Analisis O6-Metilguanin dalam darah pasien kanker yang menerima Siklofosfamid pada regimen terapi secara kromatografi cair kinerja ultra tinggi-tandem spektrometri massa = Analysis of O6-Methylguanine in cancer's patients blood during administration of Cyclophosphamide by ultra high performance liquid chromatography tandem mass spectrometry

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Abstrak

Siklofosfamid merupakan antineoplastik golongan agen pengalkilasi yang banyak digunakan dalam kemoterapi kanker. Siklofofamid bekerja dengan mengalkilasi basa DNA pada posisi N7 guanin menghasilkan N7-metilguanin. Siklofosfamid bersifat tidak selektif dan dapat mengalkilasi gugus nukleofil lain pada DNA yaitu O6 guanin menghasilkan O6-metilguanin yang berpotensi menyebabkan mutasi yang dapat memicu kanker sekunder. Pendeteksian O6-metilguanin sebagai salah satu contoh alkilguanin dapat menjadi salah satu cara monitoring terapi untuk menghindari risiko kanker sekunder pada pasien kanker yang diberikan siklofosfamid. Pada penelitian ini dilakukan analisis O6-metilguanin dalam darah pasien kanker. DNA sampel diisolasi menggunakan QIAgen DNA Mini Kits, lalu dihidrolisis menggunakan asam format. Hasil hidrolisis diinjeksikan ke KCKUTSM/ SM dengan kolom C18 Acquity UPLC BEH (1,7 μm, 2,1×100 mm) menggunakan elusi isokratik, fase gerak asam asetat 0,05% dalam aquabidestasetonitril (95:5), laju alir 0,3 mL/menit, metode ionisasi ESI+, kuantitasi MRM 166,1>149,1 dan 166,1>134,1, volume injeksi 10,0 μL. O6-metilguanin muncul pada 1,46 menit. Perhitungan menurut kurva kalibrasi memberikan batas deteksi 1,05 ng/mL dan batas kuantitasi 3,50 ng/mL. Dari 72 sampel yang dianalisis, O6-metilguanin terdeteksi pada 17 sampel, dan dapat dikuantitasi pada 1 sampel dengan kadar 5,8680 ng/mL.

<hr>Cyclophosphamide is one of the alkylating agents that widely used in cancer chemotherapy. It alkylates N7-guanine on DNA as major target, forming N7- methylguanine. Cyclophosphamide is not selective and can alkylate other nucleophilic groups such as O6-guanine forming O6-methylguanine which is potencial to causes mutation leading to secondary cancer in patients who administered it. O6-methylguanine detection as one of alkylguanine can be one way to monitor chemotherapy, therefore secondary cancer risk can be avoided. This research analyzes O6-methylguanine in cancer patients? blood. DNA samples were isolated by QIAgen DNA Mini Kits, and hydrolyzed using formic acid. The hydrolysate was injected to UPLC-MS/MS, column C18 Acquity UPLC BEH (1.7 μm, 2.1×100 mm), isocratic elution in 3 minutes, mobile phase consisted of acetic acid 0.05% in aquabidest - acetonitrile (95:5), flow rate 0,3 mL/min, ionization method ESI+, quantification traces 166.1>149.1 and 166.1>134.1, injection volume 10,0 mL. O6-methylguanine?s peak showed in 1,46 min. Extrapolation from calibration curve data gave limit of detection 1.05 ng/mL and limit of quantitation 3,50 ng/mL. Among 72 analyzed samples, O6-methylguanine was detected on 17 samples, and could be quantified on 1 sample at concentration 5.8680 ng/mL.