Analisis 4-hidroksi-n-desmetiltamoksifen dan tamoksifen dalam dried blood spot pasien kanker payudara menggunakan kromatografi cair kinerja ultra tinggi-tandem spektrometri massa = Analysis of 4-hydroxy-n-desmethyltamoxifen and tamoxifen in dried blood spot of breast cancer patients by ultra high performance liquid chromatography tandem mass spectrometry

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Abstrak

Tamoksifen merupakan obat pilihan pertama untuk terapi hormonal pada pasien kanker payudara sebagai terapi ajuvan. Efek antiestrogen dari tamoksifen sangat ditentukan oleh metabolit aktifnya, yaitu endoksifen. Pada penelitian ini dilakukan analisis tamoksifen dan endoksifen dalam sampel dried blood spot DBS dari 40 orang pasien kanker payudara yang memperoleh regimen tamoksifen. Sampel DBS diekstraksi dengan metode ultrasound-assisted liquid extraction dan dilakukan analisis menggunakan kromatografi cair kinerja ultra tinggi-tandem spektrometri massa KCKUT-SM/SM . Metode bioanalisis tamoksifen dan endoksifen serta klomifen sebagai baku dalam secara simultan dalam DBS menggunakan KCKUT-SM/SM telah divalidasi parsial dalam penelitian ini. Hasil uji akurasi dan presisi within-run dengan metode ini memperoleh nilai diff dan KV tidak lebih dari 15 dan tidak lebih dari 20 untuk konsentrasi LLOQ. Kurva kalibrasi untuk tamoksifen diperoleh pada rentang 5 ndash; 200 ng/mL dan 1 ndash; 40 ng/mL untuk endoksifen dengan nilai r > 0,99. Hasil analisis pada 40 pasien kanker payudara menunjukkan kadar tamoksifen berada pada rentang 40,28 ng/mL hingga 194,10 ng/mL dan kadar endoksifen dengan rentang 1,25 ng/mL hingga 18,02 ng/mL. Hal ini menunjukkan bahwa terdapat 4 pasien memperoleh terapi tamoksifen yang kurang efektif berdasarkan konsentrasi ambang batas endoksifen dalam sampel DBS yaitu 3,3 ng/mL.

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Tamoxifen is the first choice of hormonal therapy in breast cancer patients as their adjuvant therapy. The antiestrogen effect of tamoxifen is highly determined by its active metabolite, endoxifen. In this research, analysis of tamoxifen and endoxifen with clomiphene as the internal standard were performed in dried blood spot DBS samples of 40 breast cancer patients who received tamoxifen in their regiment. DBS samples were extracted by ultrasound assisted liquid extraction and analyzed using ultra high performance liquid chromatography tandem mass spectrometry UHPLC MS MS . A simultaneous quantification method of tamoxifen and endoxifen in DBS using UHPLC MS MS had been partially validated in this study. The diff and CV of within run accuracy and precision obtained in this method were no more than 15 and no more than 20 for LLOQ. The calibration curve range for tamoxifen obtained was 5 200 ng mL and 1 40 ng mL for endoxifen with r 0.99. The analysis results of 40 breast cancer patients showed tamoxifen levels were within the range of 40.28 ndash 194.10 ng mL and endoxifen within 1.25 ndash 18.02 ng mL. These results suggested that there were 4 patients received less effective tamoxifen therapy based on the endoxifen threshold in the DBS sample which was 3.3 ng mL.