
Poster

[P26-1] P26-1: Anticonvulsant drugs

Chair: Ikuko Yano, Japan

Tue. Sep 26, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Tue. Sep 26, 2017 12:30 PM - 1:30 PM Annex Hall)

[P26-1-4] Development and validation of phenytoin quantification from human brain, CSF and plasma by liquid chromatography tandem mass spectrometry

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Keywords: Phenytoin, LC-MS/MS, Analytical Chemistry, Brain tissue, Neurosurgery

Background

Phenytoin is of great importance in various neurosurgical conditions such as acute head injury where it is being used as prophylactic antiepileptic agent. Although plasma phenytoin concentrations and its relation with toxicity is well established, there is not much information available in literature describing the specific relationship between plasma phenytoin levels and its availability in target brain tissue site. Our paper aims to establish a sensitive and highly selective method for the estimation of phenytoin using liquid chromatography-mass spectroscopy (LC-MS) in different biological matrices which includes plasma, CSF and brain tissue.

Methods

The blank samples of brain tissue, CSF and plasma were simultaneously obtained from the tumor patients admitted in the department of neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh. All the samples were collected after obtaining proper informed consent from the patients or from the legal representatives. Before processing, the collected samples were spiked with phenytoin. The brain samples were homogenised and extracted using ammonium sulphate, tertbutyl methyl ether and hydrochloric acid while plasma and CSF were extracted using acetonitrile. The carbamazepine was used as the internal standard for all the three matrices.

Results

The mass transition ion-pair for phenytoin was m/z 253 \rightarrow 104. The linear range over which the proposed method had been validated was 0.01-32g/mL for plasma and CSF while for brain tissue it was 0.01-16 g/gm. In all the three matrices, the correlation coefficient was 0.99. As per analytical standards, the precision and accuracy were within 15% for intra-day and inter-day runs. The extraction recovery of phenytoin was found to be 82.07 - 118.9% for plasma, 62.04 - 112.13% for CSF and 83.73 - 102.69% for brain tissue. The validated lowest limit of quantification(LLOQ) for phenytoin was 0.01 g/ml for plasma and CSF while 0.01 g/gm for brain.

Conclusions

The analytical method for the estimation of phenytoin in human brain, CSF and plasma using LC-MS/MS has been successfully developed and validated. The developed method would be helpful in opening new areas of

research so that key obstacle' s in the field of neurosciences could be surpassed.