UNIVERSITI TEKNOLOGI MARA

EFFECTIVENESS OF THERAPEUTIC DRUG MONITORING (TDM) OF PHENYTOIN AND VALPROIC ACID IN ADULT PATIENTS

NURUL IZZATI BINTI HAIRUSSAM

Dissertation submitted in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons)

FACULTY OF PHARMACY

2014

ACKNOWLEDGEMENT

Alhamdulillah, grateful to the Almighty, and peace and blessings upon the Prophet Muhammad with His permission that enables me to conduct and finish this mini thesis. First of all, I would like to convey my sincere and infinite thanks to my supervisor Prof. Dr. Mohamed Mansor Manan, who had given his tireless ideas, supports, and guidance all through the process of completing this research project. Special thanks also to him for giving me an opportunity to work and learn under his supervision. My thanks also to my father, Mr Hairussam bin Yuswan and my mother,

who have sacrificed their time, energy, financially and of course their endless support and understanding not only gave me morale booster and encouragement for me from the very beginning till the end of this project. Not the least, to staff of Hospital Tengku Ampuan Rahimah and fellow colleagues who have helped and provide guidance to me. Finally, a big Thank You to all who had either involved directly or indirectly until this thesis is completed.

May Allah S.W.T bless and reward all of you.

Insya-Allah.

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ABSTRACT

The study aim to describe the effectiveness of therapeutic drug monitoring (TDM) of phenytoin and valproic acid in the control of seizures in adult patients. The data was collected from Hospital Tengku Ampuan Rahimah, Klang. A total of 233 forms were reviewed of which 98 patients are females and 135 of them are males. The patients' demographics, renal profile and pharmacokinetics were analyzed to examine the pattern correlation to phenytoin and valproic acid. The data was best describes by a one-compartment model. The analysis has shown that there is a strong correlation between total daily dose and clearance (L/day) in phenytoin polytherapy with R^2 value is 0.3031. The mean of serum level, dose per kg and clearance of phenytoin monotherapy are (9.97 ± 7.02 mg/L), (6 ± 3.59 mg/kg) and (0.362 ± 0.13 L/kg/hr) respectively. The mean of serum level, dose per kg and clearance of patients on phenytoin polytherapy are (9.14 ± 6.67 mg/L), (5.5 ± 4.18 mg/kg) and (0.36 ± 0.147 L/kg/hr) respectively. The mean of serum level, dose per kg and clearance of patients on valproic acid monotherapy are (52.12 ± 11.06 mg/L), (15 ± 5.64 mg/kg) and (10.57 ± 4.6 ml/kg.hr) respectively. Meanwhile, the mean of serum level, dose per kg and clearance of patients on valproic acid polytherapy are (38.49 ± 8.93 mg/L), (16 ± 6.03 mg/kg) and (11.68 ± 4.66 ml/kg/hr) respectively. The COV value (more than 10%) has shown high inter-patient variability in terms of pharmacokinetics. In short, the population pharmacokinetics of hospitalized adults prescribed with phenytoin and valproic acid has high intra and inter-patient variability in gender, races and drug therapy. Finally, it is necessary to monitor the patients individually and regularly in order to avoid toxicities and achieve the optimum level of therapeutic range.

CHAPTER 1

INTRODUCTION

1.1 Overview

Therapeutic drug monitoring (TDM) is a service aimed to provide the optimal level of therapeutic effects and ensure the administered drugs are in their therapeutic range by measuring the plasma concentration of drugs (Krasowski, 2011). In other words, TDM is practiced to maintain the administered drugs from leading to the toxic range or give the adverse effects.

As more of antiepileptic drugs are discovered, the effectiveness of drug need to be considered (Boon et al., 2012). The pharmacokinetic, pharmacodynamic, pharmacotherapeutics and pharmaceutics of the drug also vary in every drug. TDM is essential as each patient shows a different reaction on each drug. Therapeutic drug index for both phenytoin and valproic acid are narrow which meant only a small concentration difference between the level of therapeutic and toxicity (Crawford, Feely, Guberman, & Kramer, 2006). Then, the requirement to perform the TDM is compulsory especially for these kind of antiepileptic drugs (J. W. Wheless, Clarke, McGregor, Pearl, & Ng, 2012).