Efficacy of L-lysine in Treatment and Prevention of Feline Upper Respiratory Infection in a Traditional Shelter Setting

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Abstract

Question: Does L-lysine dietary supplementation in shelter cats reduce upper respiratory disease incidence, severity or duration?

Hypothesis: Dietary L-Lysine supplementation in shelter cats does not significantly reduce upper respiratory disease incidence.

Objectives: A literature review was conducted to identify recent research involving L-lysine in the cat. A controlled trial was conducted in a local animal shelter to determine the efficacy of dietary lysine supplementation in reducing URI incidence, severity or duration.

Background: Feline upper respiratory infection (URI) and conjunctivitis are a significant health threat in animal shelters. With a high prevalence among domestic cats, feline herpesvirus-1 (FHV-1) infection is one cause of this multi-modal disease and has been shown to be inhibited by L-lysine under certain conditions.

Methods: Upon shelter admission 32 healthy adult and juvenile cats were assigned to either the treatment (n=16) or control groups (n=16) . Over 21 days treatment cats received a once daily oral supplement of Viralys® lysine (500 mg for adults, 250 mg for kittens less than 5 months of age) in a small aliquot of canned cat food, while control group cats received canned cat food without added lysine. Cats were observed daily for URI development. Disease scoring based on clinical signs indicated severity, and disease duration was recorded. Treatment of URI was at the discretion of the shelter and included oral antibiotics. At the conclusion of 21 days, analysis of disease incidence, severity and duration between the two groups was conducted and efficacy of L-lysine evaluated, with disease management recommendations then provided to the shelter.

Results: The literature review yielded 5 articles. Analysis for quality using the American Dietetic Association's *Evidence Analysis Manual* revealed Rees et al. 2008 to be the current best evidence for L-lysine's efficacy in shelter cat populations. The authors found no effect of lysine on URI development in their shelter.

There was no statistical difference among the two groups in our lysine trial, partly owing to small sample size and unusually low disease prevalence at this shelter. The prevalence of URI ranged from 0-10%, much lower than the historic 40% observed the previous summer. During the study period the incidence rate was 0.833 incidents per 100 cat days, nearly a tenth of what it had been 13 months earlier.

Conclusion: Despite the inconclusive findings of our trial, the body of evidence is growing to support the conclusion that lysine is not effective in treating or preventing feline URI in animal shelters. The decreased disease prevalence is likely the result of improved management practices implemented in July of 2007.

Introduction

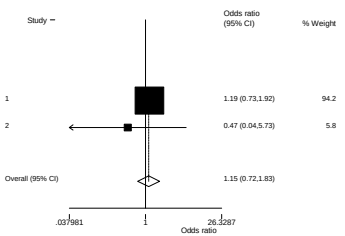
Feline upper respiratory infection (URI) is a well recognized and ubiquitous disease complex that in multi-cat environments such as animal shelters represents a significant health threat to the population. Feline herpesvius-1 (FHV-1) is one virus known to be involved in the disease.[2] FHV-1 is widespread, with up to 97% of cats showing serologic exposure evidence, and persists in a latent state within the trigeminal nerve after primary infection. Recrudescent infection and viral shedding is estimated to occur in about half of infected cats, thus providing a reservoir for FHV-1 spread to naïve cats[4,5]. Conditions associated with animal shelters promote viral reactivation resulting in acute infection, viral shedding for up to three weeks, and primary infection of susceptible cats.[3,4]

Owing to low environmental persistence and transmission mainly by direct contact or fomites, URI can be controlled where shelter management includes quarantine and isolation facilities, low cat density, ideal sanitation, good air flow, and quality care[8]. However, most shelters experience a departure from the ideal and URI outbreaks occur, with continuous infection and depopulation as possible consequences. After overcrowding, URI is the second leading cause of euthanasia in animal shelters.[2]

Adjunctive therapies for the treatment of FHV-1 infection are an appealing approach for reasons including cost, ease of administration, availability, and safety. L-lysine is known to antagonize arginine in herpesvirus protein synthesis and is used to treat infections in humans and cats. Shelters are adding L-lysine to cat diets in an attempt to prevent and treat URI. A quarter (5/20) of responding Iowa shelters indicated in our July 2007 survey that they were using lysine in an attempt to control URI disease.[11] A search of the Association of Shelter Veterinarian list serve entries over the last four years revealed that 2% of the 10,000 postings related specifically to the availability, dosage, and use of L-lysine. At a range of $0.05 to $0.50 per dose, the affordability of this approach varies. Is there an evidence based clinical justification for treating URI or conjunctivitis with L-lysine in shelters?

Author	ADA score	Dependent Variables Studied	Outcome
Stiles et al. 2002	Positive	Disease score, plasma lysine and arginine, viral shedding	Plasma lysine did not antagonize arginine; lysine treatment decreased disease symptoms.
Maggs et al. 2000	Positive	Viral titer and CRFK cell growth	Lysine inhibits FHV growth in low-arginine media. Arginine promotes FHV replication.
Maggs et al. 2003	Positive	Disease score, plasma lysine and arginine, viral shedding	Lysine treatment decreased viral shedding. No adverse arginine effects.
Maggs et al. 2007	Positive	Lysine intake, disease score, plasma lysine and arginine, viral shedding	Inconclusive; higher disease score and viral shedding in the treatment group, plasma arginine declined in both groups.
Rees et al. 2008	Positive	Disease incidence, duration to onset of disease	Lysine was found to have no effect.

Table 1 Summary of articles



Graph 1 Comparison of URI incidence between groups in Rees et al. 2008 (1) and our research (2), showing the odds ratio of the effect of lysine.

Materials and Methods

A search of PubMed, Commonwealth Agricultural Bureau (CAB), Web of Science and Veterinary Information Network (VIN) using the search terms "lysine," "FHV", "feline" and "herpes" was conducted. Upon screening for primary research and relevance selected articles were read and analyzed for quality using the American Dietetic Association's *Evidence Analysis Manual*, which considers study design, controls, blinding, relevance, methodology, statistics and research funding. Through this evaluation a Quality Rating of positive, neutral, or negative was assigned.

A controlled trial conducted in a local animal shelter evaluated the efficacy of L-lysine in treating or preventing feline URI. Upon admission to the shelter, cats were given an identification number and randomly assigned to either a treatment or control group (n=16 per group). Over 21 days treatment cats received a once daily oral supplement of Viralys® lysine (Vet Solutions, Fort Worth,TX) in the amount of 500 mg for adults and 250 mg for kittens less than 5 months of age. Lysine was mixed into a small aliquot of canned food, while controls received only canned food. URI observation and disease scoring based on clinical signs was performed daily, and disease duration recorded. Treatment was at the discretion of the shelter and according to their standardized protocol, including oral antibiotics such as enrofloxacin. PCR assay for feline URI pathogens was performed on 4 cats (2 with clinical signs of illness) and submitted to IDEXX. Incidence rate among the study population was calculated as total new URI cases/total cat days at risk. Cat days at risk were calculated as average daily population X 21 days. Statistical analysis was not considered valid due to the low power of the study population.

		URI Disease	
		Yes	No
Lysine	Yes	1	15
	No	2	14

Table 2 Disease incidence among shelter cats included in the lysine trial

Results

Table 1 demonstrates the Quality Ratings and key features of each study. All received positive ADA scores and were randomized controlled trials. Lysine was found to inhibit FHV-1 growth in vitro only with low-arginine media[6]. Lysine treatment decreased disease severity[10] and viral shedding[7] in 2 studies, while increased disease severity and incidence were found in another study[9] where group-housed and group-fed cats with enzootic URI were supplemented with dietary lysine.

Rees et al. 2008 is the first published lysine study conducted in an animal shelter. The sample size of 291 cats and the study duration of 3 months lends confidence to the authors' findings that lysine had no effect on URI incidence or duration to disease onset. A treatment group (n=144) of shelter cats received daily dietary lysine supplementation beginning at shelter admission, while control group cats received the regular shelter diet. Small sample size (n=8, n=14) was present in all but Maggs et al. 2007 and Rees et al. 2008.

Table 2 shows disease incidence over our 21 day study period, with 1 treatment cat and 2 control group cats developing URI. The mean disease score was 1 for the treatment group and 3 for the control group. These differences were not deemed significant due to the low statistical power of the small sample size. The average duration to disease onset and disease duration was 7 days for all groups. Being an open population the average daily study population was 17.1 cats, and there were 360 total cat days at risk. The incidence rate for URI was 0.833 incidents per 100 cat days. This was significantly different from the incident rate for the same time period in 2007, which was nearly twice greater at 1.52 incidents per 100 cat days.

Just one month previously at the beginning of the 2007 study the incidence rate was 8.17 incidents per 100 cat days.

Graph 1 shows the effect of lysine treatment on URI incidence for our study (2) and Rees et al. 2008 (1) in terms of odds ratio. PCR test results are pending.

Conclusions

Positive ADA scores reflect sound research, but small sample size and lack of researcher blinding are potential sources of error. *In vitro* studies support L-lysine's inhibition of FHV replication but do not represent an *in vivo* environment. SPF cats in laboratory environments eliminate some confounding variables. Conflicting results among the studies may represent a divergence from more uniform artificial populations to the more realistic shelter environment. Rees et al. 2008 presents the current best evidence regarding efficacy of L-lysine in a multi-cat environment with unknown health and disease history, such as that encountered in shelters. Their finding that lysine had no effect on URI development or duration to onset of disease is credible given the unique conditions present in shelters. The numerous health challenges shelter cats face include overcrowding, exposure to multiple cats with varied disease status, environmental stressors such as barking dogs and potentially detrimental cleaning practices. These disease risks, along with a potentially high and diverse pathogen load in the environment would presumably overwhelm any potential benefit lysine may afford.

The apparent differences between groups in our study (twice greater disease incidence and thrice the disease severity among the control group) were insignificant given the small sample size. In addition, this shelter's disease status presented a further hindrance. At their current URI prevalence of 0-10% the sample size needed to detect a statistical difference in groups would be impossibly large. To observe a 50% change in URI it was determined that the sample size must be 443 cats per group. Assuming a 35% disease prevalence, and to observe a 15% change in disease with a power of 80% each group would need to have at least 138 cats.

An odds ratio greater than 1.0 indicates an increased likelihood of the lysine group developing disease. However, the confidence interval of 0.72 – 1.83 includes 1.0 and thus relates weakness in the odds ratio. There was likely no effect between the treatment and control groups since 1.0 represents this neutrality.

Having observed this shelter for the past two summers some inferences regarding the dramatic and continued reduction in disease may be ventured. To now have incidence rate a tenth of what it was 13 months prior is likely the result of changes in management practices implemented beginning in July of 2007. Admissions began to be restricted in an attempt to control population, which has reduced overcrowding. Improved training of personnel has effected cleaning methods in which fomite transmission is less possible and cats are less stressed. Reorganization of their volunteer program may also be a factor in reducing transmission and risk, whereby untrained individuals are no longer given access to the shelter cats. Our introduction of a standardized treatment protocol based on clinical signs in June 2008 is followed at the discretion of the shelter, and while not always strictly adhered to, may still be employed adequately enough as to be of benefit to the population.

The findings of our lysine trial do not allow a definitive conclusion regarding the efficacy of L-lysine in preventing or treating feline URI in shelters. However, taken along with the findings of Rees et al. 2008 and our survey results from 20 Iowa shelters regarding their use of lysine and its lack of effect on disease[11] we conclude that the body of evidence for lysine's inefficacy in controlling URI in animal shelters is growing.

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