Techniques for Monitoring Drug Efficacy

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KEYWORDS

• Therapeutic drug monitoring • Compounded drug • Dose-response curve
• Therapeutic index • Effective dose • Lethal dose

KEY POINTS

- Drug efficacy is based on a dose-response curve, requiring a combination of pharmacokinetic and pharmacodynamic data.
- Monitoring drug efficacy includes monitoring for adverse events and should be tailored based on the drug and any reported toxicities within the species.
- Monitoring includes therapeutic drug monitoring, monitoring clinical response, imaging, and diagnostics such as complete blood count, biochemistry, and urinalysis.
- Therapeutic drug monitoring can offer an effective method to determine plasma drug concentration in the individual patient and tailor the dose based on clinical signs or adverse drug events.

INTRODUCTION

Assessing drug efficacy can be a challenge in exotic medicine due to the limited pharmacokinetic (PK) data and even fewer pharmacodynamic (PD) studies. PK reports what the body does to the drug, from absorption to metabolism, distribution, and excretion. In contrast, PD describes what the drug does to the body in a dose-dependent manner, including anticipated and unanticipated (adverse) responses. The definition of what is considered efficacious varies based on the treatment protocol, the purpose of the selected drug, the dose selection, and the dosing interval. Drug efficacy is furthermore influenced by the pharmaceutical formulation, with clinically relevant differences reported in some compounded medications compared with the approved formulations. The clinician must, therefore, critically weigh the use of compounded drugs, especially if there is a concern of therapeutic failure or an adverse event (AE). Before discussing the methods of monitoring drug efficacy, an overview of how drug efficacy is established is required.

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DRUG EFFICACY

Dose-Response Relationship

One of the fathers of toxicology, Paracelsus, is credited with the well-known saying, "All things are poison and nothing is without poison, only the dose makes that a thing is no poison."[1] Drug efficacy and toxicity is based on the dose-response relationship (**Fig. 1**) of a given drug, which illustrates the effect (response) associated with a given dose. The maximum effect a drug can have (ie, $e = 1$ or 100%) is defined as a full response and encompasses both therapeutic effects and AE. For example, at a dose corresponding to $e = 1$, the analgesic effects of fentanyl are accompanied by significant respiratory depression. Two drugs in the same class are compared and contrasted by potency and efficacy. Potency describes the dose needed for 2 drugs to provide the same magnitude of effect, whereas efficacy compares the effect that the drug has at the site of action (eg, morphine vs buprenorphine). Drugs are considered to be equal in efficacy if both induce the same magnitude of clinical response, but the drug causing the clinical response at a lower dose is considered more potent. For example, fentanyl and hydromorphone are equally effective, but a lower dose of fentanyl is required to elicit the desired response; therefore, fentanyl is more potent.[2]

Establishment of the Therapeutic Window

Once the dose-response relationship has been described, a therapeutic window can be designed for a given drug. The window reports a plasma drug maximum concentration (C_{max}) above which there is an increased risk of AE and a plasma drug minimum concentration (C_{min}) below which concentrations are ineffective (**Fig. 2**).[2] The therapeutic window is based on population statistics of the median effective dose (ED_{50}) at which at least 50% of the population has the desired response. In contrast, the median lethal dose (LD_{50}) is defined as the dose at which 50% of the population has a lethal response (**Fig. 3**). Dividing the LD_{50} by the ED_{50} establishes a therapeutic index (TI) and the larger the TI, the safer the drug.[1] This TI can vary between species

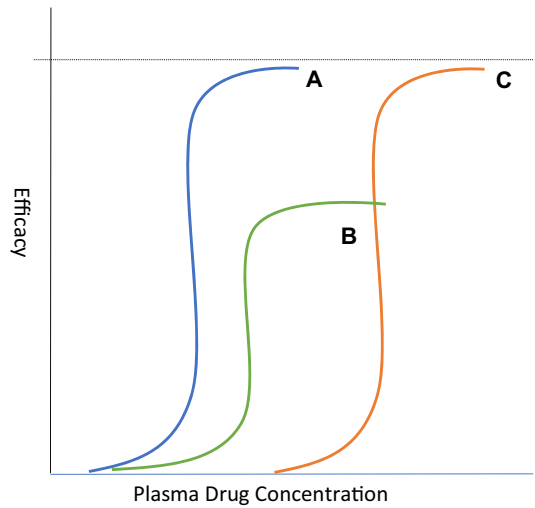

Fig. 1. Drug A and C are similarly effective; however, drug A is more potent because less of the drug is necessary. Drug A is more effective than drug B because it is 100% effective compared with the 50% effectiveness of drug B.