ABSTRAK

Perbandingan Ekspresi *Circulating* Plasma miRNA-21 dan CA 15-3 Pada Berbagai Stadium Klinis Kanker Payudara

Merlyna Savitri

Latar belakang: Kanker payudara masih menempati peringkat pertama kanker pada wanita di dunia. Beberapa *circulating* biomarker konvensional yang sudah dikenal dan digunakan dalam monitoring dan menilai progresivitas kanker payudara seperti CEA dan CA 15-3 memiliki keterbatasan karena sensitivitas dan spesifisitas yang rendah. MicroRNA (miRNA) suatu *non-coding* RNA endogen dengan panjang 22-25 nukleotida, gen targetnya adalah kelompok gen tumor supresor, sehingga miRNA-21 dapat meregulasi proliferasi sel, transformasi neoplastik, migrasi sel, dan menurunkan apoptosis sel. *Circulating* biomarker baru seperti miRNA-21 menunjukkan peran yang besar dalam hal monitoring progresivitas kanker payudara.
Tujuan: Menganalisis perbandingan antara ekspresi *circulating* miRNA-21 dan CA 15-3 pada berbagai stadium klinis kanker payudara.
Metode: Dilakukan pengukuran ekspresi *circulating* plasma miRNA-21 dan CA 15-3 pada 49 pasien kanker payudara berbagai stadium dan 16 kontrol orang sehat menggunakan metode qRT-PCR dengan miRNA-16 sebagai kontrol endogen. Nilai ekspresi relatif miRNA-21 dihitung dengan formula $2^{-\Delta\Delta Ct}$. Hasil ekspresi *circulating* plasma miRNA-21 dan CA 15-3 dibandingkan dengan kontrol pada setiap stadium dan antar stadium kanker payudara.
Hasil: Median kadar CA 15-3 pada kelompok kanker payudara secara signifikan lebih tinggi 1,60 kali dibandingkan dengan kelompok kontrol (p=0,019), masing-masing 21,00 u/ml (4,73-3000) dan 13,05 u/ml (5,2-19,9). Median ekspresi miRNA-21 pada kelompok kanker payudara secara signifikan lebih tinggi 4,92 kali dibanding kelompok kontrol (p=0,001), masing-masing 4,43 (1,11-32,22) dan 0,90 (0,16-4,53). CA 15-3 tidak bermakna pada perbandingan antara kontrol dengan semua stadium kanker payudara dan antar stadium pada kelompok kanker payudara. Ekspresi *circulating* miRNA-21 bermakna pada perbandingan antar kontrol dengan kanker payudara stadium 1 (p=0,003), stadium 2 (p=0,001), dan stadium 4 (p=0,030). Nilai *cut-off* CA 15-3 sebesar 15,05 u/ml (p=0,016) dengan sensitivitas 59,2% dan spesifisitas 62,5%. Nilai *cut-off* ekspresi *circulating* miRNA-2 2,07 (p=0,000) dengan sensitivitas 91,8% dan spesifisitas 87,5%.
Kesimpulan: Kadar CA 15-3 dan ekspresi *circulating* plasma miRNA-21 secara signifikan meningkat pada pasien kanker payudara dibandingkan dengan orang sehat. Terdapat peningkatan kadar CA 15-3 dan ekspresi miRNA-21 seiring bertambahnya stadium kanker payudara. MiRNA-21 merupakan suatu biomarker baru non-invasif yang potensial lebih baik dalam mendiagnosis dan memprediksi progresivitas kanker payudara dibandingkan CA 15-3.
Kata kunci: kanker payudara, stadium klinis, miRNA-21, CA 15-3.

ABSTRACT

Comparison of Circulating Plasma miRNA-21 and CA 15-3 at Various Clinical Stages of Breast Cancer

Merlyna Savitri

Background: *Breast cancer is still the first rank of women's cancer in the world. Conventional circulating biomarkers that are already known and used in monitoring and evaluating the progression of breast cancer such as CEA and CA 15-3 have limitations due to their low sensitivity and specificity. MicroRNA (miRNA) and non-coding endogenous RNA with a length of 22-25 nucleotides, the target gene is a group of tumor suppressor genes, so that miRNA-21 can regulate cell proliferation, neoplastic transformation, cell migration, and decrease cell apoptosis. MiRNA-21 as a circulating biomarker have a big role in monitoring the progression of breast cancer.*

Objective: *Analyzing the comparison between the expression of circulating miRNA-21 and CA 15-3 in various clinical stages of breast cancer.*

Methods*: Circulation expression of miRNA-21 and CA 15-3 in plasma was measured in 49 patients at various stages of breast cancer and 16 healthy controls using the qRT-PCR method with miRNA-16 as endogenous control. The relative expression value of miRNA-21 was calculated by the formula* $2^{-\Delta\Delta Ct}$*. The results of miRNA-21 and CA 15-3 plasma circulating expression were compared with controls at each stage and between stages of breast cancer.*

Results: *The median level of CA 15-3 in the breast cancer group was significantly higher 1.60 times compared to the control group (p=0.019), respectively 21.00 u/ml (4.73-3000) and 13.05 u/ml (5.2-19.9). The median expression of miRNA-21 in the breast cancer group was significantly higher 4.92 times compared to the control group (p=0.001), respectively 4.43 (1.11-32.22) and 0.90 (0,16-4,53). CA 15-3 was not significant in the comparison between controls with all stages of breast cancer and between stages in the breast cancer group. The expression of circulating miRNA-21 was significant in the comparison between controls with stage 1 breast cancer (p=0.003), stage 2 (p=0.001), and stage 4 (p=0.030). CA 15-3 cut-off value of 15.05 u/ml (p = 0.016) with a sensitivity of 59.2% and specificity of 62.5%. The cut-off value of circulating miRNA-2 expression is 2.07 (p=0,000) with a sensitivity of 91.8% and a specificity of 87.5%.*

Conclusions: *CA 15-3 levels and miRNA-21 plasma circulating expression were significantly increased in breast cancer patients compared to healthy people. There is an increase in CA levels 15-3 and miRNA-21 expression with increasing stage of breast cancer. MiRNA-21 is a new non-invasive biomarker that is potentially better at diagnosing and predicting the progression of breast cancer than CA 15-3.*

Key words: *breast cancer, clnical stage, miRNA-21, CA 15-3.*