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Clinicians Routinely Monitor Drug Pharmacodynamics

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Description

Therapeutic Drug Monitoring (TDM) is essential to maintain the efficacy of many immunosuppressant drugs while minimizing their toxicity. TDM has become more refined with the development of new monitoring techniques and more specific assays. It is the goal of Therapeutic Drug Monitoring (TDM) to use drug concentrations to manage a patient's medication regime and optimise outcome. Limited resources require that drug assays should only be performed when they do contribute to patient management. For this to be the case a therapeutic drug monitoring service has a far greater role than just therapeutic drug measuring. This article describes the roles and functions of a Best Practice TDM service. The features which can and should be strived for in each step of the TDM process—the decision to request a drug level, the biological sample, the request, laboratory measurement, communication of results by the laboratory, clinical interpretation and therapeutic management—are discussed..

Pharmacokinetic

There is rarely financial provision for this. Nevertheless expert interpretation of a drug concentration measurement is essential to ensure full clinical benefit. Only clinically meaningful tests should be performed and limited funds should not be wasted on measurements which cannot be interpreted and do not assist patient management. Clinicians routinely monitor drug pharmacodynamics by directly measuring physiological indices of therapeutic response e.g. lipid concentrations, blood glucose, blood pressure, clotting tests. For many drugs there is either no readily available measure of effect or it is insufficiently sensitive. Large interindividual variation in the relationship between dose and response can make individualising drug dosage difficult, for example drugs with narrow therapeutic indices, large interindividual variation in pharmacokinetics, or concentration-dependent pharmacokinetics. In other cases it is difficult to distinguish between the progress of the disease and the pharmacological effects of a drug. It is in these situations that TDM is an essential part of clinical management. Optimizing the prescription of antimicrobials is required to improve clinical outcome from infections and to reduce the development of antimicrobial resistance. One such method to improve antimicrobial dosing in individual patients is through application of therapeutic drug monitoring (TDM). The aim of this manuscript is to review the place of TDM in the dosing of antimicrobial agents, specifically the importance of pharmacokinetics (PK) and pharmacodynamics (PD) to define the antimicrobial exposures necessary for maximizing killing or inhibition of bacterial growth. In this context, there are robust data for some antimicrobials, including the ratio of a PK parameter (e.g. peak concentration) to the minimal inhibitory concentration of the bacteria associated with maximal antimicrobial effect. Blood sampling of an individual patient can then further define the relevant PK parameter value in that patient and, if necessary, antimicrobial dosing can be adjusted to enable achievement of the target PK/PD ratio. To date, the clinical outcome benefits of a systematic TDM programme for antimicrobials have only been demonstrated for aminoglycosides, although the decreasing susceptibility of bacteria to available antimicrobials and the increasing costs of pharmaceuticals, as well as emerging data on pharmacokinetic variability, suggest that benefits are likely.

Antiepileptic Drugs

Although no randomized studies have demonstrated a positive impact of Therapeutic Drug Monitoring (TDM) on clinical outcome in epilepsy, evidence from nonrandomized studies and everyday clinical experience does indicate that measuring serum concentrations of old and new generation Antiepileptic Drugs (AEDs) can have a valuable role in guiding patient management provided that concentrations are measured with a clear indication and are interpreted critically, taking into account the whole clinical context. Situations in which AED measurements are most likely to be of benefit include when a person has attained the desired clinical outcome, to establish an individual therapeutic concentration which can be used at subsequent times to assess potential causes for a change in drug response as an aid in the diagnosis of clinical toxicity to assess compliance, particularly in patients with uncontrolled seizures or breakthrough seizures to guide dosage adjustment in situations associated with increased pharmacokinetic variability (e.g., children, the elderly, patients with associated diseases, drug formulation changes when a potentially important pharmacokinetic change is anticipated (e.g., in pregnancy, or when an interacting drug is added or

removed) to guide dose adjustments for AEDs with dose-dependent pharmacokinetics, particularly phenytoin.