# CHAPTER III

# MATERIALS AND METHODS

## 1. Patients

Patients included in this study were out-patients of the neurologic clinic, paediatric out-patient department, Chulalongkorn hospital, who were selected with the following criterias :

1.1 All Thai patients , age 1 month to 15 years. Patients age over 15 years who came to this clinic were also been included as the representative of the adults.

1.2 Consumed phenobarbital long enough that the steady state had been reached.

1.3 All patients had normal renal and hepatic function as diagnosed by the physicians and the laboratory tests.

1.4 All patients had good compliance as determined by interviewed the parents or the patients.

1.5 The parents or the patients willing to be included in this study and signed the patient consent forms after receiving the information about this study.

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**2. Method**

2.1 Selected patient ;

- Investigator selected the OPD cards of the patients who had the appointment at paediatric neurologic clinic, Chulalongkorn hospital and used phenobarbital at steady state.

- While patients were waiting for the physician in neurologic clinic or after the visit, they were interviewed about the medication compliance. The inclusion criterias were

2.1.1 The patients must had good compliance at least two days before coming to the clinic. If non-compliance had happened it should not be exceeded two times in two weeks.

2.1.2 The parents and the patients were informed about the study and the advantages that they would get from the study, the parents or the patients signed the consent form.

2.2 The characteristics and the medication history of the patients were obtained from the OPD cards.

2.3 Blood samples ( 2 ml) were drawn at least 6 hours after the last dose. In each patient , blood sample were drawn two times at least two weeks apart using the same dosage regimen, the mean value of these two phenobarbital concentrations was then used to calculate the level dose ratio.

2.4 The incidence of seizures, and the side effects happened to the patients were obtained from interviewed the parents or the patients.

**3. Analytical Method**

The serum was kept at temperature 2 to 8 degree celsius or freezed in - 20 degree celsius. The serum concentration of phenobarbital determined by a homogeneous enzyme immunoassay (CEDIA®) within twenty-four hours for the samples kept at temperature 2 - 8 degree celsius and within two weeks for the samples that were freezed.

**4. Data analysis**

- Mean phenobarbital concentration was calculated from the two measured concentrations. The mean concentration was then used for calculating level dose ratio :

Level dose ratio = Serum Level (μg/ml) / Dose (mg/kg/day)

- Linear-regression-analysis was performed between phenobarbital level dose ratio and age.

- The level dose ratios between monotherapy and polytherapy regimen were compared.

- Percentages of patients whose serum phenobarbital levels were within therapeutic ranges in each age group were calculated.

- Percentages of patients with side effects whose serum phenobarbital levels were over therapeutic range , within therapeutic range, and subtherapeutic range were calculated.

- Percentages of patients whose seizure were controlled in relation with the therapeutic range were calculated.