The Use of Cephalexin in Canines and Felines

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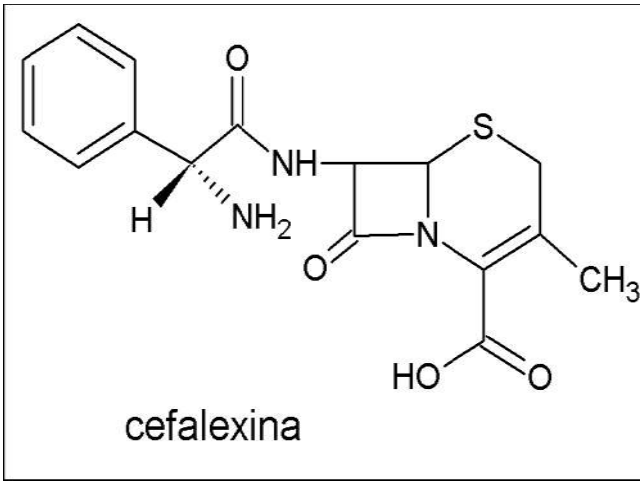
Cephalosporins are a group of antibiotics that derive from a substance produced by the fungus *Cephalosporium acremonium*. Similarly to penicillins, cephalosporins are beta-lactam bactericidal antibiotics that inhibit bacterial cell wall synthesis, thus inducing osmotic fragility. These antibiotics are generally more effective than penicillins in penetrating the external wall of Gram- bacteria and less susceptible to deactivation on the part of bacterial beta-lactamase (Greene 2006). Cephalosporins have been divided into three generations, or classes, namely chronological order of discovery, chemical structure and therapeutic activity. First generation cephalosporins are particularly active against Gram+ bacteria with the exception of some strains of resistant staphylococci. They are also active against *Escherichia*, *Klebsiella* and *Proteus Mirabilis*. Their activity against sensitive aerobes and facultative anaerobes is higher than that of Penicillin G.

Cephalosporins are relatively effective against anaerobes such as *Bacteroides*. First generation cephalosporins, unlike second and third generation ones, can be administered orally and/or parenterally. They have a variable protein bond and are extensively distributed in the pleura, pericardium, peritoneum, synovial fluids and in the major part of soft tissues. They penetrate the haematoencephalic barrier only in cases of meningitis. Most of them are excreted unmodified in urine (Greene 2006).



Cephalexin in canines and felines

Cephalexin is a first generation bactericidal agent for oral administration. It has very high efficacy against many Gram+ bacteria including *Staphylococcus spp*., a beta-lactamase-producer. It is rapidly absorbed after oral administration in dogs, and is eliminated unmodified in urine through glomerular filtration and tubular secretion (Prescott, 2006). Few side-effects have been reported for first generation cephalosporins; however, these antibiotics can occasionally cause vomiting or

diarrhoea after administration to the cat and the dog (Frank and Kunkl, 1993; Mason and Kietzmann *et al*., 1992; Vaden and Riviere, 2001).
Cephalexin is successfully delivered in cases of bacterial infections in the urinary and respiratory tracts, localised infections in soft tissues and during bacterial infections of the skin (e.g. superficial and deep pyoderma). The optimal dosage has not been determined, though good clinical efficacy has been proven with oral doses in the range of 15 - 35 mg/kg BID (Frank and Kunkle, 1993; Carli *et al*., 1999; Mason and Kietzmann, 1999; Scott *et al*., 2001).

The pharmacokinetics of orally delivered cephalexin have been extensively studied in the dog (Crosse and Burt, 1984; Silley *et al*. 1988; Wackowiez *et al*. 1997; Campbell and Rosin, 1998; Carli *et al*. 1999; Prados *et al*. 2007). Administration of cephalexin is recommended on a full stomach because food does not influence absorption of the drug (Campbell and Rosin, 1998) and it reduces the incidence of gastroenteric side-effects (nausea, vomiting, diarrhoea). The recommended dose for infections caused by Gram- bacteria such as *E. Coli* is 30-40 mg/kg BID.

Lower doses can be administered for urinary tract infections in which cephalexin can reach high concentrations (Ling and Ruby, 1983). In fact, cephalexin has been successfully delivered at a dose of 25 mg/kg BID in urinary tract infections caused by *Klebsiella pneumoniae* in the dog (Ling and Ruby, 1983). A study conducted in canines for detailed evaluation of the pharmacokinetics of cephalexin reported that maintaining effective therapeutic concentrations against *Sarcinia lutea* requires administration of 20 mg/kg PO every 6-8 hours. (Carli *et al*., 1999)

In fact, we must recall that cephalexin, like all cephalosporins, are time-dependent antibiotics; precisely, their levels can be more effectively maintained above the M.I.C. (minimum inhibitory concentration) by increasing the frequency of administration rather than the dose.

Klebsiella spp. colonies in agar-blood medium
(urine culture test of sample collected from a dog)

Epidermal collarettes in the sternal region of a male, hypothyroid, crossbred dog aged 7 years: superficial pyoderma.

Cephalexin in dermatology
Cephalexin is deemed as first choice antibiotic for the treatment of superficial and deep pyoderma in the dog (Frank and Kunkle 1993). It is also indicated for bacterial skin infections in the cat (Guaguére 1998). The recommended dose is 15-30 mg/kg PO BID on a full stomach for a minimum period of 3-4 weeks for superficial pyoderma, and 6-8 weeks for deep pyoderma (Mason and Keitzmann 1999, Scott *et al*., 2001); and, however, for a minimum period of 7-10 days after clearance of skin lesions (papules, pustules, epidermal collarettes) in cases of superficial pyoderma, with double this minimum period for deep pyoderma. Pathogens involved in cases of recurrent pyoderma and deep pyoderma are probably multi –resistant bacteria (MRSP: methicillin-resistant *Staphylococcus pseudointermedius* and MRSA: methicillin-resistant *Staphylococcus aureus*); hence the recommendation to always run a culture test along with the antibiotic sensitivity test to make a targeted choice of antibiotic.

A recent study compared two protocols for administration of cephalexin to cases of superficial pyoderma in the dog: one protocol administered cephalexin 30 mg/kg PO SID and the other administered 15 mg/kg BID (Toma *et al.*, 2008). Clinical efficacy was satisfactory and similar in both protocols probably due to the fact that the substance has a post-antibiotic effect against the various Gram+ bacterial cocci (Odenholt-Tornqvist *et al*. 1991), despite its half-life of about 6 hours (PAE *post-antibiotic effect*).

Cysts, fistulae and serohaematic exudate in a female boxer dog aged 3 years presenting atopic dermatitis: deep pyoderma.

Pustules and epidermal collarettes on the medial region of the thigh in a crossbred male dog aged 2 years presenting atopic dermatitis: superficial pyoderma.

Furthermore, cephalexin presents optimal distribution in extracellular fluids, where it later builds up (Papich, 1984; Mason and Keitzmann, 1999), and the half-life of the substance in that district is four-fold its half-life in plasma (Cardoniga *et al*., 1979). Once daily administration of cephalexin ensures greater compliance on the part of the owner, which is crucial considering the mean duration of antibiotic therapy during pyoderma.

But we must recall that the described protocol could increase the risk of selecting multi-resistant bacterial strains (MRSP and MRSA), which is an emerging and increasingly widespread problem even in veterinary medicine. It must also be underscored that the indication is only for superficial pyoderma and not for deep pyoderma, which still requires twice daily, if not thrice daily administration of cephalexin.