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THERAPEUTIC DRUG MONITORING USE –THE ROLE OF CLINICAL PHAMACOLOGIST

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ABSTRACT Therapeutic Drug Monitoring (TDM) is the clinical practice of measuring specific drugs at specified intervals to maintain a constant concentration in a patient's blood, optimizing individual dosing schedules. It is unnecessary to employ TDM for the majority of medications, and for monitoring drugs with marked pharmacokinetic variability, medications for which target concentrations are difficult to monitor, and drugs known to cause therapeutic and adverse effects. use of a combined approach involving pharmaceutical, pharmacokinectic and pharmacodynamics techniques and analyses. proper use of TDM requires more than a simple measurement of the patients blood level and comparison with a target range. TDM plays an important role in developing and individualizing safe and effective therapeutic drug . The assessment of the potential of newly marketed medicinal products to produce both advantages and disadvantages has enhanced the role of the clinical pharmacologist. pharmacoepidemiogy applies epidemiological reasoning, methodologies and knowledge to the study of drug uses and effects in human populations. The clinical pharmacologist retains an important role in monitoring medicine use in healthcare system. We currently face an irreconcilable gulf between the cost of drugs and the available resources to pay for them, which leaves the clinical pharmacologist in the key role of promoting the rational and cost-effective use of medicines. With the ever increasing number of adverse effects of drugs, prescribing errors, patients' expectations concerning drug safety and the need for appropriate new drug appraisal, the clinical pharmacologist will play an important role in reducing medication errors and in educating new prescribers and patients about their medicines.

KEYWORDS : Bloodstream, Pharmacokinetic, Pharmacodynamics, clinical pharmacologist, pharmacoepidemiogy.

INTRODUCTION

Therapeutic drug monitoring (TDM) is the clinical practice of measuring specific drugs at designated intervals to maintain a constant concentration in a patient's bloodstream, thereby optimizing individual dosage regimens. It is unnecessary to employ TDM for the majority of medications, and it is used mainly for monitoring drugs with narrow therapeutic ranges, drugs with marked pharmacokinetic variability, medications for which target concentrations are difficult to monitor, and drugs known to cause therapeutic and adverse effects. The process of TDM is predicated on the assumption that there is a definable relationship between dose and plasma or blood drug concentration, and between concentration and therapeutic effects. TDM begins when the drug is first prescribed, and involves determining an initial dosage regimen appropriate for the clinical condition and such patient characteristics as age, weight, organ function, and concomitant drug therapy.

When interpreting concentration measurements, factors that need to be considered include the sampling time in relation to drug dose, dosage history, patient response, and the desired medicinal targets. The goal of TDM is to use appropriate concentrations of difficult-to-manage medications to optimize clinical outcomes in patients in various clinical situations. Therapeutic drug monitoring (TDM) is generally defined as the clinical laboratory measurement of a chemical parameter that, with appropriate medical interpretation, will directly influence drug prescribing procedures. Otherwise, TDM refers to the individualization of drug dosage by maintaining plasma or blood drug concentrations within a targeted therapeutic range or window. By combining knowledge of pharmaceutics, pharmacokinetics, and pharmacodynamics, TDM enables the assessment of the efficacy and safety of a particular medication in a variety of clinical settings. TDM involves measuring drug concentrations in various biological fluids and interpreting these concentrations in terms of relevant clinical parameters. Clinical pharmacists and pharmacologists use pharmacokinetic principles to assess these interpretations.[1]

PURPOSE OF THERAPEUTIC DRUG MONITORING

Performing TDM requires a multidisciplinary approach. Accurate and clinically meaningful drug concentrations are attainable only by complete collaboration by a TDM team, typically comprised of scientists, clinicians, nurses, and pharmacists. Excellent communication among team members is necessary to ensure that best practices in TDM are achieved.[2] The indications for drug monitoring have widened to include efficacy, compliance, drug-drug interactions, toxicity avoidance, and therapy cessation monitoring. Plasma drug concentration measurements alone may be helpful in several circumstances, although each indication may not apply equally to every drug Measuring plasma concentrations may be helpful, however, as a low measurement reflects either poor recent compliance or undertreatment. Poor compliance is implicated if the patient is prescribed a dose that is unlikely to be associated with a measured low concentration or if a previous measurement suggested that the plasma concentration should be higher for the given dose. When initiating drug therapy, the physician may find it useful to measure the plasma drug concentration and tailor the dosage to the individual. This directive applies to all drugs, although it is most important for those with narrow therapeutic ranges such as lithium, cyclosporine, and aminoglycoside antibiotics.[3]

MEASURING PLASMA DRUG CONCENTRAION IN THERAPEUTIC DRUG MONITORING

The contribution of pharmacokinetic variability to differences in dose requirements can be identified by measuring the drug concentration at steady state and modifying the dose to attain a desired concentration known to be associated with efficacy. However, there is substantial inter-individual pharmacodynamic variability at a given plasma

concentration[4], hence a range of concentrations rather than a single level is usually targeted. For a limited number of drugs for which there is a better relationship between plasma or blood concentration-response than dose-response, the measurement of plasma or blood concentrations has become a valuable surrogate index of drug exposure in the body[5].

ANALYTICAL ISSUES IN THERAPEUTIC DRUG MONITORING

The practice of therapeutic drug monitoring requires the orchestration of several disciplines, including pharmacokinetics, pharmacodynamics, and laboratory analysis. The analytical impact on determining pharmacokinetic parameters is not well appreciated. Analytical goals in therapeutic drug monitoring should be established by determining the nature of the problem to be solved, selecting the appropriate matrix and methodology to solve the problem, and developing valid analytical schemes that are performed competently with appropriate quality and interpreted within the framework of the problem[6].

PRACTICAL ISSUES IN THERAPEUTIC DRUG MONITORING

The most important consideration in interpreting the plasma drug concentration is tailoring the treatment to the patient's physiological needs. In doing so, the clinician should take into account not only the concentration but also other clinical features that may affect the relationship between concentration and clinical effects. Thus, it is important for the clinician to know how to interpret the plasma concentration results in the context of the patient's condition, rather than making a predetermined guess as to what that measurement might mean[7]. Patient demographic characteristics are critically important so that the contributions of age, disease state, ethnicity, and other variables to inter-individual variation in pharmacokinetics and pharmacodynamics can be considered. The clinician presenting a drug assay request must communicate these details effectively to the members of the TDM team. Once the decision to monitor the concentration of a therapeutic drug has been made, it is important that a biological sample is collected to provide a clinically meaningful measurement. An appropriate pharmacokinetic evaluation requires the acquisition of properly timed blood specimens[8].

PHARMACOECONOMIC IMPACT OF THERAPEUTIC DRUG MONITORING

Over the last 30 years, in response to the lessons learned from using TDM and growing concerns among clinicians and the public about rising health care costs, the principles of pharmacoeconomics are now being applied to various fields, including TDM[9]. As an intervention method, TDM purports to improve patient responses to important life-sustaining drugs and to decrease adverse drug reactions. Furthermore, the resources consumed by TDM methods will likely be regained by positive outcomes, including decreased hospitalizations, and thus TDM is an appropriate candidate for an economic outcomes evaluation[10]. A pharmcoeconomic analysis of the impact of TDM in adult patients with generalized tonic-clonic epilepsy showed that patients undergoing TDM had much more effective seizure control, fewer adverse events, better earning capacity, lower costs to the patient, savings from lower hospitalizations per seizure, and greater chances of remission[11].

MONITORING MEDICINES USE

The term 'pharmacoepidemiology' first appeared in a *British Medical Journal* Editorial by Sir David Lawson in 1984.It may be defined as the application of epidemiological reasoning, methods and knowledge to the study of the uses and effects (be they beneficial or not) of drugs in human populations. It has been traditionally subdivided into the areas of pharmacovigilance, drug utilization and prescribing quality. With the need to examine the cost-effectiveness of newly marketed medicines, pharmacoeconomics has been added as a further subdivision[12].

THE CLINICAL PHARMACOLOGIST AND MEDICATION ERRORS

Medication errors are one of the most preventable causes of patient harm. The majority of these errors occur, not as a result of reckless behaviour on the part of health care providers, but as a result of the speed and complexity of the medication use cycle. A number of definitions exist for a medication error. One definition proposed by the National Co-ordinating Council for Medication error reporting and prevention is 'any preventable event that can cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer[13]. According to this definition, medication errors also include prescribing errors, which may be defined as the incorrect drug selection for a patient and can include the dose, quantity and indication, or prescription of a contraindicated drug[14].

A similar systematic approach to examining the causes of prescribing errors revealed that most mistakes were made by junior medical staff as a result of slips in attention or because prescribers did not apply the relevant rules[15].

Medication errors may be classified according to the their place (prescribing, dispensing or drug administration) in the medication use cycle. A more recent classification has been proposed that is based on human error theory. In this classification, errors may be subdivided into either mistakes (knowledge or rule-based errors) or skill-based errors [action-based errors (slips) or memory-based errors (lapses)][16].

REDUCING MEDICATION ERRORS

A systematic approach to medication errors and learning from other industries, such as the aviation or oil industry, should be adopted to reduce medication errors. One of the difficulties with medication errors is the low level of reporting[17]. Prescribing errors often occur because the prescriber has no immediate access to the relevant information relating to the drug or patient. Electronic prescribing can therefore support the prescribing process and help reduce prescribing errors. Computerized systems containing rules to prevent incorrect or inappropriate prescribing can help to increase the appropriateness of drug treatment and reduce errors[18].

An alternative approach to reducing medication errors is to target high-alert drugs and procedures. The implementation of carefully planned series of low-cost interventions focused on high-risk medications, driven by information derived largely from internal event reporting and designed to improve a hospital's medication safety have been shown significantly to reduce patient harm as a result of medication errors[19].

Drugs that have been identified as having a high potential for error include potassium chloride, high-strength narcotic agents, cancer chemotherapy, insulin, heparin and epidural drug infusions. The restricted supply of strong potassium chloride to reduce medication errors has long been recommended, and stocking only one strength of morphine ampoules on paediatric wards has been successful in preventing errors involving the selection of the incorrect ampoule[20]. The development of the Prescribe initiative, based on the belief that a thorough understanding of the basic principles of clinical pharmacology will translate into safe prescribing will help to support and improve prescribing in the undergraduate medical curriculum[21].

CONCLUSION

The use of TDM requires a combined approach encompassing pharmaceutical, pharmacokinetic, and pharmacodynamic techniques and analyses. The

appropriate use of TDM requires more than a simple measurement of patient blood drug concentration and a comparison to a target range. Rather, TDM plays an important role in the development of safe and effective therapeutic medications and individualization of these medications.

The clinical pharmacologist retains an important role in monitoring medicine use in today's healthcare system. Opportunities exist to improve pharmacovigilance systems through improved ADR-reporting rates, the development of hypothesis-led pharmacoepidemiological studies and the increased use of prescription databases. We currently face an irreconcilable gulf between the cost of drugs and the available resources to pay for them, which leaves the clinical pharmacologist in the key role of promoting the rational and cost-effective use of medicines. With the ever increasing number of adverse effects of drugs, prescribing errors, patients' expectations concerning drug safety and the need for appropriate new drug appraisal, the clinical pharmacologist will play an important role in reducing medication errors and in educating new prescribers and patients about their medicines.

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