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Insights into therapeutic drug monitoring

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Abstract
Therapeutic Drug Monitoring (TDM) is the measurement and interpretation of plasma or blood drug concentrations to optimize clinical efficacy while minimizing toxicity. It ensures that drug levels remain within the therapeutic window, allowing individualized dosing based on pharmacokinetic and pharmacodynamic variability. In veterinary medicine, TDM plays a vital role in managing drugs with narrow therapeutic indices, such as antiepileptics, cardiac medications, and aminoglycosides. It aids in detecting therapeutic failure, preventing adverse effects, and guiding dosage adjustments in animals with concurrent diseases or altered metabolism. Reliable sample collection, precise analytical methods, and clinical interpretation are essential for effective TDM. Incorporating TDM into routine veterinary practice enhances evidence-based decision-making, ensures treatment safety, and contributes to improved therapeutic outcomes in animal patients.

Keywords: Therapeutic Drug Monitoring, Therapeutic Window, Dose

Introduction

Definition

Measurement and interpretation of principally blood and plasma drug concentration with the purpose of optimizing a patient's drug therapy and clinical outcome while minimizing the risk of drug induced toxicity. During administration of a dosage regimen, the concentration should be maintained within the therapeutic window.

Why Therapeutic Drug Monitoring?

It guides the clinician for an effective and safe drug delivery and check serum concentrations of the drug to tailor therapy for the individual patient.

Goals for Therapeutic Drug Monitoring

It ensures that the given drug produces maximal therapeutic benefit with minimal toxic adverse effects. It also ensures appropriate concentration of the drug at the site of action to produce the required benefits.

Objectives for Therapeutic Drug Monitoring:

- Monitoring of factors like disease state, animal's characteristics, drug interactions
- Dosage adjustment in patients with pre – existing disease.
- Effective means of individualization

Use in human Medicine

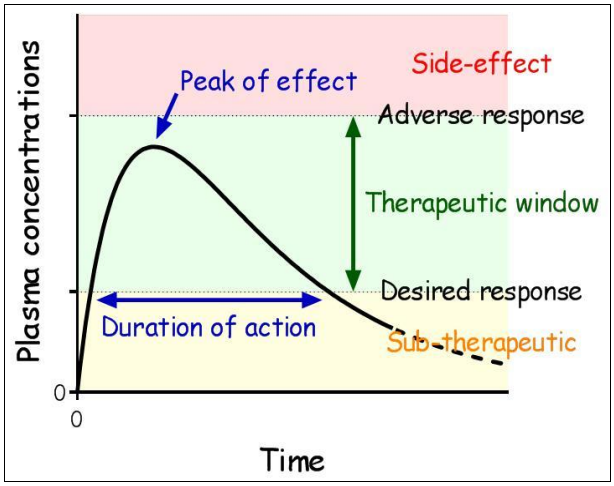
Clinical Area	Purpose
Anti-epileptics	Seizure control, avoid toxicity
Cardiac Drugs	Prevent arrhythmia, manage toxicity
Antibiotics	Ensure efficacy, prevent nephrotoxicity
Immunosuppressants	Prevent rejection, avoid toxicity
Psychiatric Drugs	Optimize effect, reduce side effects
Antineoplastics	Dosing precision, reduce toxicity
Antiretrovirals	Enhance efficacy, prevent resistance
Respiratory Drugs	Narrow index, toxicity control
Autoimmune/Oncology	Rescue timing, avoid adverse effects
Antidepressants (TCAs)	TDM in resistant/depressive cases

Use in Veterinary Medicine

Drug Category	Reason for TDM
Antiepileptics	Ensure therapeutic levels, prevent toxicity
Cardiac Drugs	Narrow therapeutic index, monitor for toxicity
Immunosuppressants	Prevent toxicity or underdosing
Aminoglycosides	Nephrotoxicity; monitor peak & trough levels
Bronchodilators	Narrow safety margin, inter-individual variation
Chemotherapy	Prevent toxic effects in sensitive patients
Endocrine Therapy	Adjust dose based on hormone levels
Antifungals	Ensure adequate blood levels; hepatotoxic risk
Behavioural Drugs	TDM in refractory cases or with side effects

Therapeutic Window/Therapeutic Range

It is the Concentration range of drug in plasma where the drug has shown to be efficacious without causing toxic effects in animals.



Sources of Variability in Drug Response

There are two main sources:

- Pharmacokinetic variability – Variation in dose and plasma concentration (more emphasis)
- Pharmacodynamic variability – Variation in drug concentration at the receptor level and the response

Factors affecting Therapeutic Drug Monitoring

- Individual's capacity for pharmacodynamics
- Enzyme induction/inhibition by other drugs/foods
- Enzyme induction – Increase rate of metabolism
- Enzyme inhibition – Decrease rate of metabolism
- Individual's capacity for pharmacokinetics
- Absorption: Rate of absorption and extent of absorption
- Drug formulation,
- Manufacturer,
- Route of administration,
- Intra-individual variations
- Bioavailability
- Distribution: Vd = dose of drug and plasma concentration
- Metabolism: protein bound (inactive) or free (active).
- Excretion: kidneys, lungs, GI or skin.
- Renal dysfunction – less drug clearance
- Concomitant disease, tropical disease and nutritional deficiencies
- Alternative system of medicine
- Medication or Sampling errors
- Laboratory errors
- Cost effectiveness

Criteria for Therapeutic Drug Monitoring

Drugs that need TDM	Drugs that do not need TDM
Narrow therapeutic index	Wide therapeutic index
Toxicity – realistic concern	Toxicity – not a realistic concern
Not follow linear kinetics	Linear kinetics
Life threatening conditions	Non – life threatening conditions
Therapeutic effect not readily assessed by clinical observation	Assessed by clinical observation
Relationship between drug concentration and pharmacologic/toxic effects	No Relationship

Process of Therapeutic Drug Monitoring

- Decision to request ???
- Any toxicity, Lack of response, Assessment of compliance, Assessment therapy after regimen change, Potential drug interactions, Chronic administration needed
- Patient demographics (e.g. Age, sex and lean body weight – renally cleared drugs)
- Time of sample withdrawal
- Trough concentration – Multiple oral doses (anti – convulsant drugs),
- Prior to next dose – steady state concentration (least variable point)
- Peak concretion – After drug absorption (2 - 4 h – oral route, 0.5 – 1 hr – i/m, s/c route)
- Collection of biological samples – Plasma/Serum/Whole Blood/Saliva/Urine/Sweat
- Laboratory measurement
- Colorimetry
- UV – Spectrometry
- Fluorescence spectrometry
- Chromatography – Gas chromatography, Mass spectrophotometry, HPLC
- Capillary electrophoresis
- Immunoassay

Clinical Interpretation of results

1. Clinical conditions requiring TDM
2. Collection of biological samples
3. Transfer to laboratory and estimation of drug concentration by suitable method
4. Interpretation of results with respect to clinical conditions

If Inadequate/Lack of clinical response

- Below Therapeutic Range – Increase dose if required.
- Within Therapeutic Range – A small change of dose should be considered
- Above Therapeutic Range – Change/Reconsider drug therapy

If Satisfactory clinical response/toxicity

- Below Therapeutic Range – Other reasons for toxicity, lab errors
- Within Therapeutic Range – Other reasons for toxicity, Lower dose can be given if relieved from disease
- Above Therapeutic Range – Discontinue therapy and restart with a low dose/alternate drug

Clinical Usefulness of Therapeutic Drug Monitoring:

- Maximise efficacy
- Avoiding toxicity
- Identify therapeutic failure
- Dose adjustment
- Individualized dose guidelines
- Avoid unnecessary medication

Problems/Limitations of Therapeutic Drug Monitoring:

- Scientific accuracy of drug assays
- Laboratory variability in reporting
- Validity of suggested target ranges
- Costs involved
- Limited accessibility and infrastructure facilities
- Lack of training/skilled lab technicians

Conclusion

- TDM is essential in veterinary medicine in optimizing therapeutic outcomes
- It helps in individualized dosing and improves treatment efficacy and safety
- It is useful for regular monitoring, which is particularly crucial
- Accurate interpretation of TDM helps in the understanding of pharmacokinetics
- Integration of TDM into routine veterinary care supports evidence-based decision-making, enhances compliance, and minimizes adverse drug reactions, ultimately improving patient outcomes.

Conflict of Interest
Not available

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Reference

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