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A Review on Therapeutic Drug Monitoring: A useful tool for individualization of dosage regimen

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ABSTRACT

To maintain a steady concentration of a certain drug in a patient's bloodstream and to optimise individual dose regimens, TDM is the clinical practise of testing the drug at predefined intervals. TDM is generally used to monitor pharmaceuticals with limited therapeutic ranges, high pharmacokinetic variability, challenging target concentrations to monitor, and compounds known to induce therapeutic and adverse effects. TDM is not necessary for the majority of prescriptions. TDM is predicated on the idea that there is a defined relationship between dose and drug concentration in the blood or plasma as well as between concentration and therapeutic outcomes.

TDM starts with the initial medicine prescription and includes figuring out an initial dosage schedule suitable for the clinical condition as well as patient traits including age, weight, organ function, and concomitant drug therapy. Consider the sample period in relation to the medication dose, the dosage history, the patient reaction, and the targeted therapeutic targets when interpreting concentration results. By employing the proper concentrations of hard-to-manage drugs, TDM attempts to optimise therapeutic outcomes in patients in a variety of clinical scenarios.The current objective is to deliver basic knowledge regarding therapeutic medication monitoring.

Keywords: Drug monitoring, criteria, utilization, drugs monitored, guidelines for TDM, analytical techniques.

INTRODUCTION

The conventional definition of TDM is the clinical laboratory measurement of a chemical parameter that, when properly interpreted by a physician, directly affects drug prescribing practices[1]. Contrarily, TDM refers to the customization of drug dosage by maintaining plasma or blood drug concentrations within a particular therapeutic range or window. Combining knowledge of pharmaceutics, pharmacokinetics, and pharmacodynamic, TDM enables the assessment of a medication's efficacy and safety in a range of clinical contexts. Personalizing therapy regimens is the aim of this strategy to maximize patient benefit. Traditionally, TDM has entailed analysing drug concentrations in a variety of bodily fluids.

Since its inception in 1970, TDM has become widely accepted. TDM's advantages have been widely publicised, thanks in large part to the accessibility of suitable analytical techniques and the commercialization of enzyme immuno assay procedures.

TDM is defined as "a measurement conducted in a laboratory of a parameter that, with appropriate interpretation, will directly alter prescribing methods" in a 1997 publication by the Joint C-TDM IATDMCT CT/IFCC group. However, it could also be an endogenous chemical prescribed as a replacement medication in a patient who is physiologically or pathologically deficient in the compound. The measurement in a biological matrix is often of a prescribed xenobiotic.

The 1960s saw the creation of TDM concepts. TDM expanded as a result of improvements in research and expertise as well as more complex laboratory techniques.

To be eligible for monitoring, a drug must meet the following criteria:

- The link between serum medication concentration and pharmacologic action should be clinically significant. The link between serum drug concentration and target tissue concentration is typically implied by this.

The relationship between drug dosage and pharmacologic impact and plasma drug concentration ought to be weaker than the other way around.

- The difference between serum concentrations that have hazardous effects and those that have therapeutic effects should be small.

- The serum concentration that results from a specific therapeutic dose is variable since there are variations in drug absorption, distribution, and excretion between and within individuals. With the medicine clomipramine, which is used to treat enuresis, it has been shown that there is a very weak association between serum levels and therapeutic dosage.
- The pharmacologic effects of medications are difficult to quantify (e.g., suppression of seizure activity is difficult to monitor clinically when administering anticonvulsant drugs).
- Drug analysis must be done quickly and accurately.

When delivering medications to children, age-related variations in drug absorption, distribution, metabolism, and clearance should be taken into account in order to maximise pharmacological efficacy and prevent toxicity. There are notable distinctions between neonates, pre-pubescent, and postpubertal children, in addition to between adults and children.

The significant differences between adults and children include the following:

- Drug absorption varies depending on the newborn period's changes in stomach pH and emptying time.
- The apparent volume of distribution differs between neonates, children, and adults due to variations in body composition (neonates have less body fat and more water).
- Immature hepatic and renal function is the primary cause of slow total medication clearance in preterm infants and neonates.
- Premature infants and newborns with immature hepatic microsomal enzyme systems have delayed biotransformation of many medications, necessitating a lower mg/kg dosage to obtain therapeutic concentrations.

Valid TDM Standards

Poor dose-effect correlation brought on by significant rater-individual pharmacokinetic variation is an acceptable TDM criteria. Monitoring is helpful in reaching effective concentrations without systemic toxicity because there is a very limited window between desirable and harmful concentrations as well as between therapeutic and toxic effects. Third, plasma concentrations and effect must be closely connected. The intensity and duration of a drug's

pharmacodynamic response must be momentarily associated with the receptor site in order to effectively show a relationship between concentration and effect.

Is TDM necessary?

Some medications cannot be evaluated clinically because the amount of the drug in the body depends on the concentration of the drug at the site of action, which in turn depends on the desired effect. The steady state concentration of a medicine cannot be predicted from the standard dose due to inter-individual heterogeneity in the processes involved between prescribing a prescription and that drug reaching an effective concentration at its site of action.

The Importance of TDM By individualised medication therapy, therapeutic drug monitoring contributes to improved drug efficacy, decreased drug toxicity, and diagnostic purposes by assisting in the design of patient-specific dosage regimens.

There is more intra-patient fluctuation between dose and effect for some medications due to their broad coefficient of pharmacokinetic variation. Therapeutic medication monitoring is quite helpful in these situations.

What Details Are Required for TDM?

- The following information is needed:
- The pharmacokinetics of the medication. The clinical state of the patient.
- The patient's clinical background in terms of prior therapy outcomes
- Schedule for dosage and sample.
- The intention of therapeutic medication monitoring, such as figuring out whether a drug is effective, harmful, or for diagnostic purposes.
- patient clinical reactions

Concept of Therapeutic Drug Monitoring (TDM)

TDM is founded on the idea that, for some medications, a close relationship exists between the drug's plasma level and its therapeutic effect. If such a link does not exist, TDM is of limited use. Like any diagnostic procedure, measuring plasma level is only appropriate when the results have the potential to be helpful. The accuracy with which the treatment outcome may be identified determines the clinical utility of plasma level monitoring. Plasma levels offer little extra information when therapeutic effects can be reliably and

objectively measured, such as during antithrombotic therapy with coumarin derivatives. On the other hand, when a precise therapeutic point is challenging to establish, monitoring medication levels may be of great therapeutic benefit.

The following criteria must be satisfied for TDM to be effective

- The medicine in question has a limited therapeutic range,
- And there is a direct link between plasma levels of a drug or a drug metabolite and its pharmacological or hazardous effects.
- Because steady state plasma levels at any given dose exhibits significant individual variability, clinical observation cannot easily evaluate the therapeutic impact.
- There are appropriate analytical methods for figuring out drug and metabolite levels.

TDM is not necessary

- When the clinical outcome is unrelated to either the dose or the plasma concentration.
- Dosage individualization is not necessary.
- Clinical quantification of pharmaceutical effects is possible.
- The relationship is still unclear when attention is impaired.
- Examples of medications with a wide therapeutic range include beta blockers and calcium channel blockers.

Indications for TDM

- A general indication for therapeutic medication monitoring is a narrow therapeutic index.
- Failure of treatment.
- Drug metabolism varies significantly.
- An uncertain clinical endpoint.
- For the diagnosis of probable toxicity and the detection of drug abuse.

TDM's Limitations

1. There are just a few medications that make good candidates for therapeutic drug monitoring, which is one of the restrictions.
2. Variation in the sensitivity and accuracy of drug detection techniques.
3. There are little infrastructure facilities in rural areas.
4. From one laboratory to the next, reports vary.
5. Insufficient or incorrect data for estimating the desired concentration range.
6. The therapeutic impact of the medicine may be influenced by its active metabolite(s), but the metabolite cannot be quantified.
7. Poor quality assurance skills and training.
8. The price for the TDM

Clinical Application of TDM

TDM data helps clinicians gain a better knowledge of the variables that affect a patient's response to pharmacological therapy. Measuring plasma levels can assist identify between a noncompliant patient and a genuine non-responder when a patient does not respond to a prescribed treatment dose. TDM also offers helpful details about individual variations in drug use habits and changes in drug usage as a result of altered physiological conditions or illness processes. When the risks and issues are considered, TDM is an effective adjuvant in the management of many patients.

- ❖ Drug monitoring is a common practise in TDM.
- ❖ A medication is an excellent candidate for therapeutic drug monitoring if it satisfies the following requirements:
- ❖ There is a lot of pharmacokinetic heterogeneity.
- ❖ The therapeutic index has limitations.
- ❖ Drugs that have a high dose-response curve

- Clinical observation alone cannot always be used to determine the treatment impact. For instance, the dose-plasma concentration relationship for anticonvulsants like phenytoin or antidepressants is unpredictable.
- Both an established range of target drug concentration in blood and an affordable technology for determining drug content in blood are available.

Currently, the following medication classes are used for therapeutic drug monitoring

- Digoxin is an antiarrhythmic drug that is used to treat heart failure.
- In both acute and maintenance doses, anti-maniacs or mood stabilisers, such as lithium and tricyclic antidepressants, are used to treat psychotic disorders.
- Antibiotics known as aminoglycosides, include gentamicin and vancomycin.
- Epileptic seizures are avoided by taking anti-epileptic drugs such phenytoin, carbamazepine, and phenobarbitone after neurosurgery or trauma.
- Anti-cancer drugs like methotrexate and immunosuppressants like cyclosporine are used to avoid transplant rejection.
- Breathing-inducing drugs like theophylline

Guidelines for Therapeutic Drug Monitoring are Now Available

- TDM entails giving the patient a dose of the medication that has been predetermined.
- Blood samples are now being taken.
- Blood sample analysis.
- Pharmacokinetic assessment of reactions.
- Clinical response assessment.
- finishing the dose schedule.

For a variety of drug categories, numerous organisations have developed standards for therapeutic drug monitoring. Guidelines for TDM of several medications are listed by the National Health Service (NHS) of the United Kingdom (UK), and they include the drug's half-life, time to reach steady state, scheduling for blood sample withdrawal, and goal range for blood concentration.

The following steps are crucial for conducting and evaluating TDM investigations, according to this particular medication guidelines and other sources:

- ✧ TDM needs supporting evidence.
- ✧ TDM includes following the law.
- ✧ Sample collection procedure
- ✧ Tests must be run before TDM is performed.

The timing of sample collection: The half-life of the drug dictates the sampling period.

- ✧ Sample concentrations.
- ✧ Sample shipping and storage.
- ✧ Patients are under observation.
- ✧ In a lab, drug levels in the blood are monitored.
- ✧ If aberrant results are seen, something needs to be done.
- ✧ Calculation, interpretation, and advice related to analytical data.

In order to find drugs in blood or other physiological fluids, analytical techniques are used

The amount of drug in bodily fluid can be determined using a variety of analytical methods.

- ➢ The technique must be able to differentiate between substances with comparable structural properties, such as the drug and its metabolites.
- ➢ Ability to pick up very little amounts.
- ➢ Simple to use; does not interfere with the administration of other medications at the same time.

The following are some of the analytical methods used to analyse drugs:

1. Spectrophotometry is an analytical method.

2. Chromatography (HPLC, GLC, etc) (HPLC, GLC, etc)

3. Radioimmunoassay (RIA) (RIA)

4. Enzyme immunoassays.

CONCLUSION

Based on their theoretical and practical knowledge, doctors try to choose the optimum medication for the treatment of a recognised disease or pathophysiologic process. The hunt for the best pharmacotherapy is made

more difficult by the emerging understanding of the huge genetic, environmental, and age-related variability in drug response. The risks, restrictions, and potential uses of the medications they recommend must be understood by knowledgeable doctors. Certain medications need to be assessed in plasma or serum, followed by any necessary dosage modifications. These problems are all made more difficult in children by other circumstances. A recent and intriguing field is the TDM of medications used to treat AIDS patients. Any combination of AIDS medications may now be measured simultaneously thanks to tandem mass spectrometry. This allows for the evaluation of patient compliance as well as the ready optimization of dosage regimens.

Based on the data presented above, it was concluded that basic information about therapeutic drug monitoring was successfully provided.

FUTURE OBJECTIVES

In the future, genotype identification may be helpful for TDM. Measuring drug concentrations in the blood will continue to be a clinical requirement because you can't predict precise serum concentrations even if you know your metabolizer status.

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