UNIVERSITI TEKNOLOGI MARA

APPROPRIATENESS OF THERAPEUTIC DRUG MONITORING OF VALPROIC ACID IN HOSPITAL TENGKU AMPUAN RAHIMAH

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ABSTRACT

TDM, although very useful in individualizing dose regimen, are often done inappropriately. For a drug lacking extensive research and having less predictable pharmacokinetics such as VPA, there is always the potential of overlooking certain factors while ensuring its optimum use. The main aim of this study is to compare the methods applied by the pharmacists in HTAR in individualizing dose regimen to the methods applied by the researcher based on literature review. Retrospective review of both TDM forms and laboratory values of HTAR in-patients taking VPA for epilepsy were carried out. Calculations of expected levels, loading dose and maintenance dose made by both the researcher and the TDM pharmacists in HTAR are compared using Wilcoxon Signed Ranks Test ($p < 0.05$) to detect significant difference between the two median values. There were significant difference ($p<0.05$) for both expected level (z ratio = ±6.900) and maintenance dose (z ratio = ±5.232) but no significant difference was found ($p>0.05$) for the loading dose (z ratio = ± 0.980). For expected level and loading dose, the calculation methods differ from those applied by HTAR pharmacist only in the choice of values of pharmacokinetic parameters and the target steady-state concentration respectively. However, the researcher has found that two important factors, hepatic function and concomitant use of hepatic enzyme inducers were not taken into account in the calculations of maintenance dose of VPA applied in HTAR. A guideline for the calculations of VPA was proposed along with this research.

CHAPTER ONE

INTRODUCTION

Therapeutic drug monitoring (TDM) can be defined simply as the individualization of drug dosage in order to maintain plasma or blood drug concentration within the target range. Major sources of variability in drug dosage are due to variability in both pharmacokinetics (the relationship between dose and plasma concentration) and pharmacodynamics (the relationship between drug concentration at the receptor and the elicited response in patients). TDM contributes to the individualization of drug dosage by reducing the variability in pharmacokinetic phase. Sources of pharmacokinetic variability include age, physiology, disease, drug interaction, environmental influences on drug metabolism and genetic polymorphisms. (Birkett, 1998).

Although TDM is useful to optimize therapy, its misuse can result in improper use of plasma or blood levels and unjustifiable cost (Ratanajamit et al, 2006). Thus expert interpretation of a drug concentration measurement is essential to ensure full clinical benefit. Only clinically meaningful tests should be performed, limited funds should not be wasted on measurements which cannot be interpreted and do not assist patient management (Gross, 1998). Monitoring is helpful in certain drugs with the following