

Pengaruh Terapi Medan Listrik Statis Frekuensi Menengah 150 kHz Intensitas Rendah terhadap Pertumbuhan Tumor Mencit dengan Induksi 7,12-
dimethylbenz[a]anthracene

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INTISARI

Kanker merupakan salah satu penyebab kematian terbesar kedua di dunia. Pengobatan kanker biasanya dilakukan dengan kemoterapi, operasi, dan radioterapi namun memiliki efek samping. Sehingga dibutuhkan alternatif terapi yang efektif dan aman. Di Indonesia sedang dikembangkan alat terapi kanker yaitu ECCT (*Electro-Capacitive Cancer Therapy*) yang menggunakan medan listrik frekuensi menengah. Penelitian sebelumnya menunjukkan bahwa medan listrik frekuensi menengah ini bersifat aman terhadap sel-sel normal. Penelitian ini bertujuan untuk mengetahui pengaruh terapi medan listrik (ECCT) terhadap pertumbuhan tumor pada mencit dengan menggunakan metode *optical imaging* dengan konfirmasi berdasarkan ekspresi GLUT1, PCNA, dan Caspase-3 pada jaringan hati, dan mengevaluasi efek samping terhadap fungsi hati. Penelitian ini menggunakan mencit galur Swiss sebagai model tumor dengan induksi senyawa DMBA. Mencit dibagi menjadi 4 kelompok, masing-masing dengan ulangan 6 individu, yakni: non induksi-non terapi (NINT), non induksi-terapi (NIT), induksi-non terapi (INT), induksi-terapi (IT). Mencit diinduksi menggunakan senyawa karsinogenik DMBA secara gastrointestinal dengan dosis 20 mg/kgbb sebanyak 10 kali selama 5 minggu. Setelah induksi, mencit diberi perlakuan terapi dan non terapi dengan total waktu perlakuan 10 jam (istirahat 2 jam diantara waktu perlakuan) per hari selama 21 hari. Pertumbuhan tumor dideteksi dengan metode *small animal imaging* (SAI). Setiap 3 hari sebelum *scanning*, mencit diinjeksi IRDye. Mencit di *scan* pada hari perlakuan ke 0, 10, dan 21 dengan alat *small animal imaging*. Pertumbuhan tumor diamati secara *in situ* berdasarkan intensitas fluorescen yang dipancarkan oleh IRDye yang berkonjugat pada protein GLUT 1. Pada hari ke 21 setelah mencit di *scan*, selanjutnya dibedah untuk diambil jaringan hatinya dan disimpan dalam NBF dan RNA Later. Ekspresi mRNA GLUT1 dan PCNA dianalisis menggunakan metode qRT-PCR. Proliferasi dan apoptosis sel tumor dideteksi menggunakan anti-PCNA dan anti-Caspase-3. Penurunan intensitas fluorescent pada tumor imaging selaras dengan penurunan ekspresi mRNA GLUT1 dan PCNA pada jaringan hati. Hasil ini telah dikonfirmasi dari ekspresi protein PCNA dan protein caspase-3 pada tumor hati mencit dengan metode hematoxilin dan eosin serta imunohistokimia. Fungsi hati diuji berdasarkan aktivitas alanine transaminase (ALT) serum darah. Hasil menunjukkan jaringan hati mencit kelompok induksi terapi mengalami penurunan ekspresi PCNA sebanyak 12,96% dan mengalami peningkatan ekspresi caspase-3 sebanyak 6.71%. Uji aktivitas ALT menunjukkan tidak ada perubahan secara signifikan pada perlakuan terapi. Kesimpulan dari penelitian ini yakni perlakuan medan listrik ECCT mampu menghambat dan menurunkan pertumbuhan tumor hati pada mencit dan masih relatif aman terhadap fungsi hati.

Kata Kunci : mencit, tumor, medan listrik, proliferasi, apoptosis.

Effect of Electric Field Therapy using Intermediate Frequency 150 kHz Low Intensity on the Growth of Tumor in Mice Induced by *7,12- dimethylbenz[a]anthracene*

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ABSTRACT

Cancer is one kind of disease which causing death in the world. Treatment that usually used to cure cancer are chemotherapy, surgery, and radiotherapy, but it has a side effect. So new and safe alternative therapy is needed. In Indonesia, ECCT (Electro-Capacitive Cancer Therapy) which used electric field with middle frequency was developed as a treatment for cancer. In the previous research showed that electric field therapy with intermediate frequency safe for normal cell. Therefore, this research is needed to find out the effect of ECCT on cancer growth in tumor mice model with optical imaging method by confirmation based on GLUT1, PCNA, and Caspase-3 expression in liver tissue and evaluate side effect of the therapy in liver function. Swiss strain mice used as a tumor model induced by DMBA. Mice divided into 4 group of 6 individuals: no induction – non therapy (NINT), no induction –therapy (NIT), induction – non therapy (INT), and induction therapy (IT). The mice induced by carcinogenic compound DMBA gastrointestinally with dosage 20 mg/bodyweight, 10 times for 5 weeks. After being induced, mice were given therapy and non-therapy treatment conduct for 10 hours/day with 2 hours rest between the treatments for 21 days. The growth of tumor observed with small animal imaging method. Every 3 days before scanning, the mice injected by IRDye 800CW. All the mice scan by small animal imaging on day 0, 10, and 21. The growth of tumor observed by it size which quantified in fluorescence intensity as a pixel unit, by the intensity fluorescence that emitted by IrDye which conjugated with GLUT1 protein in a tumor cell. In the 21th day, after the scanning the mice will be dissected to take the liver tissue and store it in NBF and RNA Later. The expression of GLUT1 and PCNA analyzed by qRT-PCR method. Proliferation and Apoptosis of tumor cell detected by anti-PCNA and anti-Caspase-3. Liver function was analyzed by ALT activity. Gradual decreases of tumor image intensity counts were related to the relative mRNA expression of GLUT1 and PCNA in liver tissue. It is confirmed by PCNA and Caspase-3 protein expression in liver tissue which analyzed with HE and IHC method. Liver tissue IT group undergone 12.96% decrease of PCNA expression and 6.71% increase of caspase-3 expression. ALT activity did not show significant different for therapy group. In conclusion, electric field exposure was able to inhibit the growth of mouse liver tumors and it save for liver function.

Keywords : mice, tumor, electric field, protein marker, caspase