CHALLENGES IN MARINE MAMMALS MEDICATION

Lack of approved drugs and pharmacokinetic data in the literature is a major concern for marine mammal veterinarians all over the world. The daily clinical practice with these animals raises challenges in many aspects leading to an extralabel use of human and domestic animal medications, pharmaceutical compounding, use of imported pharmaceutical products and sometimes extrapolating dosages and therapeutic regimes from domestic animals with little and sometimes uncertain significant basis.

The aim of the present Formulary is to assist practitioners in the selection of the most adequate medication for marine mammal patients with the highest significant basis in order to facilitate the accuracy and efficacy of the prescribed treatments minimizing potential associated risks.

Under this perspective, we must keep some general issues in mind:

A. Routes for Administering Drugs to Marine Mammals

Basically most routes used to deliver drugs to domestic animals are potentially available for drug delivery in marine mammals. However, practical considerations based on some clinical situations and anatomical adaptations frequently limit available choices.

- Oral administration (PO): is often the preferred route in regularly feeding patients or those individuals that are tube-fed for nutritional support. The major considerations are the adequate enteral absorption of the indicated drug, food interactions and other factors that might affect it (e.g. present or induced gastrointestinal disorders, physicochemical properties of the drug, stomach pH, gastrointestinal microflora, and particular anatomical singularities).
- Subcutaneous administration (SC): may be limited in several species because of the blubber layer in most cetaceans and in adult pinnipeds. It is however a common route in sea otters, bears, fur seals and in young pinnipeds (prior to the development of the thick blubber layer). Administration of drugs in the blubber could significantly interfere with the absorption and elimination curves.
- Intramuscular administration (IM): is most frequently applied in marine mammals that are out of food, difficult to restraint (sometimes through remote dart injection) or for those drugs that are not absorbed by enteral route. Caution should be paid in order to avoid superficial injection into the extensive subcutaneous blubber (long hypodermic needles are generally required), which can result in failure to achieve any appreciable systemic distribution especially with highly lipid soluble medications. Large muscle masses superficially enough to be penetrated with the needle are preferred as the site of injection. Precaution also with the local effect derived from the irritation caused by some injectable drugs and with potential vehiculation of pathogens from skin surface into the injection site (exhaustive skin disinfection is essential). Large individuals may require large volumes of drug and care should be taken to use multiple injection sites and to keep the drug volume per injection site reasonable. The recommended total volume injected per site does not increase in scale with the mass of the animal.
- Intravenous administration (IV): most species lack of superficial peripheral vessels complicating catheterization. Main vascular accession points significantly vary with species.

- Intraperitoneal administration (IP): it is not considered a common route in marine mammals. Manly used for delivery of large volumes of fluids or nonirritating drugs. Needles must be suitable to penetrate the abdominal wall without further damaging of internal organs.
- Topical administration (TA): Baths and dips. The major challenge is to achieve appropriate contact time for drug efficacy in an aquatic environment. Ointments and salves are often specially compounded for marine mammals (lipid bases such as lanolin and petroleum jelly, Orabase and other human dental bases)

Alternative routes:

- Inhalatory (IH): For induction/maintenance of general anesthesia.
- Intratracheal (IT): For rapid absorption through respiratory mucosa of emergency drugs without an accessible central vascular access.
- Aerosolization and nebulizing: For targeted delivery of medications to the respiratory system (mainly the lungs) minimizing potential systemic side effects (usage of inhaler chambers/masks or by placing animals in a nebulization chamber).

B. Dose Scaling

When specific pharmacological data for drugs in marine mammal do not exist, extrapolation of doses and pharmacokinetic parameters across species is necessary. Nevertheless, the practitioner should be cautioned that not all drugs scale well by body mass or even by body surface or basal metabolic rate. A vast array of complex allometric equations, that compare drug parameters of interest (e.g., half-life, volume of distribution, clearance) to body weight, can be found in the literature; choosing which equation to use can be daunting.

In general, it is important to know the animal physiology and the expected metabolism and excretion routes of the drug when making decisions on scaling a dose between species. It is usually accepted that shared similarities between some domestic animals and marine mammal species are related with their phylogenetic relationship. So, nearer phylogenetic species can have a more similar pharmacological response to a same medical treatment. Artiodactyla (e.g. ruminants and pigs) are phylogenetically most related with cetaceans while domestic carnivores with pinnipeds.

C. Drug interactions

At present, little data exists concerning drug interactions in marine mammals, but we must be at least prepared for the possibility of any drug interaction described in terrestrial species.

In the present formulary, any user must pay attention to the comments on each section, where previously described drug interactions in different species are noted. When new combinations are considered, it is always best to administer one drug at a time not mixing them in the same container.

One of the strengths of the present formulary is to facilitate daily clinicians an easy way to report interactions, side effects and adverse reactions with of the different drugs in the different marine mammal species. This valuable data will be updated routinely in the app in order to increase a rational and safety use of drugs by other colleagues.