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Research Article

TDM IN THE ESSENTIAL IN VITRO DRUG LIST AND PRIORITISATION OF DIGOXIN, VANCOMYCIN, AMIKACIN TO BE NEEDED – REVIEW

Akshaya Abraham., Helana Jose., Christeena Jacob and Rosmin Jacob*

Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala

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A B S T R A C T

Therapeutic drug monitoring is a branch of clinical chemistry and clinical pharmacology that specializes in the measurement of medication level in blood. Essential diagnostic are, Diagnostic that satisfy the priority health care needs of the population and are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and accuracy and comparative cost- effectiveness; similar to the definition of an essential medicine.

Aim

To determine the necessity of TDM in essential drug list and prioritisation of digoxin, Amikacin and vancomycin.

Objective

1. Establish the priority of digoxin, Vancomycin, Amikacin to be included in TDM.
2. Provide evidence and evaluate the effect to include TDM in essential drug list.

INTRODUCTION

When there is large inter individual variation between dose and effect of individualising drug dosage is difficult. This is relevant for the drugs with narrow therapeutic range (NTI Drugs).Concentration measurements of a drug is necessary to correlate the desired or ADR with plasma concentration. The present report suggest that evidence supporting TDM for a list of drugs included in the WHO essential medicines list with the aim of being considered as part of essential diagnostic list.

Therapeutic Drug Monitoring

TDM is a tool which can help in rational prescribing process. Therapeutic drug monitoring refers to the individualisation of dosage by maintaining plasma concentration within a target range (therapeutic range, therapeutic window).

TDM is useful when the following criteria are met:

- A good correlation exists between the pharmacologic response and plasma concentration.
- Drug concentrations cannot be predicted from a given dose, as result of interindividual variability.
- The drug has a narrow therapeutic index (i.e., the therapeutic concentration is close to the toxic concentration).
- The pharmacological effects of the drug cannot be monitored easily (e.g., monitoring blood pressure for antihypertensives) or the adverse effects cannot be easily differentiated from lack of efficacy of a drug. If the clinical effect can be readily measured (e.g. heart rate, blood pressure), it is obviously better to adjust the dose on the basis of response.

Where this cannot be done, therapeutic drug monitoring is used in two major situations: -

- Drugs used prophylactically to maintain the absence of a condition such as seizures, cardiac arrhythmias, depressive or manic episodes, asthma relapse.
- To avoid serious toxicity as with the aminoglycoside antibiotics which, unlike most antibiotics, have a narrow therapeutic range

For the majority of drugs, routine monitoring is not supported and should only occur if it can be accurately interpreted and subsequently contribute to patient management. Drug concentrations need to be interpreted in the context of the individual patient without rigid adherence to a target range. This requires knowledge of the pharmacokinetics, sampling time, drug history and the patient's clinical condition.

Essential Diagnostics

The present report analyses evidences supporting TDM for a list of drugs included in the WHO Essential Medicines List with the aim of being considered as part of the Essential

Corresponding author:* **Rosmin Jacob
Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala

Diagnostics List (EDL). The first EDL thus encompasses a minimum set of IVDs that should be made available in primary care, hospitals and reference laboratories, with a focus on common diseases with public health importance and the WHO defined priority infectious diseases.

As defined by WHO, Essential diagnostics are: "Diagnostics that satisfy the priority health care needs of the population and are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and accuracy, and comparative cost effectiveness; similar to the definition of an essential medicine". .TDM is suggested for: Amikacin, carbamazepine, cyclosporine , digoxin, gentamicin, lithium, methotrexate, phenobarbital, phenytoin, Valproic acid and vancomycin.

Digoxin

Digoxin, together with some antiepileptics drugs and antibiotics such as aminoglycosides, has been traditionally in the list of medicines which require TDM.A careful analysis of analysis of the published evidences associated with TDM of digoxin allow to minimise previous recommendations. Most authors agree on the fact that the risk of digoxin toxicity is potentiated in elderly patients and in those with renal impairment (as digoxin is predominantly renally cleared), electrolyte disturbances , acidosis, hypoxia, hypothyroidism or co-administered P-glycoprotein inhibitors.

A study conducted on analysing of aliquots from 261 routine digoxin samples by accredited laboratories using commercially available immunoassays showed that the reproducibility of the digoxin assay is such that through the course of digoxin therapy, patient samples analysed by different laboratories and medical practitioners may be unacceptably inconsistent. The authors concluded that this extensive variation in digoxin monitoring has significant implications, as it makes drug concentrations difficult to interpret.

Studies give the evidence for the clinical relevance of digoxin therapeutic monitoring is proved but the serum digoxin concentrations required for optimal clinical efficacy and acceptable toxicity remains controversial. A considerable variation in the routine monitoring of digoxin, which makes TDM difficult to interpret and complicates clinical management. Thus, clinical monitoring of heart rate and adverse effects may be more helpful than TDM.

Amikacin

In a detailed revision published in 2014, Hall worth concludes that the value of monitoring of aminoglycosides is high: "Monitoring is essential to achieve effective therapy while avoiding toxicity, particularly in infants, the elderly, the obese and patients with cystic fibrosis, if high doses are being used or if renal function is impaired.

McCudden adds that the combination of MIC requirements and toxicity risk is the basis for aminoglycoside TDM. The use of alternative approaches, such as consensus opinion and a review of current practice, will be required to develop guidelines to maximize therapeutic outcomes and minimize toxicity with amikacin".

Vancomycin

Vancomycin is a reserve antibiotic either used IV or orally.Hallworthauthor concludes that the value of monitoring vancomycin blood concentrations is moderated: "like the aminoglycosides, the glycopeptides are poorly absorbed, not metabolized, excreted renally and are potentially nephrotoxic and ototoxic. There is definitely a role for monitoring in patients with poor renal function to achieve maximum effect with minimal toxicity. In a chapter on TDM of antimicrobials published in a specialized book of Clinical Chemistry, Dasgupta concluded : "TDM of aminoglycosides and vancomycin is essential in order to avoid drug toxicity especially nephrotoxicity and irreversible ototoxicity". McCudden refers to joint guidelines for TDM targets for vancomycin published in 2009, guidelines recommend that trough vancomycin concentrations should be higher than 10 mg/L to reduce development of resistance.

RESULT

TDM should be considered within the framework of the rational prescribing process, in those patients that could benefit from it because of their physiological or clinical conditions, the presence of cotreatments which could produce drug-drug interactions, etc.

- For non-complicated patients receiving digoxin, it seems that close clinical control can be enough in most cases, and routine TDM seems unnecessary. The recommendation for TDM can be categorized as 'low' because of the inconsistencies.
- In the case of Vancomycin, guideline quality for vancomycin TDM is not optimal, efforts are needed to improve guideline quality, especially in the domain of rigor of development and stakeholder involvement".
- The use of alternative approaches, such as consensus opinion and a review of current practice, will be required to develop guidelines to maximize therapeutic outcomes and minimize toxicity with amikacin.

DISCUSSION

TDM is dynamic and techniques are evolving quickly. These advances affect aminoglycosides and vancomycin, but also other antimicrobial.

WHO EML group	Drug	Reference
Antibacterial	Amikacin(Aminoglycoside)	Monitoring is essential to achieve effective therapy while avoiding toxicity, particularly in infants, the elderly, the obese and patients with cystic fibrosis, if high doses are being used, for treaments longer than 5 days or if renal function is impaired. Value of monitoring: high Indications for monitoring have been controversial, but there is definitely a role for monitoring in patients with poor renal function to achieve maximum effect with minimal toxicity, for treatments longer than 5 days. Value of monitoring: moderate
	Vancomycin (glycopeptide)	
Antiarrhythmic medicines Medicines used in heart failure	Digoxin	Clinical monitoring of heart rate and adverse effects may be more helpful than TDM. For some drugs, clinical monitoring may be more helpful than TDM and in all cases, it is imperative that drug. Value of monitoring: low

Although the scope of TDM is broadening from the traditional focus on prevention of toxicity, to include optimization of antibiotic exposure thereby improving patient outcomes., "the evidence relating TDM practice with improved clinical outcome remains limited.

It is also very important to highlight that TDM is not just having a laboratory with the necessary tools to obtain plasma concentrations, but also to have specialists with enough expertise to interpret these results in the clinical context of each patient, as well as to have clinicians with expertise to adapt dosages to the results of TDM.

In non-complicated patients, the recommendation for TDM of vancomycin could be considered 'moderate', according to Hallworth and also to Ye, *et al*. These authors found that despite the availability of clinical practice guidelines for TDM of vancomycin, vancomycin serum concentrations still do not reach therapeutic concentrations.

There is also a need to discuss about the importance of the involvement of clinical pharmacology, assurance of accurate data (e.g. time of collection and dosing) and recognition of risk factors (e.g. renal impairment) for aminoglycoside TDM.

CONCLUSION

TDM is essential to ensure that a drug has reached its therapeutic concentration in body. This is of importance in the case of patients with renal impairement, liver impairement etc. For some drugs, clinical monitoring may be more helpful than TDM and in all cases, it is imperative that drug concentrations are interpreted in the patient's clinical context. Clinical monitoring of heart rate and adverse effects may be more helpful than TDMin the case of Digoxin.TDM is of high value in Amikacin and is moderate for Vancomycin.

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Reference

1. de Vries TPGM, *et al*. Guide to good prescribing. WHO/DAP/94.11, Geneva, 1994.
2. Ghiculescu, RA. Therapeutic drug monitoring: which drugs, why, when and how to do it. Aust Prescr 2008; 31:42-41.
3. Birkett, DJ. Therapeutic drug monitoring. Aust Prescr 1997; 20:9-11.
4. Saha, N. Clinical Pharmacokinetics and Drug Interactions. In Pharmaceutical Medicine and Translational Clinical Research, 2018.
5. Lucas C, Donovan, P. 'Just a repeat' When drug monitoring is indicated. Austr Fam Phys2013; 42:18-22.
6. Gross, AS. Best practice in therapeutic drug monitoring. Br J Clin Pharmacol 2001; 52: 5S–10S.
7. Nwobodo, N. Therapeutic drug monitoring in a developing nation: a clinical guide. Journal Of the Royal Society of Medicine Open 2014; 5:1–5.
8. Cooney, L; Loke, YK; Golder, S; Kirkham, J; Jorgensen, A; Sinha, I and Hawcutt, D. Overview of systematic reviews of therapeutic ranges: methodologies and recommendations for practice. BMC Medical Research Methodology 2017; 17:84.
9. Flanagan, RJ; Brown, NW; Whelpton, R. Therapeutic Drug Monitoring (TDM). CPD Clinical Biochemistry 2008; 9: 3–21.
10. Le Guellec, C; Simon, N; Hulot, JS; Billaud, EM; https://t.me/c/1200403665/1363: 29-34.
11. McCudden, CR. Quality, origins and limitations of common therapeutic drug reference intervals. Diagnosis (Berl.) 2018; 5:47-61.
12. Yusuf, E; Hammer, RL. What the WHO's List of Essential Diagnostics means for clinical microbiology laboratories and antimicrobial stewardship practice worldwide. Clin Microbiol Infect 2019; 25:6-9.
13. Schroeder, LF; Guarner, J; Amukele, TK. Essential Diagnostics for the Use of World Health Organization Essential Medicines. Clin Chemistry 2018; 64: 1148-1157.
14. Hallworth, M. Antimicrobial drugs. In: William J. Marshall (Ed.) Clinical Biochemistry: Metabolic and Clinical Aspects (3rd. Edition), Churchill Livingstone, 2014.
15. Jenkins, A; Thomson, AH; Brown, NM; Semple, Y; Sluman, C; MacGowan, A; Lovering, AM;Wiffen, PJ, and the BSAC Working Party on Therapeutic Drug Monitoring. Amikacin use and therapeutic drug monitoring in adults: do dose regimens and drug exposures affect either outcome or adverse events? A systematic review. *J Antimicrob Chemother* 2016; 71:2754-9.
16. Dasgupta, A. Advances in antibiotic measurement. In: GS Makowski (Ed.) Advances in Clinical Chemistry Volume 56, Elsevier, 2012: 75-104. Volume 56, Elsevier, 2012: 75-104.

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