

Analisis simultan siklofosfamid dan 4-Hidroksisiklofosfamid dalam dried blood spot pasien kanker secara kromatografi cair kinerja ultra tinggi-tandem spektrometri massa = Simultaneous analysis of cyclophosphamide and 4-hydroxycyclophosphamide in dried blood spot of cancer patients by ultra high performance liquid chromatography-tandem mass spectrometry

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Abstrak

Siklofosfamid merupakan obat antikanker berupa pro-drug yang diaktifkan oleh enzim sitokrom P450 menjadi 4-hidroksisiklofosfamid 4-OHCP. Kadar 4-OHCP dalam tubuh dapat menggambarkan pembentukan fosforamid mustar yang dapat mengalkilasi DNA dan memberikan efek sitotoksik terhadap sel kanker. Analisis siklofosfamid dan 4-OHCP dilakukan pada Dried Blood Spot DBS 17 pasien kanker Rumah Sakit Kanker Dharmais yang diberikan rejimen siklofosfamid secara KCKUT-SM/SM sebagai upaya pemantauan terapi obat. Pengambilan darah dilakukan pada jam ke-2 dan ke-4 setelah pemberian kemoterapi melalui ujung jari.

Hasil validasi metode bioanalisis parsial menghasilkan akurasi dan presisi intra hari dengan diff dan koefisien variasi KV tidak lebih dari 15 dan tidak lebih dari 20 pada konsentrasi LLOQ. Kurva kalibrasi yang linear didapat pada rentang 50-30.000 ng/mL untuk siklofosfamid dan 10-1000 ng/mL untuk 4-OHCP. Metode ini telah memenuhi syarat akurasi dan presisi intrahari sesuai European Medicines Agency EMEA tahun 2011. Hasil analisis pada 17 pasien kanker menunjukkan kadar siklofosfamid berkisar antara 6045,980 ng/mL hingga 37024,403 ng/mL dan 4-OHCP berkisar antara 33,155 ng/mL hingga 246,362 ng/mL. Hasil yang diperoleh dapat menjadi salah satu parameter pemantauan terapi siklofosfamid.

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Cyclophosphamide is an anticancer in the form of prodrug activated by cytochrome P450 enzyme into 4 hydroxycyclophosphamide 4 OHCP. 4 OHCP levels in the body can describe formation of phosphoramid mustard that can alkylate DNA and give cytotoxic effects to cancer cells. Analysis of cyclophosphamide and 4 OHCP was performed on 17 Dried Blood Spots DBS of cancer patients who received cyclophosphamide as chemotherapy regiment from Dharmais Cancer Hospital by KCKUT SM SM for therapeutic drug monitoring. Samples were taken at 2nd and 4th hours after drug administration with finger prick method. The results of partial validation method produced intra day accuracy and intra day precision with diff and coefficient of variation CV were not more than 15 and not more than 20 in LLOQ concentration. Linear calibration curves were obtained in the range of 50 ndash 30,000 ng mL for cyclophosphamide and 10 1000 ng mL for 4 OHCP. This method has been fulfilled for intra day accuracy and precision according to European Medicines Agency EMEA Guidelines, 2011. The results of the 4 OHCP concentration analysis in 17 cancer patients showed that cyclophosphamide levels ranging from 6045.980 ng mL to 37024.403 ng mL and 4 OHCP was in the range of 33.155 ng mL to 246.362 ng mL. The results could be one of the monitoring parameters of cyclophosphamide therapy.