Current Issue
Browse Issues
Search
About this Journal
Instruction to Authors
Online Submission
Subscription
Contact Us
RSS Feed

Acta Medica Iranica
2009;47(4) : 34-40

Evaluation of phenytoin pharmacokinetics in neurotrauma patients

Shohrati M., Rouini M.R., Mojtahedzadeh M.,. Firouzabadi M.

Abstract:

Previous studies have suggested that drug metabolism may be altered in patients with severe neurotrauma. The purpose of this prospective study was to observe the alteration of phenytoin pharmacokinetic and the resulting drug plasma level among these patients. Twenty patients with severe head injury (Glasgow Coma Scale≤8) requiring intravenous phenytoin were included in the study. Phenytoin sodium was diluted to a concentration of 25mg/ml and infused for 20 minutes at the rate of not faster than 25mg/min. Maintenance dose of phenytoin sodium was administered in the first day of head trauma and vital signs were monitored at hourly intervals while the patients remained in the neurosurgical intensive care unit. Blood samples were obtained for peak and trough concentrations. Free and total phenytoin levels were determined by both liquid chromatography and fluorescence polarization immunoassay (Éclair) of plasma samples after ultrafiltration and deproteinization respectively. Based on the reported Km (Km = 5.4 mg/l), predicted population Vmax was calculated to be (7.3 ± 0.4 mg/kg/d) which was significantly lower than calculated individual Vmax (9.3 ± 3.2 mg/kg/d) (P=0.026). Moreover, significant differences was found between mean daily dose of phenytoin administered to patients (257 ± 4 mg/d) and calculated mean daily dose based on individual Vmax (479 ± 3 mg/d) (p=0.0015). Mean plasma concentrations determined by fluorescence polarization immunoassay (FPIA) (6.11 ± 2.9 mg/l) and HPLC method (5.78 ± 2.8 mg/l) were not statistically different Metabolic rate increased non-proportionally with increase in phenytoin concentration, and as a result decrease in clearance. Significant alteration in the metabolism of phenytoin occurred after severe neurotrauma. Based on our results, to keep phenytoin concentrations in the range of 10-20 mg/l, an increase in the phenytoin maintenance dose and more frequent monitoring of concentration is commonly required.

Keywords:

Neurotrauma

TUMS ID: 3193

Full Text HTML Full Text PDF 258 KB

top