Therapeutic drug monitoring using Rapid High Performance Liquid Chromatographic for simultaneous determination of multiple antiepileptic drugs in human serum: Analysis of 45 patients in an epilepsy camp

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Background and Objective: Therapeutic drug monitoring (TDM) is essential to check toxicity, compliance, and dose titration in uncontrolled chronic epilepsy. Majority of Indian patients cannot afford TDM due to high cost of Fluorescence Polarization Immuno assay method (INR 600 per test, IDR 45 = USD 1). Rapid High Performance Liquid Chromatographic (HPLC) method of drug assay cost lower (INR 50 per test), and can be performed rapidly with sample preparation and analysis time approximately 23 min for 5 antiepileptic drugs (AEDs). This study aims to assess the applicability of Rapid HPLC among the participants of an epilepsy camp.

Methods: 45 patients who were enrolled in an epilepsy camp where AEDs were given free were recruited in the study. TDM of phenytoin (PHT), valproate (VPA), carbamazepine (CBZ), lamotrigine, phenobarbital were done by Rapid HPLC method. Serum was collected in the morning at 11 am just before the next dose (trough concentration). The plasma level were categorized as Therapeutic: 10 - 20 mcg/ml (PHT), 50-100 mcg/ml (VPA), 4-12 mcg/ml (CBZ); Subtherapeutic: <10 mcg/ml (PHT), <50 mcg/ml (VPA), <4 mcg/ml (VPA); Toxic: >20 mcg/ml (PHT), >100 mcg/ml (VPA), >12 mcg/ml (CBZ); Not detectable (zero): 0.1 mcg/ml for all drugs.[1]

Results: There were 18 females and 17 males with age ranging from 6 to 51 years, with different seizure types. Of the patients, 16 (36%) were on monotherapy, and 29 (64%) on two or more AEDs. Normal levels was seen in 21 patients (47%), subtherapeutic levels in 24 patients (53%), toxic levels in 10 patients (22%), and not detectable in 2 patients (4%). PHT toxicity manifested as cerebellar ataxia in 3 patents, megaloblastic anemia from folate deficiency and osteomalacia from vitamin D deficiency in 2 patients.[2] The patients improved after reduction of PHT dose.

Conclusion: Rapid HPLC method of TDM is cost effective. It was able to identified AED toxicity in a fifth, and non-compliance in 4% of participants in an epilepsy camp, who were provided with free drugs.

Table 1: Thrapeutic drug monitoring of 45 patients in an epilepsy camp

	Therapeutic	Subtherapeutic	Toxic	Zero
Phenytoin, n=14	2 (29%)	6 (43%)	5 (36%)	1 (7%)
Valproate, n=22	12 (55%)	5 (23%)	5 (23%)	none
Carbamazepine, n=9	6 (67%)	2 (22%)	none	1 (11%)

References

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2. Penucca E, Richens A. Antiepileptic drugs: Clinical aspects. In: Richens A, Marks, eds: Therapeutic Drug Monitoring. Edinburgh: Churchill Livingstone. 1981; 320-44