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Three-year duration of immunity for feline herpesvirus and calicivirus evaluated in a controlled vaccination-challenge laboratory trial

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ABSTRACT

Feline vaccination guidelines recommend less frequent boosters for the core vaccines (rhinotracheitis, calicivirosis and infectious panleucopenia). Most guidelines recommend boosters at 3-yearly intervals after a basic vaccination including primary vaccination and revaccination one year later.

The objective of this study was to assess the duration of immunity induced by PUREVAX® RCPCh FeLV, a non-adjuvanted vaccine against feline rhinotracheitis, calicivirosis, infectious panleucopenia, chlamydiosis and leukemia. After primary vaccination followed by revaccination one year later with a vaccine formulated at minimum dose, the cats were kept in a confined environment and challenged 3 years later with a virulent heterologous strain of feline calicivirus (FCV) and subsequently a virulent strain of feline herpesvirus (FHV). Clinical signs and viral excretion were recorded for two weeks after each viral inoculation. Contemporary unvaccinated cats and new animals added at the time of challenge were used as controls.

The vaccination regimen induced a stable and long-lasting humoral response. Vaccination resulted in a significant reduction in the severity of the disease after FHV challenge and in the frequency of cats showing a severe calicivirosis (defined as a combination of systemic clinical symptoms and oronasal ulcers). As opposed to the significant reduction of excretion observed a few weeks after primo-vaccination or even one year after vaccination for FCV, viral shedding was not reduced 3 years after revaccination.

This study showed that primary vaccination and revaccination one year later with PUREVAX® RCPCh FeLV was able to induce 3-year duration of immunity against FCV and FHV. The results and conclusion of this study are consistent with current vaccination guidelines and will allow the veterinarian to adapt the vaccination regimen to the way of life of the cat.

1. Introduction

Feline herpesvirus 1 (FHV) and feline calicivirus (FCV) are major pathogens of the cat highly prevalent with a worldwide distribution. FHV is responsible for upper-respiratory tract disease (URTD), which can be severe and

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even life-threatening in case of bacterial super-infection. FCV infection is associated with oral ulcerations and occasionally with severe systemic disease. Along with feline parvovirus (FPV), FHV and FCV are considered core vaccine components that all cats should receive.

In the last decade, annual revaccination of pets has been challenged, especially in cats, where injection-site sarcomas raised the question of the benefit/risk of annual revaccination. Three international panels, the American Association of Feline Practitioners (AAFP) Feline Vaccine Advisory Panel, the World Small Animal Veterinary Association Vaccine Guidelines Group (WSAVA VGG) and the European Advisory Board on Cat Diseases (ABCD) provided veterinarians with guidelines on the use of feline vaccines. Despite some differences, the three groups recommend boosters for the core vaccines at intervals of more than one year. Primary-vaccination with two injections 3–4 weeks apart followed by revaccination 1 year later is the current recommendation for FHV and FCV vaccination. Subsequent boosters should be given every 3 years except in high risk situations (Day et al., 2007; Radford et al., 2009; Scherk et al., 2013; Thiry et al., 2009; Schultz, 2006).

The duration of immunity (DOI) can be demonstrated by following some immune parameters but in the absence of valid surrogate marker, infectious challenge is the most unambiguous means to assess DOI. Only a few long-term DOI studies for FHV and FCV based on challenge data have been published (Gore et al., 2006; Lappin et al., 2002; Scott and Geissinger, 1999) suggesting that attenuated or adjuvanted killed vaccines could induce a long DOI. Unlike FPV vaccines which induce a long-lasting complete protection, FHV and FCV vaccines reduce clinical signs but do not provide complete protection, and vaccine-induced protection may decrease with time requiring regular boosters (Poulet, 2007).

The objective of this study was to evaluate the 3-year DOI of a feline non-adjuvanted multi-valent vaccine (PUREVAX®[1] RCPCh FeLV, Merial) in cats after the recommended basic immunization regimen including primary vaccination followed by revaccination one year later. This vaccine was previously shown to induce 3-year DOI against FPV and 1-year DOI against FHV (reduction of clinical signs) and FCV (reduction of both clinical signs and viral shedding) (PUREVAX® RCPCh FeLV: European public assessment report, http://www.emea.europa.eu/ema/index.jsp).

2. Materials and methods

2.1. Vaccine

A lyophilisate containing a non-adjuvanted inactivated FCV antigen (FCV G1 and 431 strains) and attenuated strains of FHV (F2 strain), *Chlamydophila felis* and infectious panleucopenia virus was reconstituted with 1 ml of recombinant canarypox-FeLV. The vaccine lyophilisate was formulated at a low dose corresponding to the minimum protective dose for each antigen. Apart from the lower antigen content, the vaccine batch used in this study was representative of PUREVAX® RCPCh FeLV.

2.2. Cats

Twenty specific pathogen-free (SPF) cats (Hill Grove strain, Charles River Laboratories, France) aged between 10 and 11 weeks were assigned to a treatment group (15 cats) and a control group (5 cats). For logistical reasons, half of the control group was enrolled at the beginning of the study and five additional SPF cats were included and assigned to the control group four months before the challenge. They were between 2 and 4 year-old at the time of challenges.

Groups were housed separately to avoid potential contamination of the controls by the FHV vaccine strain. Animals were confirmed to be seronegative for FCV and FHV at the beginning of the study. All animals were kept in a confined environment (Animal Biosafety Level 2). Cats were fed with specific food for cats and water was freely available. Veterinary care and treatment for non-study related health issues were provided throughout the study. This animal experiment and the associated procedures were reviewed and approved by the Merial Ethical Committee.

2.3. Immunization

Cats in the control group were not immunized and served as controls for the challenge. They also served as sentinels to show the absence of FHV or FCV contamination during the immunization phase. Cats in the treatment group were vaccinated twice subcutaneously at 28 day-interval (Day 0 and Day 28) with 1-ml dose of vaccine. A booster injection was given by subcutaneous route one year later (Day 392).

One vaccinated cat was found dead approximately one year after the annual booster injection. Necropsy showed that the sudden death was likely related to a cardiac and/or a renal failure. This cat was excluded from the study.

2.4. ELISA antibody assay

All cats were periodically tested for FCV and FHV antibodies during the immunization phase. Blood samples were collected from the jugular vein on dry tubes on Day 0, 28, 56, 84, 175, 266, 357, 392, 420 and then at 3 month intervals until challenge. Blood was also collected after challenge.

Sera were stored at −20 °C until testing for FCV and FHV antibodies by a blocking ELISA test. Microplates were coated with a capture antibody for 18 h at 5 °C, then rinsed. In separate dilution plates, the sera under test and positive and negative controls were incubated with a feline calicivirus p66 antigen or a purified feline herpesvirus antigen for 18 h at 5 °C. The serum/antigen mixture was then transferred to the ELISA plate coated with the capture antibody. Plates were then incubated for 3 h at 37 °C and then rinsed. A broadly cross-reactive anti-feline calicivirus p66 or anti-feline herpesvirus gB monoclonal antibody,

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