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Introduction of Therapeutic Drug Monitoring (TDM)

- 1. TDM is generally defined as the clinical practices of measurement & interpretation of specific drug at designated intervals to maintain a constant concentration within a target range for optimizing dosage regimens with appropriate medical interpretation.
- 2. TDM refers to the individualization of drug dosage by maintaining plasma or blood drug concentrations within a targeted therapeutic range or window.

History of Therapeutic Drug Monitoring

1960s: The science of TDM introduced a new aspect of clinical practice in the 1960s with the publication of initial pharmacokinetic studies linking mathematical theories to patient outcomes

 $\mathbf{\Omega}$



Indications for Therapeutic Drug Monitoring



2

Contraindications for Therapeutic Drug Monitoring



e.g. Penicillin

Hit and run drugs e.g. Omeprazole

6

Process of Therapeutic Drug Monitoring



• Therapeutic management

Advantages of Therapeutic Drug Monitoring

- Maximized efficacy and minimal toxicity
- Facilitates in adjustment of doses
- Achieving consistent concentration of drug in the blood to maximize clinical benefits
- Useful in the drugs which have narrow therapeutic ranges or high pharmacokinetic variability

Disadvantages of Therapeutic Drug Monitoring

1. Time Lag in Results:

- 1. TDM involves analysing blood samples to determine drug concentrations. This process takes time, and during this period, a patient's condition may evolve or change.
- 2. The delay in obtaining results could lead to suboptimal adjustments in drug dosage, especially in situations where quick intervention is crucial.

2. Inter-Individual Variability:

- 1. Individuals can respond differently to the same drug due to factors such as genetics, age, and overall health.
- 2. Establishing a universal therapeutic range that suits all patients can be challenging, as some may require higher or lower drug concentrations for optimal therapeutic effects.

3. Intra-Individual Variability:

- 1. Even within the same individual, drug response may vary over time. Factors like changes in metabolism, organ function, or concurrent illnesses can influence drug levels.
- 2. TDM results taken at a single point might not accurately represent the ongoing dynamics of drug metabolism and efficacy.

4. Complexity of Drug Interactions:

- 1. Concomitant use of multiple medications can affect the pharmacokinetics of the monitored drug.
- 2. TDM may not fully account for all possible interactions, leading to challenges in predicting the combined effects of different drugs on an individual's therapeutic response.

5. Limited Availability of TDM for All Drugs:

- 1. Not all drugs have well-established therapeutic ranges, and not all healthcare settings have the infrastructure or resources for routine TDM.
- 2. This limits the widespread application of TDM and its benefits across the entire spectrum of medications.

Factors affecting Therapeutic Drug Monitoring

1. Patient demographics

Age, sex and lean body weight are particularly important for renally cleared drugs as knowledge of these allows calculation of creatinine clearance.

2. Individuals' capacity to absorb/distribute/metabolize/excrete the drug

3. Concomitant disease, tropical disease and nutritional deficiencies E.g. Infections, Diarrhea, Worm infestations, Tuberculosis, Nutritional deficiencies Diabetes and AIDS.

4. Patient Compliance

If the concentration of the drug is lower than expected, the possibility of noncompliance should be considered before a dose increase is recommended.

5. Alcohol & Tobacco use

Chronic use of alcohol \rightarrow cause non-specific hepatic microsomal enzyme induction, resulting in increased clearance and decreased serum concentrations of hepatically cleared drugs.

Cigarette smoking- \rightarrow increases the hepatic clearance of theophylline and patients who have recently stopped smoking may have unexpectedly high theophylline concentrations.

6. Medication or sampling errors & laboratory errors



Drugs That Commonly Require TDM

Types of Drugs

Antibiotics

Cardiac drugs

Vancomycin, Gentamicin, Amikacin

Digoxin, Procainamide, Lidocaine

Names

Anti-seizure drugs

Drugs treat autoimmune diseases

Drugs that treat bipolar disorder

Phenytoin, Phenobarbital, Lamotrigine Cyclosporine, Sirolimus, Tacrolimus, Methotrexate

Lithium, Valproic acid

Drugs whose TDM may be useful in some circumstances but not generally practised

- Amiodarone
- Beta Blockers
- Caffeine
- Clozapine
- Flucytosine
- Morphine
- Olanzapine
- Tricyclic antidepressants

Conclusion

- 1. TDM may be useful for establishing initial dosing and monitoring certain medications.
- 2. TDM can not compensate for error in diagnosis, poor choice of drugs, errors in dispensing and dosages, errors in sampling, non compliance etc.
- 3. However, when used in combination with good clinical observation, it can lead to optimal drug therapy with minimal side effects.
- 4. TDM data provides the clinician with greater insight into the factors determining the patients response to drug therapy.
- 5. It can help to distinguish a noncompliant patient and a patient who is a true non-responder.
- 6. Thus, TDM is a useful adjunct in treating many patients provided the potential pit falls and problems are considered.
- 7. TDM is a valuable tool in optimizing drug therapy, its effectiveness is constrained by factors such as delayed results, individual variability, complex drug interactions, and the limited availability of monitoring for all drugs.





- 1. Which of the following factors can influence drug metabolism and, consequently, the need for TDM?
 - a. Age
 - b. Gender
 - c. Diet
 - d. All of the above
- 2. Which of the following is NOT a limitation of TDM?
 - a. Complex drug interactions
 - **b.** Intra-individual variability
 - c. Universal therapeutic range
 - d. Limited availability for all drug
- 3. Which body fluid is commonly used for monitoring drug levels in TDM?
 - a. Urine
 - b. Saliva
 - c. Blood
 - d. Sweat
- 4. For which class of drugs is TDM often recommended due to the potential for toxicity and individual variability in metabolism?
 - a. Antibiotics
 - b. Analgesics
 - c. Antihistamines
 - d. Anticonvulsants
- 5. What is meaning of the term "peak concentration" in TDM?
 - a. The highest drug level in the bloodstream after administration
 - b. The lowest drug level in the bloodstream after administration
 - c. The average drug concentration over time
 - d. The concentration of drugs in the tissues

Ans: (1)-D, (2)-C, (3)-C, (4)-D, (5)-A.

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Message from the Executive Director

"I heartily congratulate the department of pharmacology for bringing this informative newsletter on "Therapeutic Drug Monitoring" – an emerging technique in clinical pharmacology and therapeutics. My best wishes to the entire team......

Dr. (Col) CDS Katoch, Executive Director, AIIMS, Rajkot.

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