INTISARI

TINGKAT EKSPRESI GEN *HETEROGENOUS NUCLEAR RIBONUCLEOPROTEIN E2* (hnRNP-E2) PADA PASIEN *CHRONIC MYELOID LEUKEMIA* (CML) FASE KRONIK DAN FASE *BLAST CRISIS* DI RSUP SARDJITO, YOGYAKARTA

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Latar Belakang : *Chronic Myeloid Leukemia* (CML) merupakan keganasan hematologi yang ditandai dengan peningkatan granulosit matur pada fase kronik (CML-CP), dan ditemukan ≥20% granulosit imatur (sel *blast*) pada fase *blast crisis* (CML-BC). Pada 50% kasus CML, fase kronik akan mengalami progresi langsung menuju fase *blast crisis* tanpa melewati fase akselerasi (CML-AP). Kromosom *Philadelphia* dapat ditemukan pada lebih dari 90% kasus CML akibat translokasi kromosom 9 dan 22, menghasilkan gen fusi BCR-ABL. Gen fusi BCR-ABL ini menginduksi beberapa jalur *signaling*, salah satunya RAS yang bila teraktivasi akan menginduksi aktivasi MAPK – ERK 1/2. Fosforilasi ERK 1/2 memicu proliferasi sel dan menekan apoptosis, serta meningkatkan ekspresi, translasi, dan stabilitas hnRNP-E2. Peningkatan aktivitas hnRNP-E2 akan menghasilkan akumulasi sel *blast* dan diduga dapat menjadi marker progresi CML-CP menuju CML-BC.
Tujuan : Penelitian ini bertujuan untuk mengetahui perbedaan rerata tingkat ekspresi gen hnRNP-E2 pada CML-CP dan CML-BC.
Metode : Penelitian ini menggunakan desain *cross sectional* yang melihat perbedaan tingkat ekspresi hnRNP-E2 pada pasien CML-CP (n=10) dan CML-BC (n=10). sampel cDNA dari pasien CML dengan BCR-ABL positif RSUP Sardjito Yogyakarta (2010 – 2016) pada kali pertama terdiagnosis diambil dari penelitian payung CML. Pengukuran tingkat ekspresi hnRNP-E2 dilakukan menggunakan metode *quantitative Real Time*-PCR dengan mesin RT-PCR ABI 7500 *Fast*.
Hasil : Tingkat ekspresi gen hnRNP-E2 pada pasien CML-BC lebih rendah dibanding CML-CP, tetapi tidak ada perbedaan yang signifikan secara statistik ($p>0.05$). Apabila dibandingkan dengan individu normal, peningkatan ekspresi hnRNP-E2 terjadi pada 50% sampel pasien fase kronik dan 40% sampel pasien fase *blast crisis*.
Kesimpulan : Tidak terdapat perbedaan rerata tingkat ekspresi gen hnRNP-E2 yang signifikan pada pasien CML fase kronik dan fase *blast crisis*.
Kata Kunci : *chronic myeloid leukemia*, *blast crisis,* hnRNP-E2

ABSTRACT

EXPRESSION LEVEL OF HETEROGENOUS NUCLEAR RIBONUCLEOPROTEIN E2 (hnRNP-E2) GENE ON CHRONIC MYELOID LEUKEMIA (CML) PATIENTS AT CHRONIC PHASE AND BLAST CRISIS PHASE IN SARDJITO HOSPITAL, YOGYAKARTA

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Background: Chronic Myeloid Leukemia (CML) is a hematological malignancy characterized by increasing number of mature granulocyte at chronic phase (CML-CP), and having ≥20% of immature blast cells at blast crisis phase (CML-BC). Approximately 50% of CML cases of the chronic phase will directly progress into blast crisis without passing through the accelerated phase (CML-AP). Philadelphia (Ph) chromosome can be found in more than 90% CML cases as the consequences of chromosome translocation (9 and 22) result in BCR-ABL fusion gene. BCR-ABL fusion gene induce some signaling pathways including RAS pathway. Activated RAS will induce MAPK – ERK 1/2 activation. The ERK phosphorylation induce cell proliferation and inhibit apoptosis, and also increase the expression, translation, and stability of hnRNP-E2. Increased hnRNP-E2 activity will result in blast cells accumulation in CML, therefore it is considered as progression marker from CML-CP to CML-BC.
Objective: This study aims to analyze the mean differences of hnRNP-E2 expression level in CML-CP and CML-BC.
Methods: This cross sectional study evaluated the mean differences of hnRNP-E2 expression in CML-CP (n=10) and CML-BC (n=10). cDNA samples of CML patients with BCR-ABL positive in RSUP Sardjito Yogyakarta (2010 – 2016) at the first time diagnosed were taken from the sample archive of CML umbrella research. The level of hnRNP-E2 expression was measured quantitatively using Real Time-PCR method with RT-PCR ABI 7500 Fast machine.
Results: The level of hnRNP-E2 expression is slightly lower in blast crisis than in chronic phase but there is no significant difference statistically ($p>0.05$). Compared to normal individual, 50% samples showed increasing level of hnRNP-E2 expression in chronic phase and 40% in blast crisis.
Conclusion: There is no significant differences of hnRNP-E2 expression in chronic and blast crisis CML.
Keywords: chronic myeloid leukemia, blast crisis, hnRNP-E2