论文

新生儿庆大霉素的群体药代动力学模型及其预测血药浓度能力的评价

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摘要：

目的　建立庆大霉素的群体药代动力学模型并考察该模型预测血药浓度的能力。方法　收集常规血药浓度监测中的30例新生儿80对庆大霉素血药浓度时间数据进行分析;根据Sheiner等提出的群体药代动力学思想,编制估计群体参数和个体参数的程序,目标函数最小值以MonteCarlo算法求得;预测能力通过计算ME和RMSE来考察。结果　新生儿庆大霉素的群体药代动力学参数分别为:k_e:0.22±0.022h^{-1},V_d:0.51±0.06L·kg^{-1},Cl:112±10mL·h^{-1}·kg^{-1};群体分析组和预测组的预测血药浓度与实测值显著相关(γ=0.920和0.946）;预测组ME和RMSE分别为0.001mg·L^{-1} 和0.84mg·L^{-1} 。结论　该模型能较好地预测新生儿庆大霉素的血药浓度。
关键词： 群体药代动力学　庆大霉素　蒙特卡罗法　新生婴儿

POPULATION PHARMACOKINETIC MODEL FOR GENTAMYCIN AND ITS PREDICTIVE VALUE

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Abstract:

AIM To construct a population pharmacokinetic model to describe gentamycin concentrations in serum in newborn infants and to validate the predictive ability of this model. METHODS Data used in this study were obtained from 30 neonates with 80 serum samples. A one-compartment open model was used to describe the kinetics of gentamycin after intravenous infusion. Following Sheiner's idea of population pharmacokinetics, a programs to estimate population parameter and individual parameter of gentamycin was made. The target function minimality was obtained from Monte Carlo algorithm. The predictive ability of the developed model was evaluated by computing precision and accuracy of serum concentration predicted using the parameter estimates. RESULTS Fitted population pharmacokinetic parameters (mean±standard deviation) were as follows: k_e: 0.220±0.022 h^{-1}, V_d: 0.51±0.06L·kg^{-1}, Cl: 112±10 mL·h^{-1}·kg^{-1}. For the population analysis sample and the predictive sample, predicted and observed concentrations were all close with correlation coefficient 0.920 and 0.946, respectively. Mean prediction error (ME) and root mean squared error (RMSE) were 0.001 mg·L^{-1} and 0.84 mg·L^{-1} for the predictive sample, respectively. CONCLUSION Observed gentamycin serum concentrations were explained very well by this model. We propose the use of this population pharmacokinetic model to optimize gentamycin clinical therapies in our institution and others with similar patient population characteristics.

Keywords: gentamycin　Monte Carlo method　newborn infant　population pharmacokinetics

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