Feline upper respiratory tract infections – current treatment strategies

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Introduction
Feline upper respiratory tract disease (FURTD) is also known as feline upper respiratory infection or “cat flu”. FURTD is caused by several agents and a common problem in kittens and young cats, especially in multi-cat households, e.g. animal shelters. Upper respiratory infections in cats are one of the leading causes of euthanasia in these environments. Transmission is facilitated by close contact between cats.

Which pathogens are involved in FURTD?
In FURTD, several primary pathogens can be involved. Most important in this context are feline herpesvirus 1 (FHV-1), feline calicivirus (FCV), Chlamydia (C.) felis, and Bordetella (B.) bronchiseptica. In 80% of cases of FURTD, one or both of the 2 viruses, FHV-1 and FCV, are involved. Infection can occur despite vaccination, and clinical signs can vary slightly depending on which pathogen is involved.

What strategy is recommended for symptomatic treatment in FURTD?
Management of these infections can be fairly difficult. Investigating the etiology is therefore recommended to enable appropriate treatment. Regardless of the causal organism, fluid therapy is important when treating a cat with FURTD. Cats often need encouragement to eat, and food can be warmed to enhance the smell and therefore to compensate for the cat’s inability to smell due to nasal congestion. If oral lesions are present, blending or pureeing food can decrease the pain associated with eating. Antipyretic and analgesic drugs can help to reduce fever and relieve pain associated with mucosal lesions. Broad-spectrum antibiotics should be administered to guard against secondary bacterial infections.

Which drugs are effective against FHV-1?
FHV-1 causes approximately 50% of the cases of upper respiratory disease in cats worldwide. FHV-1 has an affinity to epithelial conjunctival cells and the upper respiratory tract. It replicates in neurons, where the virus establishes life-long latency. FHV-1 is susceptible to most commercially available disinfectants, antiseptics, and detergents. In the environment, the virus remains infective for about 1 day. At 37°C, it is inactivated within about 3 hours.

In vitro studies have demonstrated activity of several common antiviral compounds against herpesviruses. However, field data are sparse for many agents. Several of these agents seem to be effective when used topically for ocular manifestations of FHV-1 infection, but adverse side effects occur when used systemically.

Cidofovir: The drug of choice for local ocular treatment is cidofovir (1 drop 0.5% cidofovir q 12 h) because it only needs to be applied q 12 h, in contrast to all other local antivirals.

Few drugs can be given systemically.
Acyclovir: Acyclovir, the well-known nucleoside analog found to be highly effective against human herpesvirus, is not potent against FHV-1.

Valacyclovir: Valacyclovir, a prodrug for acyclovir that has an identical antiviral spectrum but superior oral bioavailability, has not only produced disappointing results, but has been shown to be highly toxic. In one placebo-controlled study, cats with FHV-1 infection treated with valacyclovir orally developed renal tubular epithelial and hepatocellular necrosis and severe bone marrow suppression.

Famcyclovir: A very promising new drug is famcyclovir (40 mg/kg q 8 h until improvement of clinical signs). This drug showed very good efficacy in several case series without development of any adverse effect even if used long term.

Human interferon-α: Interferons have also been used in treatment of FHV-1 infection. Human interferon-α is commonly applied topically for treatment of FHV-1-induced ocular changes. Its topical use is preferred over systemic use because an antiviral effect can develop directly at the application site. Frequent application is important, and combination therapy with acyclovir has been shown to produce a synergistic effect against FHV-1. In a placebo-controlled study, human interferon-α (10^8 IU/kg SC q 12 h for 2 consecutive days) was effective in reducing clinical signs over a 14-day period.

Feline interferon-ω: In vitro studies on feline interferon-ω suggest that it might be more effective than human interferon-α for treating FHV-1-infected cell lines, but one placebo-controlled double-blinded study in naturally infected cats study demonstrated no efficacy.

L-lysine: Another agent used against FHV-1 is L-lysine, an amino acid. L-Lysine acts by reducing viral replication through antagonizing arginine, which is present in large quantities in the capsid coat surrounding the DNA of FHV-1. In vitro studies have shown that L-lysine effectively inhibits FHV-1 replication. In experimental studies, oral administration of L-lysine resulted in less severe manifestation of FHV-1-related conjunctivitis when cats were treated soon after infection. Also, the onset of clinical signs of infection being
was delayed in cats receiving L-lysine. L-lysine also prevented recurrence of clinical signs in latently FHV-1-infected cats after a stressful situation. However, in studies in which L-lysine was given as a component of commercial food to shelter cats in a high exposure environment, no efficacy was demonstrated. Thus, L-lysine might be beneficial in cats with FHV infection but should be used as early as possible after infection is established. It also can be recommended as long-term treatment in cats with recurring clinical signs of FHV-1 infection to prevent reactivation of latent infection. However, a recently published meta-analysis on L-lysine did conclude that L-lysine is effective in cats. The current recommendation is to administer L-lysine as a bolus of 500 mg PO q 12 h mixed in small amounts of moist food.

Immunoglobulins: Commercially available specific immunoglobulins are also used to treat cats with FHV-1 infection. In one placebo-controlled double-blinded study, treatment with specific immunoglobulins lead to a faster improvement of clinical signs in cats with natural FHV-1 and/or FCV infection. There was a significant difference in improvement of clinical signs on day 3 of treatment between immunoglobulin-treated cats and cats that had received placebo. On day 7, however, cats in both groups had improved equally and showed almost no more clinical signs.

Which drugs are effective against FCV?
FCV is a highly contagious pathogen with widespread distribution in the feline population. FCV has a small single-stranded RNA that enables the virus to evolve quickly. The genome is surrounded by multiple copies of the immunodominant capsid protein. Between FCV isolates, antigenic differences can be observed that impair vaccine cross-reactivity. FCV can stay infectious in the environment for about 3 weeks. Few antiviral compounds are available to treat RNA virus infections, like FCV infection.

Ribavirin: Ribavirin is one of the few agents that have been shown to inhibit FCV replication in vitro, but is very toxic to cats when used systemically.

Feline interferon-ω: Feline interferon-ω also inhibits FCV replication in vitro, but to a lesser extent than other feline viruses. In one placebo-controlled double-blind field study, administrations of feline interferon-ω (one subcutaneous injection followed by oral administration) was not effective.

Immunoglobulins: Commercially available specific immunoglobulins have also been used to treat cats with FCV infection. In one placebo-controlled double-blinded study treatment with specific immunoglobulins lead to a faster improvement of clinical signs in cats with natural FHV-1 and/or FCV infection. There was a significant difference in improvement of clinical signs on day 3 of treatment between the immunoglobulin-treated cats and those that had received placebo. On day day 7, however, cats in both groups had improved equally and showed almost no more clinical signs.

Which drugs are effective against Chlamydia felis?
C. felis is a gram-negative rod-shaped coccoid bacterium that is unable to replicate autonomously. The organism attaches to sialic acid receptors of host cells, enabling it to enter the cytoplasm of the host’s epithelial cells. Eventually the epithelial cells rupture, liberating infectious elementary bodies that will infect other epithelial cells. Some C. felis isolates contain plasmids, which can play a role in host colonization and pathogenicity.

Doxycycline: C. felis can be effectively treated with doxycycline. However, doxycycline can be associated with various adverse effects. Doxycycline can cause esophageal strictures, increased liver enzyme activity, as well as anorexia and vomiting.

Enrofloxacin: Enrofloxacin has been shown to be almost as effective, but its use can cause retinal degeneration in cats.

Pradofloxacin: A safe alternative is available in form of the fluoroquinolone pradofloxacin which does not cause these retinal changes. In a placebo-controlled double-blind study, efficacy of pradofloxacin was compared to that of doxycycline in 39 cats with clinical signs of FURTD due to C. felis infection. Cats in both groups improved clinically during the 6 weeks of treatment, and there was no significant difference in the improvement of clinical signs or in the general health status. However, doxycycline was significantly more effective in completely eliminating the organism (no cats receiving doxycycline were shedding C. felis after 6 weeks, while 4 cats receiving pradofloxacin were still shedding).

Which drugs are effective against Bordetella bronchiseptica?
B. bronchiseptica is an aerobic, gram-negative proteobacterium (coccobacillus) that is widespread in the cat population. Its role as a primary pathogen in cats is not fully understood, but respiratory disease can be experimentally induced in specific pathogen-free cats after aerosol or intranasal challenge with B. bronchiseptica. Most of the B. bronchiseptica isolates were originally associated with cases of bronchopneumonia in laboratory cats; however, the agent was also detected as a primary pathogenic agent in diseased cats from breeding colonies and private households.

Doxycycline: Doxycycline is the treatment of choice for B. bronchiseptica infection (5 mg/kg q 12 h for three weeks). Studies suggest, however, that doxycycline might not be able to completely eliminate the organism during later stages of infection.
Suggested Reading References


Other references can be provided by the author on request.