RINGKASAN

PENGARUH PAPARAN MEDAN MAGNET *EXTREMELY LOW FREQUENCY (ELF)* DENGAN INTENSITAS 20 – 32 μT TERHADAP MODULASI IMUNITAS PADA MENCIT BALB/C

Sudarti

Penelitian ini adalah penelitian eksperimental. mencit Balb/C secara in vivo dipapa medan magnet ELF pada intensitas 20 – 32 μ T, secara intermiten 8 jam/hari selama 15 hari dan 30 hari. Paparan medan magnet ELF bersifat tak terhalangi, maka secara langsung dapat berinteraksi sel, dilaporkan dapat menimbulkan stress cells (Golfert, 2001), dan mempengaruhi terhadap perilaku sel (Lee, 2000). Oleh karena itu penelitian ini menggunakan paradigma patobiologi dengan konsep *stress cells*. Paparan medan magnet ELF dalam penelitian ini dipandang sebagai *stressor*, sementara sel mengalami stres adalah sel imunokompeten. Diduga sel T dan sel B termasuk sel imunokompeten mengalami stres. Oleh karena itu penelitian ini dilakukan untuk mengungkap mekanisme modulasi imunitas sel imunokompeten yang stres pada mencit Balb/C yang di papar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam per hari selama 15 hari dan 30 hari, mengingat sistem imun memegang peranan penting pada mekanisme pertahanan tubuh terhadap berbagai penyakit, termasuk perkembangan berbagai tumor atau kanker.

Perilaku sel T dan sel B yang stres dicerminkan oleh perubahan komponen, sitokin atau imunoglobulin yang dihasilkannya. Oleh karena itu sebagai variabel perubahan perilaku sel T adalah IFN-gamma untuk sel Th1, dan IL-10 untuk sel Th2,

sementara IgG dan IgM untuk sel B. Pemeriksaan terhadap Il-10, IFN-gamma, IgG, dan IgM dilakukan melalui pemeriksaan secara morfofungsi dengan menggunakan metode imunohistokimia. Analsis hasil penelitian ini menggunakan analisis multivariat, mengingat modulasi imunitas merupakan perubahan biologis sistem imun sebagai akibat interaksi dari semua variabel terkait. Analisis diskriminan dilakukan untuk mendapatkan variabel diskriminator (variabel dominan yang berperan sebagai pembeda) atas modulasi imunitas suatu individu termasuk dalam kelompok terpapar medan magnet ELF selama 15 hari atau 30 hari. Selanjutnya dibangun pola diskriminan yang mencerminkan kontribusi fungsi setiap diskriminator terhadap proses modulasi imunitas pada mencit Balb/C yang dipapar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam per hari selama 15 hari dan 30 hari.

Berdasarkan hasil analisis *multivariate analysis of variance (Manova)* menunjukkan bahwa hasil pengamatan antara peneliti dan pengamat konsisten, maka untuk analisis selanjutnya digunakan data hasil pengamatan peneliti yang secara statistik berdistribusi secara normal (uji *Kolmogorov Smirnov*, $p > \alpha$; $\alpha = 0{,}05$). Hasil uji pengaruh maturasi, menunjukkan bahwa perubahan pada ke empat variabel penelitian tidak dipengaruhi oleh proses maturasi baik selama 15 hari maupun selama 30 hari. Hasil penelitian ini menyatakan bahwa terjadi modulasi imunitas pada mencit Balb/C yang dipapar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam/hari baik selama 15 hari maupun 30 hari, yang dicerminkan oleh peningkatan persentase jumlah limfosit penghasil IL-10 dan prosentase jumlah sel

plasma penghasil IgM secara signifikan ($p < 0,05$), yang disertai dengan penurunan persentase jumlah limfosit penghasil IFN-gamma dan prosentase jumlah sel plasma penghasil IgG secara ignifikan ($p < 0,05$). Hasil analisis diskriminan menunjukkan bahwa, variabel IgM dan IFN gamma sebagai diskriminator yang dapat digunakan untuk membedakan kedua kelompok perlakuan tersebut. Berdasarkan pola diskriminstor, tampak bahwa kontribusi IFN-gamma maupun IgM dalam modulasi imunitas mencit Balb/c yang di papar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam perhari meningkat baik setelah paparan baik selama 15 hari maupun 30 hari adalah meningkat. Kontribusi IgM tampak lebih dominan pada modulasi imunitas 15 hari, sementara kontribusi IFN-gamma lebih dominan pada modulasi imunitas 30 hari. Peningkatan modulasi imunitas pada mencit Balb/c setelah di papar medan magnet ELF selama 15 hari, menjadi turun setelah paparan selama 30 hari. Kontribusi IFN-gamma maupun kontribusi IgM tampak menurun pada modulasi imunitas 30 hari, kontribusi IgM menurun menjadi 1/5 dan kontribusi IFN-gamma menurun menjadi ½. Hal ini diduga bahwa terjadi respons imunodefisiensi pada mencit Balb/c yang dipapar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam perhari setelah paparan selama 30 hari.

Berdasarkan uraian tersebut, dapat disimpulkan bahwa terjadi respons menuju *adaptation stage* pada mencit Balb/C setelah terpapar medan magnet ELF pada intensitas 20 – 32 μ T secara intermiten 8 jam/hari selama 15 hari yang dicerminkan oleh peningkatan modulasi imunitas pada kelenjar getah bening, namun terjadi respons *exhausted* dalam bentuk *imunodefisiensi* yang dicerminkan oleh

penurunan modulasi imunitas setelah paparan selama 30 hari. Tampak bahwa penurunan IFN-gamma baik pada kelompok terpapar 15 hari maupun 30 hari ternyata memberikan kontribusi yang tinggi pada modulasi imunitas mencit Balb/c setelah di papar medan magnet ELF baik selama 15 hari maupun 30 hari.

Mekanisme modulasi imunitas pada mencit Balb/c yang dipapar medan magnet ELF pada intensitas 20 - 32 μ T secara intermiten 8 jam/hari selama 15 hari dan 30 hari adalah melalui stress sel T, yang dicerminkan oleh peningkatan Ca2+ sitosol. Peningkatan Ca^{2+} sitosol akan meningkatkan ikatan Ca^{2+} - calmodulin dan terbentuk komplek Ca^{2+}-calmodulin di sitoplasma. Ikatan Ca^{2+}-calmodulin tersebut mengaktivasi *calcineurin*, dan Calcineurin yang telah diaktivasi oleh ikatan Ca^{2+}-calmodulin kemudian mendefosforolasi proteinndari NF-ATc (*nuclear factor of activated T-cell cytoplasmic*). NF-ATc yang kehilangan fosfat akan menembus menbran inti dan mengikat *enhancer*. Ikatan NF-AT terhadap *enhancer* akan memicu terjadinya transkripsi gen sitokin, sehingga terjadi translasi yang dapat mengakibatkan sel Th2 memproduksi IL-10, sehingga jumlah sel T penghasil IL-10 meningkat. Peningkatan IL-10 akan menghambat aktivitas sel Th1 untuk memproduksi IFN-gamma, sehingga jumlah sel T penghail IFN-gamma menurun. Penurunan IFN-gamma berpengaruh pada penurunan aktivasi terhadap sel plasma untuk melakukan switching rantai μ ke rantai γ, sehingga terjadi akumulasi IgM dan penurunan produksi IgG.

SUMMARY

THE INFLUENCE OF MAGNETIC FIELD EXPOSURE OF *EXTREMELY LOW FREQUENCY (ELF)* WITH 20 – 32 μT INTENSITY TOWARD IMMUNITY MODULATION OF BALB/C MICE

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This is an experimental research of Balb/C mice by in vivo exposed on *extremely low frequency* (ELF) magnetic field with 20 – 32 μT intensity 8 hour/day intermitently for 15 days and 30 days. ELF magnetic field exposure has unobstructive characteristic, so direct interaction of cell could happen. It is reported that the condition can cause stress cell (Golfret, 2001) and influences cell behaviour (Lee, 2000). Understanding the condition, the research used pathological paradigm with *stress cell* concept in which ELF magnetic field exposure plays as *stressor* while cell experiencing stress are immunocompetent cell. It is assummed that T cell and B cell are immunocompetent cell which face a certain stress. Therefore the research is conducted to investigate the mechanism of immunity modulation on immunocompetent cell facing stress of Balb/C mice exposed on *extremely low frequency* (ELF) magnetic field with 20 – 32 μT intensity 8 hour/day intermitently for 15 days and 30 days with special consideration on the fact that immune system plays important role on the mechanism of body resistance toward any diseases including the development of tumour or cancer.

Behavior of stress cell on T cell and B cell is indicated by the alteration of component as cytokine and immunoglobuline produced. Accordingly the altering variable of T cell behaviour is IFN gamma for Th1 cell , and IL-10 for Th2, while IgG and IgM for B cell. Observation to Il-10, IFN-gamma, IgG, and IgM are conducted through morphofunctional observation using immunohistochemical method. Multivariat examination is used for data analysis by considering that immunity modulation is biological changing of immune system as a result of interaction of all related variables. Discriminant analysis is conducted to get discriminator variable which can be used to classify whether one belong to which group of treatment; 15-day or 30-day exposure of ELF magnetic field. Later discriminant pattern illustrating the constribution of all discriminators to the process of immunity modulation of Balb/C mice is developed.

Result of analysis using *multivariate analysis of variance (Manova)* shows that there is a consistency between reseacher observation and observer examination, so the next analysis could use the data from researcher observation which statistically has normal distribution (*Kolmogorov Smirnov Test*, $p > \alpha$; $\alpha = 0{,}05$). The result of masturation influence test indicates that alternation on four research variables are not influenced by the process of masturation even for 15 days or 30 days. Research result states that immunity modulation is happened on Balb/C mice exposed on ELF magnetic field with 20 – 32 μ T intensity 8 hour/day intermittently for 15 days or 30 days, represented by the significant increase ($p < 0{,}05$) of lymphocite producing IL-10 and the percentage of the number of plasma cell producing IgM together with

decreasing percentage significantly ($p < 0,05$) of the number of lymphocite producing IFN-gamma and the percentage of plasma cell producing IgG. The result of discriminant analysis shows that IgM and IFN-gamma variables be as disciminator which can be used to classify the two group of treatments. The pattern of discriminator indicates that IFN-gamma and IgM contribution on immunity modulation of Balb/C mice exposed on ELF magnetic field with 20 – 32 μ T intensity 8 hour/day intermittently for 15 days or 30 days is increased. IgM constribution seems more dominant on immunity modulation of 15 days while participation of IFN-gamma has its dominance on 30 days immunity modulation. The increased immunity modulation on Balb/C mice after exposed on ELF magnetic field for 15 days decreases on their 30-day exposure. IFN –gamma and IgM contribution seems decreased on 30 days immunity modulation in which IgM contribution becomes 1/5 and IFN-gamma to ½. This is assummed that the response of imunodeficiency is occurred on Balb/C mice exposed on ELF magnetic field with 20 – 32 μ T intensity 8 hour/day intermittently after 30 days exposure.

From above explanation, it can be concluded that the response to adaptation stage is occurred on Balb/C mice after exposed on ELF magnetic field with with 20 – 32 μ T intensity 8 hour/day intermittently for 15 days, which is indicated by the increase of immunity modulation on lymphnode but exhausted response happened in the form of immunodeficiency represented by decreasing immunity modulation after 30 days exposure. The decreasing of IFN-gamma both on two group of treatments; 15

days and 30 days exposure, gives the highest contribution on immunity modulation of Blab/C mice.

Mechanism of immunity modulation of Balb/C mice exposed on ELF magnetic field with with 20 – 32 μ T intensity 8 hour/day intermittently for 15 days and 30 days are through T cell stress, indicated by the increase of Ca2+ cytosol. Increasing Ca^{2+} cytosol would strengthen the bond of Ca^{2+} -calmodulin and Ca^{2+}-calmodulin complex would be formed in cytoplasma. The bond of Ca^{2+}-calmodulin will activate *calcineurin*, and Calcineurin activated by Ca^{2+}-calmodulin bond, later will dephospolarate protein of NF-ATc (*nuclear factor of activated T-cell cytoplasmic*). NF-ATc which loses its phospat will perforate the core membrane and bind *enhancer*. NF-AT on *enhancer* will initiate the process of cytokine gene transcription, so translation causing Th2 cell to produce IL-10 will occur, and the number of T cell producing IL-10 will increase. Increasing IL-10 will obstruct the activity of Th1 cell to produce IFN-gamma that leads to decreasing number of T cell producing IFN-gamma. Decreasing IFN-gamma influences the activation of plasma cell to do chain switching from μ to γ, so accummulation of IgM and decreasing production of IgG will happen.

ABSTRACT

THE INFLUENCE OF MAGNETIC FIELD EXPOSURE OF *EXTREMELY LOW FREQUENCY (ELF)* WITH 20 – 32 μT INTENSITY ON IMMUNO MODULATION OF BALB/C MICE

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The objective of the study is to reveal the mechanism of immuno modulation on Balb/C mice wich were exposed to extremely low frequency magnetic field with 20 – 32 μT intensity 8 hour/day intermitently for 15 days and 30 days. The variable used in this study are IL-10, IFN-gamma, IgG, and IgM detected by using immunohistochemical method.

The 15-day exposure in mice with extremely low frequency magnetic field with 20 – 32 μT intensity showed a significance corelation with immuno modulation, reflected by the increase of IL-10 and IgM along with the decrease on IFN-gamma and IgG values. The increased IL-10 may posibly inpair the activity of Th1 cell in produce IFN-gamma, cousing the decrease of number of T cell producing IFN-gamma. The decrease in IFN-gamma may influence the activation of plasma cell to produce immunoglobulin by switching the μ to γ chain, hence the accummulation of IgM and decreased production of IgG.

However the decreased IL-10 and IgM and the increased IFN-gamma and IgG occured only after exposure for 30 days. The immuno modulation remain following Th1 and Th2 balance although in decreasing quality. IFN-gamma and IgM contribution seems to decrease after 30-days exposure respectively 50% and 20%.

The result of the study reveals that the mechanism of immuno modulation after exposure for 15 days is still in the adaptation stage, meanwhile the exhausted stage in the form of immunodeficiency posibly occur only after 30-day exposure.

Keywords: *extremely low frequency magnetic fields, exhausted stage, adaptation stage, immunodeficiency, Immuno Modulation*

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