MEDICAL TREATMENT OF INFECTIOUS OTITIS EXTERNA AND MEDIA CASES

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Categories : Vets

Date : March 5, 2012

Filippo De Bellis discusses the methodologies available for these conditions, such as ear flushing and using topical and systemic medicinal approaches

Summary

Otitis externa (inflammation of the external ear canal), with or without middle ear involvement, is very common in dogs and quite common in cats. Ear disease is seen in both first opinion and referral practice and, due to its frequently recurrent nature, constitutes a frustrating problem for owners and veterinarians alike. Many different factors can cause or exacerbate otitis, and recognition and correction of these is the key to successful management. Based on history and clinical presentation, management of ear diseases includes medical and surgical options. The aim of these notes is to describe the medical interventions available in the course of otitis externa and media, discussing principles of ear cleaning, ear flushing, and use of topical and systemic medications, and the issues related to ototoxicity.

Key words

ear, otitis media, skin, cleaning

ONCE an otic infection has been diagnosed, medical options include topical and systemic therapy, co-adjuvated, when appropriate, by ear cleaning.

Ear cleaning – when?

While it is commonly accepted that cleaning is not necessary in healthy ears, it is beneficial in the following conditions:

• seborrhoeic ears (Figure 1);

• hairy ears (Figure 2);

• stenotic ears (Figure 3);

• pendulous ears; and

• purulent discharge (Figure 4).

Ear cleaning is an important part of any treatment regimen, as it can remove debris and pus, and permit complete diagnostic evaluation of the ear canal and tympanic membrane.

The cleaning fluids most commonly contain:

• cerumenolytics, surfactants and foaming agents, such as sodium docusate;

• astringents or drying agents, such as isopropyl alcohol; and

• antimicrobial agents, such as parachlorometaxylenol (PCMX).

In one study (Swinney et al, 2008), the antimicrobial efficacy of different ear cleaners against *Staphylococcus intermedius*, *Pseudomonas aeruginosa* and *Malassezia pachydermatis* was evaluated. Antimicrobial activity appeared to be associated with the presence of isopropyl alcohol, PCMX and a low pH. The owners can perform manual cleansing at home, but it is important to instruct them on how to perform the cleaning and how often to use the different preparations.

Although not normally recommended to be used more than every 48 hours, in a study (Cole et al, 2003) one cleaner used up to twice daily caused no adverse effects.

Manual cleansing doesn’t remove tightly adherent debris or material present in the deep portion of the ear canal and, therefore, is best used as routine cleansing at home once ear flushing has been performed.

Ear flushing

Ear flushing is indicated when the entire external ear canal and/or the middle ear need thoroughly

cleaning.

It should always be performed under general anaesthesia, with an endotracheal tube placed and cuffed to avoid the fluids running from the ear to the respiratory tract through the eustachian tube. In the presence of hyperplastic, stenotic or particularly inflamed ear canals, it is recommended to provide systemic glucocorticoid treatment (0.5mg/kg to 1.0mg/kg once daily) two to three weeks prior to the flushing. Ear flushing is best performed using a videootoscope or, if unavailable, with a urinary catheter or a feeding tube connected to a syringe and fluids (sterile saline), preferably through a three-way tap.

Before ear flushing is performed, some cases may require the use of an ear cleansing solution to emulsify and remove debris.

If the eardrum cannot be visualised, care should be used as ear cleaners are not licensed for applications in the middle ear, and are all potentially ototoxic.

Myringotomy

Iatrogenic rupture of the tympanic membrane is indicated when otitis media is suspected and/or confirmed by diagnostic imaging techniques, to take samples for cytology and culture from the tympanic bulla and to allow flushing of the middle-ear cavities.

It should be performed under general anaesthesia and direct visualisation after lavage of the external ear when the canal is dry. The preferred method used by the author is using a six French urinary catheter cut obliquely to 60° and attached to a 2ml syringe containing sterile saline solution. The catheter is advanced through the ventral and posterior quadrant of the membrane, with subsequent aspiration of the fluids. An aliquot can be used for direct cytological examination, and the remaining for culture.

Topical therapy

In the majority of infectious otitis externa cases, topical therapy alone is sufficient.

Antimicrobial agents can rarely reach, systemically, therapeutic concentrations in the skin of ear canal and topical therapy, chosen empirically based on otic cytology and otoscopic examination, represents an appropriate choice. Antibiotic sensitivity data reflect the serum levels needed systemically, and it is less useful with topical drugs, where concentrations 100 to 1,000 times superior to the minimum inhibitory concentration (MIC) may be reached. Topical therapy is usually characterised by high efficacy and, with regard to the antimicrobial agents, no systemic side effects in the presence of an intact tympanic membrane.

Ingredients of topical antibacterials

• Fusidic acid

– Bacteriostatic.

– Effective against grampositive cocci.

– Mechanism of action: interference with bacterial proteins synthesis.

• Aminoglycosides

– Bactericidal.

– Large spectrum.

– Mechanism of action: interference with bacterial proteins synthesis.

– Impaired in an acidic environment – cleansing agents should be used at least one hour prior to their use.

– Topical agents include mainly neomycin and gentamicin. Amikacin is not available in topical preparations, but injectable formulations, diluted in sterile saline, can be used topically.

• Polymyxin B

– Bactericidal.

– Effective against gram-negative bacteria.

– Mechanism of action: alteration of cytoplasmic membrane permeability.

– Ototoxic.

– Inactivated by cellular debris, thus the association with ear cleaning is important.

• Fluoroquinolones

– Bactericidal.

– Large spectrum.

– Mechanism of action: inhibition of DNA replication.

– Effective against grampositive and gramnegative bacteria.

– Topical agents, available as veterinary formulations, include marbofloxacin and orbifloxacin. Enrofloxacin injectable solution dilute in sterile saline can be used topically.

• Carboxypenicillins

– Expanded-spectrum penicillins.

– Activity against gramnegative organisms (including *Pseudomonas* species).

– Mechanism of action: penetrate the gram-negative cell membrane.

– Reconstituted ticarcillin, diluted with sterile water, is the carboxypenicillin for which topical use has been most commonly reported in treating canine *Pseudomonas otitis*.

Topical antimycotics

• Azoles

– Imidazoles (clotrimazole, miconazole, posaconazole and ketoconazole).

– Mechanism of action: inhibition of ergosterol synthesis.

• Polyenic

– Nystatin.

– Mechanism of action: binds to ergosterol causing alterations of the cellular wall permeability.

Other topical antimicrobials

• Silver sulfadiazine (SSD).

This has broad-spectrum antibacterial activity (most notably against *P aeruginosa*). Concentrations as low as 0.02 per cent have shown 100 per cent efficacy against *P aeruginosa* and *Staphylococcus* species. It is available as a cream and, although not readily miscible in water, a homogeneous emulsion can be achieved with gentle mixing.

• Tromethamine-ethylenediamine-tetraacetate (TrisEDTA). This is commonly used as either a

pre-soak or a carrier vehicle in the treatment of gram-negative infections. EDTA promotes increased permeability to extracellular solutes and increased sensitisation to antibiotics, whereas Tris serves as a buffer. Recently (Guardabassi et al, 2010), the in-vitro antimicrobial activity of a commercial ear antiseptic containing chlorhexidine (0.15 per cent) and Tris-EDTA was evaluated; according to the results, this product was active against all the pathogens most commonly involved in canine otitis.

• **Bacteriophage treatment.** One publication (Hawkins et al, 2010) reported the results of a veterinary clinical trial of a bacteriophage treatment of infection. The results show administration of this topical bacteriophage mixture leads to lysis of *P aeruginosa*in the ear without apparent toxicity.

Glucocorticoids

Glucocorticoids have antiinflammatory, antipruritic and antiproliferative properties.

They can also reduce sebaceous and ceruminous gland secretions. They can be systemically absorbed, with the adrenal gland function suppressed up to two weeks or more after administration of some glucocorticoids for more than one week.

Long-term treatment can cause cutaneous atrophy, comedones and demodicosis.

Their potency depends on:

• intrinsic potency;

• concentration; and

• vehicle.

An example of a potency scale follows.

• Hydrocortisone: one.

• Prednisolone: five.

• Triamcinolone: five.

• Dexamethasone: 25.

• Betamethasone: 25.

• Fluocinolone: 100.

According to manufacturers' data, hydrocortisone aceponate has a potency similar to dexamethasone and betamethasone.

The reader should remember that all the UK-licensed polypharmaceutical topical ear medications are not licensed to be used in absence of tympanic membrane, and owners should be made aware of the risks of using these medications when the tympanic membrane cannot be assessed.

Systemic therapy: antibiotics

As stated by Morris (1994): "Unless the ear canal epithelium has been eroded or ulcerated extensively, systemic (oral) antimicrobials are unlikely to achieve therapeutic concentrations within the fluid and waxy exudates of the external canals in which the infectious organisms are harboured."

Systemic antimicrobial treatment is indicated in cases of:

• stenosis;

• ulcerations and deep infections; and

• otitis media.

Considering the middle ear (tympanic bulla) contains a highly vascular mucous membrane lining, drugs may diffuse from the vascular compartment to the bulla space better than in the external ear canals. The choice of systemic antibiotics for treating the middle ear diseases is also indicated, as the tympanic bulla may present a problematic access to topicals. The choice should be based on culture and susceptibility testing and, results pending, empirical treatment – based on examination of cytological specimen from the bulla content – should be started.

Antibiotics recognised as being effective for treating otitis media include:

• enrofloxacin 5mg/kg to 20mg/kg once daily;

• marbofloxacin 2mg/kg to 5mg/kg once daily;

• ciprofloxacin (off label) 10mg/kg to 20mg/kg once daily;

• orbifloxacin 2.5mg/kg once daily; and

• cephalexin 20mg/kg to 30mg/kg twice daily.

In case of multiresistance:

• ceftazidime (off label) 30mg/kg four times daily;

• ticarcillin (off label) 40mg/ kg to 80mg/kg three times daily; and

• meropenem (off label) 8mg/kg twice daily.

Systemic therapy: antimycotics

The administration of systemic antimycotic agents is needed in the course of otitis media caused by *Malassezia* species or when topical therapy is not an option.

Drugs used include:

• ketoconazole (off label) 10mg/kg once daily;

• itraconazole (off label) 5mg/ kg once daily; and

• fluconazole (off label) 2.5mg/kg to 5mg/kg once daily.

Systemic therapy: glucocorticoids

Administered systemically, they can:

• reduce stenosis;

• reduce oedema;

• reduce hyperplasia;

• allow a better cleaning process; and

• allow otoscopic examination.

The initial treatment consists of doses of 0.5mg/kg to 1.0mg/ kg once daily, depending on the severity of clinical signs. Dose and frequency of administration should be reduced until discontinuation, when the medication is no longer needed.

Ear wicks

Ear wicks are made of polyvinyl alcohol (PVA) and are characterised by a hard, compact structure.

They are inserted in the ear canal under general anaesthesia and then soaked with a solution usually containing antibiotics with or without TrisEDTA and/or glucocorticoids. The expansion produces a structure that adapts to the contours of the ear canal, slowly releasing the medicaments.

In this author’s experience, ear wicks can be a useful alternative to daily topical therapy in those patients that do not tolerate administration of topical medications. It is paramount the ear canals and (in the presence of otitis media) the tympanic bullae are aseptically cleaned prior to the placement as, if the canal is not adequately fl ushed, the wick can act as a lid, thus trapping infections. Additionally, in dogs with large ear canals, they often do not expand sufficiently to fill the entire diameter of the ear canal.

Ototoxicity

An ototoxic agent can cause damage to the ear in any of its anatomical components.

Ototoxicity can usually be divided into cochlear damage with consequent deafness or vestibular damage with consequent vestibular syndrome. In both cases, the damage occurs to the inner ear. The ototoxic agent can reach the inner ear via the haematogenous route or directly through openings in the tympanic membrane. In particular, given that the middle and inner ear component can be damaged by topical medicaments, it is important that, before administrating a topical treatment, the clinician performs otoscopic examination.

• Systemic ototoxicity

Examples of molecules that cause ototoxicity after topical administration are aminoglycosides, antibiotics, furosemide, cisplatin, vinblastine and vincristine.

• Local ototoxicity

– Cleaning agents.

According to Mansfield et al (1997), the only non-ototoxic agent is squalene. With regard to chlorhexidine, recent studies have demonstrated that, if used at a 0.2 per cent or inferior concentration, it doesn’t carry a risk of ototoxicity.

– Antibiotics.

Aminoglycosides can cause cochlear damage, with the exclusion of gentamicin, which in a study (Strain et al, 1995), failed to cause damage when instilled in the middle ear of dogs for 21 days. Agents with recognised ototoxic potential are polymyxin B in guinea pigs and ticarcillin in chinchillas.

Agents with low ototoxic potential are fluoroquinolones, some cephalosporins (such as ceftazidime), the antifungal clotrimazole, miconazole, nyastin and tolnaftate, the steroids dexamethasone and fluocinolone, and TrisEDTA solution.

In pathological conditions, even the use of a simple saline solution during ear flushing may cause, although infrequently, complications. For this reason, it is always important to inform owners about potential risks of ear flushing and topical therapy.

Finally, it is paramount to highlight that the majority of the studies on ototoxicity have been performed on laboratory animals, or have been extrapolated by human studies. Despite these studies representing guidelines for the clinician, further studies on other species are needed.

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