Developing Pharmacokinetics – Pharmacodynamics Model of Valproic Acid Syrup Based on Prediction of Population Pharmacokinetics Parameter and Seizure Frequency in Indonesian Pediatric Epilepsy Outpatients

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Background: Valproic acid is a broad spectrum antiepileptic drug with known efficacy profile in pediatric patients, despite of its narrow therapeutic index. There is lack of valproic acid’s pharmacokinetics profile in Indonesian pediatric subjects. This study aimed to identify valproic acid’s population pharmacokinetics (PK) parameters at steady state level and pharmacodynamics (PD) properties in pediatric epilepsy outpatients.

Method: This observational study was conducted prospectively at Sanglah General Hospital during June – December 2019. The subject of this study were 38 Indonesian epilepsy patients aged 6 – 18 years old who adhered to valproic acid syrup monotherapy for at least 1 month. Five subject randomly selected for blood sample collection. Blood valproic acid concentration level was compared to its concentration predicted from Yukawa’s steady state equation. Monolix® software was used to identify valproic acid population PK-PD parameters at steady state level.

Results: Population PK-PD of valproic acid syrup were Vd pop = 3.78 L, Cl pop = 3.19.e⁻¹⁵, IC50 pop = 7.29.e⁻⁶. Mean prediction error between predicted steady state concentration levels of 5 subjects and their related blood levels was ≤ 25% and accepted as within clinically acceptable limit.

Conclusion: It needs further study to develop best matched PK-PD model of valproic acid syrup at steady state concentration in Indonesian pediatric epilepsy.

Keywords: valproic acid, pediatric, epilepsy, PK-PD, seizure frequency
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