UNIVERSITI TEKNOLOGI MARA

EFFECTIVENESS OF THERAPEUTIC DRUG MONITORING OF PHENYTOIN AND VALPROIC ACID IN CHILDREN IN A HOSPITAL SETTING

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ABSTRACT

The study was conducted to predict the effectiveness of phenytoin and valproic acid Therapeutic Drug Monitoring (TDM) in children in a hospital setting. The data of patients were collected from Hospital Sultanah Aminah, Johor Bharu (HSAJB) and consisted of 88 patients at which 57 patients are male and 31 patients are female. Patients' demographics and pharmacokinetic data were evaluated to observe the correlation between parameters. The evaluation has shown that there is a strong relationship between the drug level of phenytoin and its clearance with R^2 value of 0.5629 while valproic acid shown moderate relationship with R^2 value of 0.4474. Clearance of both phenytoin and valproic acid were also analysed against dose per kg and dose per day. The mean of clearance of phenytoin in this study is (0.49 ± 0.31 L/kg/hr) while the mean of clearance of valproic acid is (14.35 ± 7.75 ml/kg/hr). The pharmacokinetic of patients in terms of the coefficient of variance (COV) has shown high inter-patient variability for value of more than 10%. The pattern and trend of pharmacokinetic parameters in children treated with phenytoin and valproic acid is also identified. There is no significant difference of pharmacokinetic parameters between gender and race. The most affected parameter is clearance and it is relevant to monitor both drugs to ensure the therapeutic effectiveness can be optimized.

CHAPTER 1

INTRODUCTION

1.1 Overview

Epilepsy is the most common neurologic disorder in children, and both the incidence and prevalence of seizures among children are higher than among the adults (Ma et al., 2009). During the period of children's growth and development, the cause, diagnosis, treatment, prognosis, and pharmacokinetics of pediatric epilepsy differ considerably from those of adults, and the application of antiepileptic drugs (AEDs) in children is more complicated than that in adults (Ma et al., 2009).

Therapeutic drug monitoring (TDM) may be defined as the use of drug measurements in body fluids as an aid to the management of patients receiving drug therapy for the cure, alleviation or prevention of disease (Sharpe, Morrow and Trimble, 1995). TDM is useful in the clinical management of AED therapy (Krasowski, 2010). A common reason is that the pharmacokinetics of the drug shows significant inter-individual variability (Krasowski, 2010). Metabolism (biotransformation) is a major pharmacokinetic factor that can affect AEDs. Variability in metabolism may be due to impaired organ function (typically kidney or liver), genetic factors (pharmacogenetics), or drug-drug or drug-food interactions (Krasowski, 2010).

Convulsions are the commonest and most alarming of neurological problems in children. The reported prevalence of febrile convulsions in children under the age of 10 years is 5.2 to 8.1 per thousand (Thilothammal, Banu and Ratnam, 1996). Children with