

REPTILE DRUG THERAPY

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Reptiles provide clinicians with unique challenges due to their varied and unique anatomy and physiology. Drug therapy is therefore challenging in reptiles, due to a variety of adaptations which do not exist in mammalian or avian patients. In order to optimize the outcome of reptile patients undergoing drug therapy for treatment or prevention of diseases or for induction of anesthesia or analgesia, it is important to consider these unique adaptations.

Effect of body temperature

Reptiles are ectothermic, and therefore their body temperature is directly affected by the environmental temperature. In their natural environment reptiles regulate their body temperature through various behaviors, but in captivity reptiles may be maintained outside of their preferred optimal temperature zone (POTZ). Since body temperature in reptiles is not kept constant but will vary based on the environmental temperature, clinicians have to expect varied response to drug therapy in reptiles and should ensure that reptile patients are maintained at their POTZ prior to and during drug therapy. Drug absorption, distribution, metabolism and excretion are all affected by body temperature. An increase in body temperature will lead to acceleration of these processes, while lower temperatures will result in a delay in drug absorption, distribution, metabolism and excretion. If sedation or anesthesia is induced with injectable drugs, reptiles may show a delayed or no onset of sedation if they are below their POTZ, and the duration of drug effects will be prolonged, delaying complete recovery due to the delayed metabolism and excretion of the administered drugs. In contrast, reptiles which are maintained at the high end of their POTZ or above will show a more rapid onset of sedation or anesthesia, but the duration of effect (plateau phase) will be shortened due to the acceleration in drug metabolism and excretion.

Temperature is also of particular concern if reptiles receive antimicrobials for treatment of infections, since their immune system will only function optimally within the POTZ.

Routes of drug administration

The oral route for drug administration is rarely indicated in reptiles, and large variation in drug bioavailability has been reported. In any systemically sick reptile, oral drug administration should be avoided and instead parenteral administration (i.e. subcutaneous or intramuscular injections) considered. Reptile owners and keepers can be trained to administer drugs by injection, which will result in more reliable and consistent drug delivery than oral drug administration. However, certain drugs, such as antifungals (e.g. terbinafine, itraconazole) can only be administered by the oral route and often require long-term administration. Placement of esophageal feeding tubes in chelonians and lizards is therefore recommended if long-term oral drug administration is necessary.

Historically intramuscular (IM) drug administration has been considered superior to the subcutaneous route. However, for most drugs administered the subcutaneous route is the preferred method of administration by the author, since it is less painful, allows for delivery for larger volumes and can be performed with less restraint than IM injections.

Intravenous (IV) drug administration is rarely indicated in reptiles, with the exception of the administration of certain anesthetic induction agents (e.g. propofol, alfaxalone, ketamine). In most cases placement of an intravenous catheter prior to IV drug administration cannot be easily accomplished and therefore IV injections are performed using hypodermic needles or butterfly catheters. Intraosseous catheters are a suitable alternative to IV catheters in lizards, but are considered painful, and are therefore only recommended in cases of emergency or if intravascular access is required during anesthesia.

The intracoelomic administration of drugs and fluids has been reported, but is not recommended by the author due to the risk of internal organ damage, in particular in female reptiles with developed ovarian follicles.

Other routes of administration include nebulization of antimicrobials for skin and respiratory tract infections, intranasal administration of anesthetics and their reversal agents, and the topical administration of antiparasitics.

Renal portal system

Historically the administration of drugs in the caudal body half in reptiles has been controversial. Blood draining from the hindlimbs and tail in reptiles can directly reach the kidneys, due to the presence of a

renal-portal system and therefore it has been assumed that renal tissue damage may occur if nephrotoxic drugs are administered. An additional concern is that insufficient drug levels may be reached, if drugs excreted by the renal tubules are administered. Several studies have been performed to investigate the effects of hindlimb vs. forelimb injection on plasma levels of a variety of antibiotics which undergo excretion by either glomerular filtration (e.g. gentamicin) or tubular excretion (e.g. carbenicillin). It was concluded from these studies that generally the effects of hindlimb administration of drugs are unlikely to be clinically significant and that the caudal body half is a suitable parenteral drug administration site in reptiles.¹ Therefore injection site is considered irrelevant in regards to drug kinetics by some authors, which recommend to administer drugs anywhere in the reptile body. However other authors recommend that drug administration in the caudal body half should only be considered for specific drugs and if the administration of drugs in cranial body half is not feasible. It has been recommended to adjust the drug dose if drugs are administered in the caudal body half, in order to account for the renal and hepatic first pass effects on drug plasma levels. In contrast to the great amount of attention paid to the effects of the renal portal system on drug kinetic in reptiles, the hepatic-portal system and how the venous vasculature differs in reptiles compared to birds and mammals has not received much attention in the literature, but in fact it has a much greater clinical impact than the effects of the renal portal system.

Hepatic portal system

The venous blood flow from the hindlimbs and tail in reptiles differs substantially from other higher vertebrates. In mammals and birds, the blood from the hindlimbs and tail drains into the caudal vena cava, that enters the right atrium of the heart. In contrast, the venous blood flow from the hindlimbs and tail region in reptiles drains into the ventral abdominal vein(s), which connect to hepatic portal vein to enter the liver. Hence, any drug administered in the hindlimb or tail (caudal body half), enters the liver first, before reaching the systemic circulation, resulting in a hepatic first-pass effect if the drug undergoes hepatic metabolism or excretion. The hepatic first-pass effect is one of the reasons why oral administration of many drugs is ineffective. The same effect has to be considered in reptiles when drugs are administered in the caudal body half, but not in mammals or birds because of the difference in how blood drains from the caudal body half. In red-eared sliders the administration of ketamine and dexmedetomidine failed to induce anesthesia if the drugs were administered by intramuscular injection in the hindlimbs, while anesthesia was reliably induced in all animals following forelimb injection. A study on alfaxalone in turtles demonstrated the lack of anesthetic efficacy of this drug following

intramuscular hindlimb injection, while when administered intravenously in the jugular vein, anesthesia could be reliably induced. A pharmacokinetic study on buprenorphine in red-eared sliders showed 80% lower plasma levels following hindlimb administration compared to forelimb administration. Hindlimb injection of tramadol in turtles, resulted in 20% higher metabolite levels, compared to forelimb injections, which is clinically desirable, since the metabolite has analgesic properties.

It cannot be assumed that hindlimb injection is a generally acceptable or unacceptable drug administration method in reptiles. Drugs that are metabolized or excreted predominately by the liver will undergo a hepatic first-pass effect (e.g. opioids, most anesthetics, oxytocin, etc.) and should therefore not be administered in the caudal body half. In contrast, drugs that do not undergo a significant hepatic first-pass effect (e.g. fluroquinolones, many cephalosporins, aminoglycosides, etc.) can be administered in the caudal body half in reptiles without concerns about altered drug kinetics. However, as a general rule the drug administration in the cranial body half is preferred over administration in the caudal body half because of the reduced risk of injection site dependent effects on drug kinetics.