SMALL MAMMALS – CLINICAL TECHNIQUES

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SUPPORTIVE CARE

Supportive care is indicated in all small mammals that are anorexic or hyporexic, which is the case in most systemically ill small mammal patients. Supportive care can be performed on an outpatient basis if the patient is stable (e.g. normothermic) or in-patient basis if the patient requires thermal support and more aggressive supportive measures.
Subcutaneous fluids are indicated for all anorexia or hyporexic patients and can be safely administered in most small mammals. However, anesthesia may be required in small species. Intravenous fluids are indicated in patients with moderate to severe dehydration, moderate hypothermia, or shock. In rabbits, intravenous catheters can be safely placed and maintained in the marginal ear veins. In ferrets, rabbits, and guinea pigs the cephalic veins can be used for intravenous catheter placement. Most ferrets will eventually attempt to remove the intravenous catheter once they feel better. Therefore, ferrets may need to be sedated if the catheter is to be maintained for longer periods. If intravenous catheters cannot be placed due to patient size or hypotension, intraosseous catheters can be placed in any vertebrate species and allow for the delivery of intravascular fluids and drugs. The proximal tibia or the proximal humerus are preferred sites for interosseous catheter placement, which is a painful procedure therefore local anesthesia at a minimum should be provided and ideally, it should be performed under general anesthesia or sedation.
Nutritional support should be provided to all anorexic or hyporexic patients, but it should be prioritized in hindgut fermenting species (rabbits, guinea pigs, chinchillas) as well as small species (rats, hamsters, etc). Several commercial nutritional support formulas are available and manufacturer instructions should be followed. In addition, appetite stimulants such as capromorelin can be used to promote voluntary food intake, if dental or other forms of intraoral disease have been ruled out.

SEDATION

Sedation is beneficial in stressed patients as well as patients in respiratory distress. Procedural sedation is used to facilitate positioning for radiographs or computed tomography, restraint for ultrasound, or minor procedures such as ear flushes or urinary catheterization. In combination with local anesthetics sedation can also be used to perform minor surgical procedures such as laceration repair. Various injectable drug protocols are used in small mammals. Midazolam, butorphanol, dexmedetomidine, ketamine, and alfaxalone are used in various combinations, based on the species, the patient's condition, and the desired depth of sedation. Completely reversible sedation protocols (i.e. dexmedetomidine-midazolam) or partially reversible protocols (dexmedetomidine-ketamine, midazolam-butorphanol) are generally preferred. While injectable

protocols have many benefits for the patient and veterinary staff, they may result in a negative impact on post-sedation food intake compared to gas anesthesia. Therefore, based on the procedure to be performed and on the species, isoflurane or sevoflurane anesthesia should also be considered, in particular in smaller rodents. In rabbits and ferrets' isoflurane-induced sedation or anesthesia without premedication is not recommended.

ANALGESIA

Research on the efficacy of analgesic drugs is largely focused on rats due to their use in many research studies. Information on analgesic drug efficacy and safety is limited for other species. Tramadol and gabapentin are not analgesic in most small mammal species and therefore their routine use is not recommended. Gabapentin has sedative effects in rabbits and can be used to reduce stress-induced negative effects in this species. Buprenorphine and hydromorphone are effective in most small mammal species, but doses vary widely, and sedation can be seen at higher doses. Lidocaine constant rate infusion is an effective analgesic in rabbits following abdominal surgery and for the treatment of small intestinal obstructions.

ANTIBIOTIC THERAPY

Antimicrobials are amongst the most common drugs routinely prescribed to rabbits and rodents by veterinarians for the treatment of prophylaxis of bacterial infections. However, rabbits, as well as guinea pigs, chinchillas, and degus, are strict herbivorous hindgut fermenting species, which differ substantially in their tolerance of oral antibiotic drug use, compared to dogs, cats, ferrets, or hedgehogs. In addition, other rodents, such as rats, hamsters, and gerbils, while omnivorous and not hindgut fermenters also are more sensitive to certain oral antibiotics and their effect on their intestinal flora.[1]

In rabbits and hindgut fermenting rodents, the cecum is the exclusive site of microbial fermentation and production of volatile fatty acids used as an energy source by these species. The physiological cecal flora consists predominately of anaerobic bacteria as well as gram-positive aerobes, in addition to low numbers of motile protozoa in some species and yeast. The normal microflora ensures optimal utilization and fermentation of ingested dietary fiber as well as prevention of infection by transient enteric pathogens, such as E. coli. Therefore, any disturbance of the normal flora in hindgut fermenting species will lead to dysbiosis with secondary consequences such as hypomotility and increased gas production both resulting in tympany, as well as abnormal fecal consistency, bacterial translocation, and potentially sepsis. A variety of factors can lead to dysbiosis, such as excessive intake of simple carbohydrates (e.g. fruits, treats), primary enteric pathogens, or the inappropriate oral administration of` certain antibiotics. This session will provide an overview on the safe and effective use of antibiotics in hindgut fermenting species to allow veterinarians to make sound treatment choices for the therapy and prophylaxis of bacterial infections.[1]

ORAL ANTIBIOTICS TO AVOID

Antibiotics that have excellent activity against anaerobic bacteria and aerobic gram-positive bacteria (which represent the majority of normal cecal flora in hindgut fermenters) should never be administered orally in these species, since they will lead to dysbiosis and associated complications including death. The acronym **PLACE** is frequently used to remember which drugs should not be used orally in rabbits, chinchillas, and guinea pigs.

- **P**enicillins (e.g. penicillin G)
- **L**incosamides (e.g. clindamycin)
- **A**moxycillin
- **C**ephalosporins (e.g. cephalexin)
- **E**rythromycin

ORAL ANTIBIOTICS THAT ARE SAFE TO USE

- Trimethoprim-sulfamethoxazole (TMS)
- Fluoroquinolones
- Azithromycin
- Metronidazole
- Doxycycline
- Chloramphenicol

Trimephoprim-sulfamethoxazole (TMS) and similar potentiated sulfonamide combinations are inexpensive and have good bactericidal efficacy against many bacterial pathogens and should be used as first-line antibiotics whenever possible in small mammals.[2] Sulfonamides have good activity against many aerobic gram-positive and gram-negative bacteria. In addition, moderate activity against anaerobic bacteria has been reported but this drug should not be used solely for confirmed or suspected anaerobic infections, but instead be combined with metronidazole. Potentiated sulfonamides are not effective against Pseudomonas, Bacteroides, or intracellular organisms. Sulfonamides are highly effective against coccidia and frequently used for this indication in small mammals.[2] Adverse effects as reported in dogs and cats (e.g. keratoconjunctivitis sicca) are not of clinical relevance in small mammals.

Fluoroquinolones (e.g. enrofloxacin) are bactericidal but have no activity against anaerobic bacteria. Therefore they need to be combined with other drugs (e.g., metronidazole) to extend activity against anaerobic bacteria, for treatment of odontogenic abscesses for example. Fluoroquinolones have excellent activity against most gram-negative and gram-positive pathogens. The empiric use of fluoroquinolones is discouraged unless no suitable alternatives are available or the patient is critically ill. Newer generation fluoroquinolones are available for veterinary use and these have an activity against anaerobic bacteria. A licensed veterinary 3rd-generation fluoroquinolone is pradofloxacin (Veraflox), which has however been shown to lead to severe appetite suppression in chinchillas and its use is not recommended in hindgut fermenters at this time.[3] Fluoroquinolones also have activity against intracellular bacteria, such as Mycoplasma spp. and Chlamydia spp.

Azithromycin is a macrolide antibiotic synthesized from erythromycin. It is bactericidal at high concentrations, which are often achieved due to the high tissue levels reached with this drug due to this drug concentrating in many cells including macrophages.[2,4] In general, macrolides are not effective against most gram-negative bacteria but are effective against many gram-positive aerobic and anaerobic bacteria, in addition to intracellular bacteria such as Mycoplasma spp. and Chlamydia spp. The use of azithromycin has been controversial due to is almost exclusive gram-positive and aerobic activity, which should theoretically result in dysbiosis, as would other antibiotics, including erythromycin another macrolide. However, azithromycin is considered safe in rabbits and hindgut-fermenting rodents and it is routinely used. It is assumed that near complete intestinal absorption occurs in the small intestine and therefore no significant amount of drug will enter the cecum leading to a low risk of dysbiosis. Azithromycin is usually dosed at 30 mg/kg PO q24h in hindgut-fermenting small mammals.

Metronidazole is the treatment of choice for anaerobic infections and is the most effective treatment against anaerobic bacteria available.[2] It is not active against aerobic bacteria but is effective against a variety of motile protozoa (e.g. Giardia, Trichomonas, etc). It is bactericidal and well tolerated in rabbits and guinea pigs at published doses even for long-term use. Chinchillas are prone to develop food intake reduction which is dose-dependent and varies between individuals.[5-6] Therefore the use of metronidazole should be avoided in chinchillas. Instead, tinidazole (20 mg/kg PO q12h) can be used in chinchillas without the risk of food intake reduction. Tinidazole has the same antimicrobial spectrum as metronidazole and is safe for long-term use in chinchillas.[7]

Doxycycline is bacteriostatic and its activity is limited to mostly gram-positive bacteria as well as intracellular bacteria (e.g. Chlamydia and Mycoplasma). It has immune-modulatory effects but its indications are limited in hindgut fermenting small mammals.

Chloramphenicol is effective against a large spectrum of both aerobic and anaerobic bacteria. However, its bacteriostatic effects and human health risks (blood dyscrasias) limit its use in small mammals and this drug should not be used unless no other suitable alternatives are available and the susceptibility of the isolated bacteria has been confirmed. The author does not recommend the routine use of chloramphenicol.

Aminoglycosides have no anaerobic activity and are therefore theoretically safe to use orally. However, since aminoglycosides do not get absorbed from the GI tract, oral use is not recommended. However, using aminoglycosides topically (e.g. eye drops, skin ointment) is safe due to the lack of anaerobic activity.

PARENTERAL ANTIBIOTIC USE

In general, all antibiotics can be administered parenterally (IV, SC, IM) in hindgut fermenters, since these drugs will not reach significant drug levels within the cecum to result in dysbiosis.

Ceftiofur crystalline free acid (CFA) is a bactericidal long-acting 3rd-generation cephalosporin, which is routinely used in rabbits, guinea pigs and chinchillas, without adverse effects. It has excellent gram-negative efficacy (but not against *Pseudomonas aerguinosa*, which is common

in chinchillas) and good anaerobic efficacy (except for *Bacteroides fragilis*). It has good activity against most gram-positive cocci.[4]

Penicillin G benzathine/procaine or Penicillin G benzathine is a long-acting drug formulation, which is currently challenging to obtain and therefore less frequently used. In addition to the availability of PK data for ceftiofur CFA, its use in rabbits and other hindgut fermenters is declining.

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