PROFIL MIKRO RNA RESPON IMUN MAKROFAG PADA PLASMA DARAH SUKARELAWAN SEHAT DENGAN PERLAKUAN PAPARAN MEDAN LISTRIK STATIS FREKUENSI MENENGAH DAN INTENSITAS RENDAH

INTISARI

Latar Belakang. Saat ini masih diperlukan pengobatan atau terapi kanker payudara yang lebih efektif dan murah. Kemoresistensi, kekambuhan, dan metastasis masih menjadi masalah besar pada terapi kanker termasuk kanker payudara. Salah satu terapi kanker yang sedang dalam pengujian yakni menggunakan medan listrik statis berupa rompi *electro-capacitive cancer therapy* (ECCT). Melalui uji praklinis telah dilaporkan ECCT mampu menghambat pertumbuhan sel kanker dan menjadi terapi kanker komplemen yang menjanjikan serta dapat mengurangi efek samping terapi kemoresistensi. Mekanisme ECCT dapat menghambat pertumbuhan tumor dapat dikaji dari sudut pandang epigenetik yakni dari ekspresi *miRNA*. Molekul *miRNA* juga dapat digunakan sebagai penanda biologis salah satunya dalam aktivitas peningkatan respon imun makrofag. Adanya perubahan *miRNA* kemungkinan berpengaruh terhadap perubahan dari aktivitas makrofag, khususnya dalam paparan ECCT.

Tujuan Penelitian. Mengetahui perubahan profil ekspresi *miRNA* terkait respon imun makrofag M1 (*Hsa-miR-19a-3p, Hsa-miR-146a-5p*) dan M2 (*Hsa-let-7a-5p, Hsa-miR-21-5p, Hsa-miR-27a-3p Hsa-miR-223-3p*) dengan paparan medan listrik ECCT pada wanita sukarelawan sehat. Serta menganalisis pengaruh perubahan *miRNA* secara *in silico* terhadap jumlah gen yang ditarget melalui jalur persinyalan *Foxo* dan *TGF-β*.

Metode Penelitian. Masa perlakuan penggunaan ECCT berlangsung selama 21 hari dengan jadwal pemakaian rompi ECCT 10 jam per hari dengan jeda 4 jam setelah 5 jam pemakaian pertama dan pemeriksaan klinis total sebanyak dua kali yaitu pre dan post paparan. Sebanyak 5 mL plasma darah dari 8 sukarelawan diambil *pre* dan *post* perlakuan ECCT, selanjutnya dilakukan isolasi total RNA untuk digunakan dalam sintesis cDNA. Metode pengujian profil *miRNA* menggunakan qRT-PCR. Hasil kemudian di analisis dengan perangkat lunak Biorad CFX 96 Manager™, metode livak dan analisis *in silico* menggunakan *software* berbasis *web* seperti *DIANA Mirpath v.3*.

Hasil. Hasil analisis kuantifikasi qRT-PCR menunjukkan tidak ada perubahan signifikan pada ekspresi *miRNA* setelah paparan ECCT. *Heatmap* dari profil ekspresi *miRNA* dianalisis secara *in silico* untuk mengetahui target *miRNA* yang terkait dengan sistem kekebalan tubuh. Pada jalur *Foxo*, *Hsa-miR-19a-3p* mengalami *upregulated* mentarget gen AKT, P13K, PTEN, MAPK, SKG1, IRS1, IGF1R. Sementara itu, jalur utama kelompok *downregulated miRNA* adalah jalur persinyalan *TGF-β*, dengan *miRNA* paling signifikan yaitu *Hsa-miR-27a-3p* mentarget gen THBS1, BAMBI, TGFBR, SMAD7.

Kata kunci: ECCT, *miRNA*, Respon Imun, Makrofag, Sukarelawan Sehat

MICRO-RNA EXPRESSION PROFILE OF MACROPHAGE RESPONSES IN BLOOD PLASMA HEALTHY VOLUNTEERS EXPOSURE TO MEDIUM-FREQUENCY AND LOW-INTENSITY STATIC ELECTRIC FIELD

ABSTRACK

Background. Currently, there is still a need for more effective and inexpensive breast cancer treatment or therapy. Chemoresistance, recurrence, and metastasis are still major problems in cancer therapy, including breast cancer. One of the cancer therapies currently under testing is using an electric field in the form of an electro-capacitive cancer therapy (ECCT) vest. Through preclinical trials, it has been reported that ECCT is able to inhibit the growth of cancer cells and the expected complementary cancer therapy and can reduce the side effects of chemoresistance therapy. The mechanism by which ECCT can inhibit tumor growth can be studied from an epigenetic point of view, namely from *miRNA* expression. *MiRNA* molecules can also be used as biological markers, one of which is in the activity of increasing the immune response of macrophages. The presence of *miRNA* changes may influence changes in macrophage activity, especially in ECCT therapy.

Purposes. Knowing the changes in *miRNA* expression profile related to the immune response of M1 (Hsa-miR-19a-3p, Hsa-miR-146a-5p) and M2 (Hsa-let-7a-5p, Hsa-miR-21-5p, Hsa-miR-) macrophages 27a-3p Hsa-miR-223-3p) with ECCT electric field exposure in healthy female volunteers. As well as analyzing the effect of in silico *miRNA* changes on the number of targeted genes through Foxo and TGF-β signaling pathways.

Methods. The period of use of ECCT lasts for 21 days with ECCT usage time of 10 hours per day with an interval of 4 hours after the first 5 hours of use and a total clinical examination twice, namely pre and post exposure. A total of 5 mL of blood plasma from 8 volunteers was taken before and after ECCT treatment, then total RNA was isolated for use in cDNA synthesis. *MiRNA* profile testing method using qRT-PCR. The results were then analyzed using the Biorad CFX 96 ManagerTM software, the livak method and in silico analysis using web-based software such as DIANA Mirpath v.3.

Results. The results of the qRT-PCR quantification analysis showed no significant changes in *miRNA* expression after ECCT exposure. Heatmaps of *miRNA* expression profiles were analyzed in silico to identify *miRNA* targets associated with the immune system. In the Foxo pathway, Hsa-miR-19a-3p was upregulated targeting the AKT, P13K, PTEN, MAPK, SKG1, IRS1, IGF1R genes. Meanwhile, the main pathway for the downregulated *miRNA* group was the TGF-β signaling pathway, with the most significant *miRNA* being Hsa-miR-27a-3p targeting the THBS1, BAMBI, TGFBR, SMAD7 genes.

Keywords: ECCT, *miRNA*, Immune Response, Macrophages, Healthy Volunteer