Profil Farmakokinetika Fenitoin dalam Dried Blood Spot (DBS) Subjek Sehat Menggunakan Kromatografi Cair Kinerja Tinggi-Photodiode Array (KCKT-PDA) = Pharmacokinetic Profile of Phenytoin in Dried Blood Spot (DBS) of Healthy Subjects Using High Performance Liquid Chromatography Photodiode Array (HPLC-PDA)

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Abstrak

Fenitoin merupakan obat antiepilepsi yang memiliki rentang terapeutik sempit dan mengikuti farmakokinetika non-linear, sehingga diperlukan penentuan parameter farmakokinetika. Penelitian ini bertujuan untuk memperoleh data validasi parsial metode analisis dan profil farmakokinetika fenitoin dalam Dried Blood Spot pada enam subjek sehat. Pengambilan sampel darah dilakukan sebanyak 15 kali. Kondisi analisis fenitoin dan baku dalam karbamazepin menggunakan sistem KCKT-PDA dengan kolom C18 SunFireTM (5 µm; 4,6 mm x 250 mm); fase gerak menggunakan kombinasi metanol, asetonitril dan air (44:10:46, v/v/v); laju alir 1,0 mL/menit; suhu kolom 35oC; waktu analisis 15 menit; dan menggunakan detektor photodiode array pada panjang gelombang 205 nm. Hasil validasi parsial, termasuk parameter linearitas, akurasi, dan presisi intra-hari, dinyatakan memenuhi syarat (EMA, 2022; US FDA, 2022). Parameter profil farmakokinetika fenitoin dalam DBS yang diperoleh, yaitu Cmaks berada pada rentang 3,18-4,90¼g/mL; tmaks berada pada rentang 3-9 jam; t1/2 berada pada rentang 7,69-15,54 jam; AUC0-t berada pada rentang 29,15-144,12¼g.jam/mL; dan AUC0-berada pada rentang 33,84-150,43 Î¼g.jam/mL. Profil farmakokinetika fenitoin dalam DBS dapat digunakan sebagai alternatif pendukung penetapan dosis karena menunjukkan kemiripan dengan profil fenitoin dalam plasma.

.....Phenytoin had a narrow therapeutic range and followed non-linear pharmacokinetics; thus, pharmacokinetic parameters determination was needed. This study aimed to obtain partial validation data of the analytical method and the pharmacokinetic profile of phenytoin in Dried Blood Spot of six healthy subjects. Blood sampling was carried out 15 times. The conditions used to analyse phenytoin and IS carbamazepine were HPLC-PDA system with a C18 SunFireTM column (5 µm; 4.6 mm x 250 mm); a combination of methanol, acetonitrile, and water (44:10:46, v/v/v) as the mobile phase; flow rate was 1.0 mL/min; column temperature was 35oC; analysis time was 15 minutes; and photodiode array detector at 205 nm. The results of partial validation, which evaluated the linearity, within-run accuracy, and precision, were within the criteria acceptance range (EMA, 2022; US FDA, 2022). The pharmacokinetic profile parameters of phenytoin in DBS included Cmax ranging from 3.18-4.90 ¼g/mL; tmax ranging from 3-9 hours; t1/2 ranging from 7.69-15.54 hours; AUC0-t ranging from 29.15-144.12¼g.hr/mL; and AUC0-ranging from 33.84-150.43¼g.hr/mL. The pharmacokinetic profile of phenytoin in DBS can be used as an alternative to support dosage individualization because it was similar to the profile of phenytoin in plasma.