

Best Practices in Otitis: Maximizing the Value of Topical Therapy (SA288)

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Best practices for treating otitis externa include 1) using the proper diagnostic procedures, done properly; 2) preparing the ear for topical treatments (cleaning); 3) choosing wisely to select medications that will be the most likely to resolve or clear infections or control unwanted clinical signs; 4) **administering those topical medications properly**; 5) performing some quality control, usually at recheck examinations, to ensure that your treatment has been effective; 6) switch to some maintenance therapy in patients with chronic or recurring otitis...after successful treatment...to reduce flare-ups and relapse; and 7) identify and control the underlying (i.e., primary) factors of otitis.

Once your (wise) selection of topical therapy has been made, it is important to apply/instill these medications in a manner to give them the best possible opportunity to be effective.

Apply Treatments Properly

There are four aspects of proper application:

1. Using the proper dose of medication
2. The physical application of the medication to reach the areas involved
3. The necessary frequency of treatments
4. The duration of treatment required to clear the infections

Proper Dose

When considering the necessary amount of medication to be instilled into an ear, we must consider the desired effect. It is common sense that we would like enough medication in the canal to coat the surface of the canal with the medication. This may be either grossly (visible to the naked eye) or microscopically (on a pharmacological level). The truth is, we do not know how much of medications, especially with the wide variety of commercial products, it takes to accomplish this effect. It seems logical that a proper dose reflects the use of adequate volumes of topical medications to reach or coat (macro- or microscopically) all of the surface of the ear canal.

The volume of medication applied into the ear during treatment appears to be **critical**. There is little to no data to demonstrate exactly how much medication needs to be given to coat the ear canal. Volumes recommended in this paper to achieve adequate penetration **down** the canal are based on existing literature concerning volumes of ear canals and pilot studies performed by the author.

Table 1. Commercial veterinary otic preparations

| Product | Manufacturer | Drops/mL* | Label dosing | Maximum Tx time (days)‡ |
|-----------|--------------|-----------|---------------------------------|-------------------------|
| Animax | Dechra | 49 | 3–5 drops Variable frequency | — |
| Aurizon** | Vétoquinol | 50 | 10 drops once daily | 7–14 |

| | | | | |
|--------------|----------------------|-------|---|----|
| Baytril Otic | Bayer Animal Health | 30 | <35 lb: 5–10 drops twice daily >35 lb: 10–15 drops twice daily | 14 |
| EasOtic** | Virbac Animal Health | NA*** | 1 pump daily | 5 |
| Mometamax | Merck Animal Health | 40 | <30 lb: 4 drops once daily >30 lb: 8 drops once daily | 7 |
| Otomax | Merck Animal Health | 37 | <30 lb: 4 drops twice daily >30 lb: 8 drops twice daily | 7 |
| Posatex | Merck Animal Health | 39 | <30 lb: 4 drops twice daily >30 lb: 8 drops twice daily | 7 |
| Surolan | Vetoquinol | 45 | 5 drops twice daily | 7 |
| Tresaderm | Merial | 40 | 5–15 drops twice daily | 7 |

*Determined manually by author. Estimates \pm 2 drops/mL.

** Not currently available in USA.

***One pump actually measures out to 0.7–0.8 mL (Unpublished data, JON)

‡ Label instructions

Table 2. Newer extended-activity otic preparations

| Product | Manufacturer | Active ingredients | Labeled dosing |
|----------|----------------|---|--|
| Claro | Bayer | Florfenicol, terbinafine, mometasone | Clean ears and dry. Instill one tube. |
| KetoCort | TrilogicPharma | Ketoconazole, hydrocortisone | Clean ears and dry. Instill adequate amount and repeat as necessary. |
| Osumia | Elanco | Florfenicol, terbinafine, betamethasone | Clean ears and dry. Instill one tube, massage 1–2 minutes. Repeat in one week. |

Dose (Volume) Recommendations

- Small dogs (<15 kg): 0.4–0.5 mL
- Medium dogs (15–20 kg): 0.7–0.8 mL
- Large dogs (>20 kg): 1.0 mL
- Giant breed dogs (>50 kg): 1.5 mL

Keep in mind that higher volumes of otic medication may increase the likelihood of absorption of otic medications, especially glucocorticoids. It is important to understand that there may be systemic side effects if potent glucocorticoids are used. Administration of topical commercial products in this manner is “extra-label” use of these drugs.

The integrity of the tympanic membrane is critical in determining the best treatment options for a patient with otitis. The possibility of ototoxicity is greater if the medication is instilled directly into the middle ear. The best practice is to avoid topical therapy if the tympanic membrane is torn or absent. However, based on limited data and anecdotal evidence, some topical therapies, such as vinegar: water (1:2), enrofloxacin (parenteral formulation), and Baytril Otic, appear to be safe if instilled into the middle ear. There is little clear evidence of the safety of commercial otic medications. One clinical review found that some antimicrobial agents, such as marbofloxacin and gentamicin, instilled into the middle ear did not result in hearing deficits when instilled into the middle ears of dogs with otitis media, while tobramycin and ticarcillin did lead to evidence of reduced hearing.

Systemic administration of glucocorticoids is indicated in severe cases of otitis externa, especially for patients with painful ears, which may prevent or limit the ability of the owner to instill topical medications. They are also indicated for general purposes of reducing inflammation and in patients with hyperplastic/stenotic ear canals. Dosages range from 0.5 mg/kg of prednisone (or equivalent) orally (PO) once daily for inflammation to 2.2 mg/kg PO once daily for severe hyperplastic changes. Glucocorticoids (e.g., prednisone) are generally prescribed by the author as follows (Example): 1 mg/kg/day PO for 5–7 days, then 1 mg/kg PO once daily every other day for 5 doses (10 days), then 0.5 mg/kg PO every other day for 5–7 doses. At this time, the patient will be re-examined to assess the effects of treatment and for further considerations. If glucocorticoids are still indicated, topical glucocorticoids should be effective from this point forward.

Physical Application of Topical Medications

Failure to apply sufficient quantities to penetrate and cover the entire ear canal is potentially a major cause of treatment failure. Asking an owner to count drops is unreasonable, especially considering the application device (i.e., bottle) on some products has a long tip that is designed to be placed deeper into the canal. (You can't see how many drops are applied!) Dosing syringes work well to accurately measure volumes of otic medications. Owners are easily trained to measure out the product and are then taught to apply the medications properly.

This should include a demonstration of proper application by one of the medical staff, followed by asking the owner to instill medication, **in the presence** of the Veterinarian or technician. Owners should be taught to massage ears for 15–30 seconds after instilling medications and to use proper amounts of medications. They may need to be shown how to administer medications in the ears with the dog in lateral recumbency to help deliver medications deep into the canals.

You may promote distribution of otic medicine deeper into the canal by using “positional installation,” which is administration of the medication in the “up” ear while the animal is lying on one side. (It is best to do each ear at a different time to avoid losing the advantage of gravitation effects of distribution of medications.) Massaging the ear for 15–30 seconds after instillation may also help distribute medication deeper in the canal.

Frequency of Applications

Once the medication is instilled into the canal, it may be 1) shaken out and lost, 2) absorbed, 3) bound to wax or hair to render it unavailable, or 4) evaporate. Metabolism of drugs placed in the ear (i.e., topically) is significantly different from that of drugs administered parenterally. Once-daily treatment is generally sufficient for most cases of otitis, although severe infections **may** benefit from twice-daily treatment. There are no data available to compare dosing frequencies.

Treat for a Sufficient Time

Practically speaking, the goal of our therapy is the improvement of the clinical condition of otitis: reduced swelling, erythema, pain, and restoration of function. However, for long-term success in managing ear disease, it is important to **clear** the infections. This generally requires longer treatment periods and higher doses. For most infectious problems in dermatology, we recommend treating for 1–2 weeks past clinical cure, as mentioned above. This principle also applies for topical otic therapy as well as systemic therapy of otitis. Clinical cure is demonstrated by 1) return of the ear canal to normal (or near-normal) appearance, 2) absence of infectious agents on cytology or culture, **and** 3) absence of other clinical features of otitis (i.e., inflammation) such as pruritus, head tilt, pain, etc.

As mentioned previously, folliculitis and furunculosis are actually common in chronic otitis, so an appropriate minimum time for therapy is 30 days. At that time, the patient should be reexamined and re-evaluated with appropriate diagnostics.

Adjunctive Therapy

Tromethamine (Tris) edetate disodium dehydrate (EDTA), known more commonly as Tris-EDTA solution, is commonly used as adjunctive therapy for bacterial otitis. Several commercial products (e.g., TrizEDTA Aqueous Flush-Dechra, and T8 Keto Flush-DVM) contain this solution. There is good evidence that the Triz-EDTA is highly effective for *Pseudomonas* when used

concurrently with an appropriate antimicrobial (some fluoroquinolones or aminoglycosides), silver sulfadiazine, or chlorhexidine. Tris-EDTA alone is bacteriostatic *in vitro*, but is not bactericidal, and has been shown *in vitro* to reduce the minimum inhibitory concentrations (MICs) for neomycin, gentamicin, and marbofloxacin (but not enrofloxacin or polymyxin B) in biofilm-embedded bacteria. Additional studies show that Tris-EDTA enhances antibiotic efficacy of marbofloxacin and gentamicin against multidrug-resistant *Pseudomonas in vitro*. Clinically, these products are often administered into the infected ear 15–30 minutes prior to an antibiotic; however, data suggest they may be administered concurrently. Anecdotally, Tris-EDTA appears to be safe when instilled into the middle ear, but there is no scientific evidence to support that clinical impression.

N-Acetylcysteine (NAC) is a mucolytic agent used extensively in human medicine. It has been shown to disrupt mature biofilm and reduce production of extracellular polymeric substances (EPS), the main structural component of biofilm. In addition, NAC has been shown to modulate antibiotic activity in bacteria. Alone, NAC has anti-*Pseudomonas* activity *in vitro*, with the MIC values for six isolates calculated (May 2016) to be 10.3 mg/mL. Concurrent use of NAC with an antibiotic has been studied *in vitro*, with synergy shown for some antibiotics (e.g., enrofloxacin), but antagonism (reflected by increased MICs) shown with others (fluoroquinolones, gentamicin). NAC may be used as a flushing agent during/after cleaning: 2% solution used 30 minutes prior to antibiotic infusion. Clinical trials (*in vivo* studies) have not been reported.

Glucocorticoids are present in most commercial otic products for good reasons. They will help reduce the pain associated with otitis, which will facilitate the ability to deliver medication down the ears. The anti-inflammatory properties are crucial to reduce swelling and help to “open” up the canal, which also allows medications to reach deeper into the canal. The only reason that glucocorticoids would be contraindicated in otitis would be 1) if the patient was scheduled for intradermal allergy testing in the near future, or 2) if the patient was diabetic or had some other conditions where any systemic glucocorticoid might interfere or complicate management of that disease. All topical (otic) glucocorticoids are absorbed systemically to some extent, but there is great variability with the formulation and specific steroid used. In general, hydrocortisone, hydrocortisone aceponate, and mometasone are minimally absorbed. Dexamethasone, betamethasone, and fluocinolone are more readily absorbed and may show systemic effects. Glucocorticoids with more pronounced anti-inflammatory effects (i.e., more potent) include fluocinolone, mometasone, hydrocortisone aceponate, betamethasone, dexamethasone, and triamcinolone, while hydrocortisone and prednisolone have less pronounced effects.

Summary

Choosing wisely is, of course, a key step in proper management of otitis in dogs and cats. However, even the best ear medications will result in limited success if those medications are not applied properly. The practices described above (proper doses, proper instillation, best frequency of applications, and treating for an appropriate time) will maximize the efficacy of your medications to clear an infection or control inflammation and value of your treatment.

References

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SPEAKER INFORMATION

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