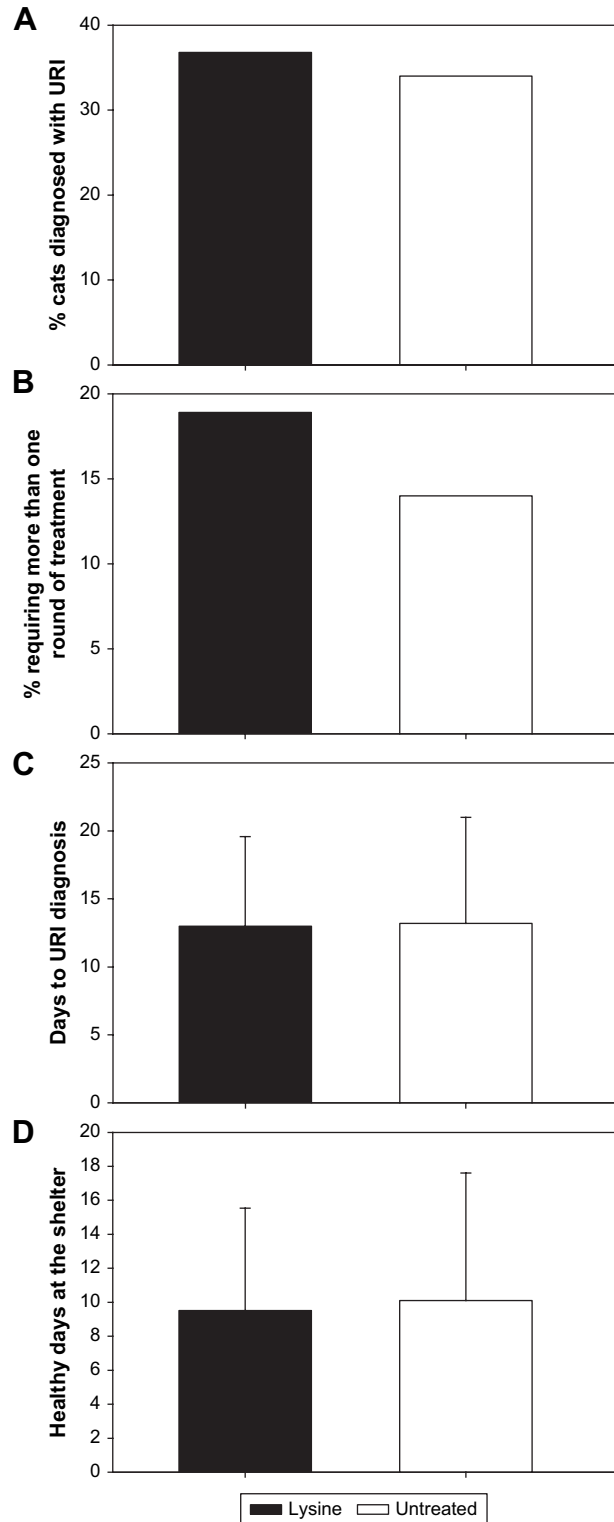


Fig 1. Clinical findings from lysine supplementation. Lysine treated group $n = 144$; untreated group $n = 147$. (A) Percentage of cats diagnosed with URI or conjunctivitis. Not significantly different between groups using the χ^2 test ($P > 0.5$). (B) Percentage of those cats treated for URI who required more than one round of standard treatment for their signs to resolve. Not statistically different between groups

the cat received its first dose of lysine. Some cats were reluctant to eat the canned food, which is a limitation of the canned food method of administration, but the number of cats who did not choose to eat their canned food every day was small and not different between the two treatment groups. This limitation may affect the overall outcome but there is no satisfactory way to overcome the reluctance to eat without further stressing the cat. In actuality, this reluctance to eat may be an indication of stress and demonstrates even more the stressful situation cats surrendered to animal shelters potentially endure.

We chose to give the lysine once daily to accurately reflect the most likely shelter paradigm due to staffing and financial constraints. A significant decrease in viral shedding was demonstrated among a small group of adult cats receiving 400 mg lysine once daily (Maggs et al 2003), so the dose chosen was reasonable. Although one study demonstrated that high levels of lysine supplementation did not cause arginine antagonism (Fascetti et al 2004), we also wished to be careful in light of cats' sensitivity to arginine deficiency (Morris and Rogers 1978), as we were not able to determine plasma concentrations of lysine and arginine in this study.

Although we do not know what percentage of URI is directly related to FHV infection in our shelter, historic data determined at other animal shelters would suggest that a large percentage of the cats residing in the shelter are actively shedding virus. Therefore, given the large sample size, we would expect to see an effect if lysine is effective in preventing URI in a shelter setting. It is possible that during this study the upper respiratory disease was caused by other pathogens such as feline calicivirus (FCV) or bordetella, which could explain a lack of efficacy of lysine in prevention of the illness. However, no oral ulcers, limping, or excessive coughing were seen in our ill population. Although this does not rule out the possibility of an FCV or bordetella outbreak, it does make it less likely to have played a major role. It may be possible that the stress of residing in a shelter is too great to be overcome by a nutritional supplement, but that lysine would be effective in a lower stress environment such as a private home.

Stress reduction is a critical step in ensuring the health of cats residing in shelters, as stress has been shown to contribute to virus reactivation and illness (Gaskell and Povey 1977). Overcrowding, proximity to dogs, small cages, and lack of enrichment can stress cats. Equally

important to stress reduction is the implementation of proper sanitation procedures to prevent the spread of illness through improperly cleaned cages and fomite transmission. Staff should be trained to clean cages with proper detergents and disinfectants. Handling of cats should be closely monitored to prevent fomite transmission of infectious disease.

Lysine supplementation is commonly used in shelters empirically as a method to suppress or prevent URI, with the assumption that a large percentage of URI is caused by FHV. Although these findings are specific to one shelter and one set of circumstances, these findings suggest that lysine supplementation may not be effective in preventing URI in a stressful shelter situation. Time, staffing, and money may be better spent in working toward developing infection control practices, limiting fomite transmission, and general stress reduction.

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