The estimation of pharmacokinetic parameters of lithium in children by pharmacokinetic modeling: a pilot study at Yuwaprasart Waithayopathum Child Psychiatric Hospital


Keywords: Lithium, Pharmacokinetics, Children, Pharmacokinetic Modeling

Background
Since the dose adjustment of Lithium in pediatric patients still has problematic. In our hospital, more than half of the patients had serum Lithium outside therapeutic range (0.6-1.2 mg/L). The estimation of pharmacokinetic parameters of Lithium in children by pharmacokinetic modeling to produce the dose adjustment may be useful. Therefore, the purpose of the study was to estimate the pharmacokinetic parameters and calculate the precision (%RMSE) of the predicted Lithium concentration equation.

Method:
This research was a study of blood Lithium levels of children who had visited Yuwaprasart Waithayopathum Child Psychiatric Hospital during 1 January 2011-31 December 2009 by the following criteria; Age lower than 18 years, Receiving Lithium continuously not less than 1 week, the laboratory of renal and liver function were available, good compliance. These blood levels information were used as part of pharmacokinetic modeling process to establish the equation for prediction of Lithium concentrations in blood. The accuracy and precision of the equation were evaluated by the mathematical principle. The assist package software (WIN-NONLIN) was used to create pharmacokinetic parameters.

Results
Twenty-nine patients were recruited. The characteristics presented as the following; age (mean ±SD) was 15.79± 2.64 years, weight (mean ±SD) was 69.75± 22.28 kg and the average daily dose of Lithium (mean+ SD) was 858.62 ±274.53 mg. The trough Lithium concentrations (mean± SD) was 0.56± 19 mg/L. The kinetic parameters (Mean± SD) presented as the following t1/2 (7.23± 3.38 hr), Ke (0.12± 0.07 hr⁻¹), Vd ((48.83± 15.60 L), AUC0-12 (11.01± 5.61 mg*hr/L). The population pharmacokinetic parameters; Ke, and AUC(0-∞) presented as 0.0151 hr⁻¹ and 169.8113, mg*hr/L respectively. The modified equation from Yukawa equation for Lithium clearance calculation and prediction Lithium concentrations were CL (mL/min) = [36.5+(0.242x BW (kg)-7.79]/Scr (mg/dL) and Lithium Concentration (mg/L) = 4 x Dose (mg)/ CL (mL/min) x 73.89, respectively with 6.39 %RMSE (test for 20 patients data).

Conclusions
There were variations of Lithium pharmacokinetic parameters in children. The modified Yukawa equation may be able use for predict Lithium concentration with 6.39% RMSE. However, prospective use of this equation in large population is needed.