INTISARI

Pendahuluan. Hewan model digunakan untuk mempelajari patogenesis dan mengembangkan terapi berbagai penyakit, salah satunya kanker mammae. Penggunaan mencit sebagai hewan model kanker mammae memiliki keuntungan yaitu lebih hemat bahan uji dan biaya pemeliharaan yang lebih murah dibandingkan tikus.
Tujuan. Penelitian ini bertujuan untuk membandingkan metode induksi DMBA dan kombinasi DMBA dengan estrogen pada mencit berdasarkan kecepatan timbulnya nodul dan diameter nodul, jumlah nodul/ekor serta tipe gambaran histopatologi kanker mammae yang dihasilkan.
Metode. Mencit BALB/c betina, dibagi menjadi 5 kelompok induksi DMBA yaitu kontrol, DMBA oral (DMBA O), DMBA oral-estrogen (DMBA O-E), DMBA subkutan (DMBA S), DMBA subkutan-estrogen (DMBA S-E), masing-masing terdiri dari 5 ekor mencit. Pemeriksaan berat badan dan nodul dilakukan setiap minggu. Saat terminasi nodul diambil untuk dilakukan pemeriksaan histopatologi menggunakan pewarnaan *hematoxylin-eosin* (HE) dan imunohistokimia menggunakan antibodi anti reseptor estrogen, reseptor progesteron dan CD3 untuk mengamati sel T. Analisis statistika perubahan berat badan menggunakan *one way ANOVA*, diameter nodul dan jumlah nodul/ekor dianalisis menggunakan Kruskal Wallis, dengan nilai $p \leq 0,05$ dianggap signifikan secara statistika.
Hasil. Pada saat terminasi minggu ke-7 jumlah mencit hidup kelompok DMBA S paling rendah diantara kelompok lainnya (2/5). Pada minggu ke-7 terdapat perbedaan berat badan (p=0,026), diameter nodul (p=0,033), jumlah nodul/ekor (p=0,014). Kelompok DMBA S-E memiliki rerata berat badan paling tinggi (36,5 $\pm$ 3,69 gram), rerata jumlah nodul/ekor paling banyak yaitu (1,6 $\pm$ 0,40 nodul/ekor), diameter nodul/ekor paling besar, yaitu (11,12 $\pm$ 1,64 mm). Pada kelompok DMBA O dan DMBA O-E sampai waktu terminasi (minggu ke-20) tidak dijumpai adanya nodul di glandula mammae area abdomen. Tetapi, ditemukan nodul kanker mammae di area *cervical* pada kelompok DMBA O-E (1/5). Pemeriksaan histopatologi menunjukkan, nodul pada DMBA S, dan DMBA S-E merupakan infiltrasi sel radang yang membentuk massa berkapsul namun terwarnai negatif CD3. Pada DMBA O, DMBA S dan DMBA S-E terdapat epitel yang hiperplasia dan nukleus yang hiperkromatik, sedangkan nodul kanker mammae yang ditemukan pada DMBA O-E mengindikasikan keganasan tipe *solid adenokarsinoma* subtipe RE+/RP-. Secara umum ekspresi reseptor estrogen dan reseptor progesteron pada jaringan mammae area abdomen kelompok perlakuan lebih tinggi dibandingkan kontrol.
Kesimpulan. Kombinasi induksi DMBA subkutan dan estrogen pada mencit mampu menghasilkan nodul pertama lebih cepat, rerata diameter nodul lebih besar dan rerata jumlah nodul/ekor lebih banyak, namun nodul tidak mengindikasikan kanker mammae. Kombinasi induksi DMBA oral dan estrogen menghasilkan kanker mammae dengan tipe *solid adenokarsinoma* subtipe *RE+/RP-*.
Kata kunci: Kanker mammae, DMBA, estrogen, BALB/c

ABSTRACT

Introduction. Animal model is used to learn pathogenesis and therapy development for any diseases, especially mammary cancer. Mice as mammary cancer animal model has advantages, such as less material using and cost-effective in maintenance.
Objective. This study aims to develop mouse model for breast cancer, by comparing different method of DMBA and estrogen induction, based on first nodules appearance, nodules diameter, nodules quantity and histopathological examination.
Methods. Five weeks of virgin female BALB/C divided into 5 groups, control (NC), oral-induced DMBA (DMBA O), combination of oral-induced DMBA and estrogen (DMBA O-E), subkutan-induced DMBA (DMBA S), combination of subkutaneous-induced DMBA and estrogen (DMBA S-E). Body weight measurement and nodule palpation was done weekly. Hematoxylin-eosin and immunohistochemistry stainings for detection of Estrogen receptor (ER), progesteron receptor (PR) and CD3 (T lymphocyte) was performed on the nodules. One-way ANOVA continued with post-hoc test were used to compare average body weight, Kruskal Wallis test was used to analyze diameter of nodules and number of nodules/head. The p value $\leq$0.05 was considered as statistically significant.
Results. Statistical analysis was done in the 7th week. The survival rate of DMBA S was the lowest among the other groups (2/5). We observed, differences in average body weight (p=0.026), nodule diameter (p=0.033), nd number of nodules/head (p=0.014). The DMBA S-E group had the highest average weight (36.5 $\pm$ 3.69 grams), number of nodules/head (1.6 $\pm$ 0.40 nodules/head) and average nodules diameter (11.12 $\pm$ 1.64 mm), compared to other groups. On the termination time (20th week), DMBA O and DMBA O-E groups showed no nodules in the mammary glands of the abdominal area. However, mammary cancer nodule was found in the cervical area of the DMBA O-E group (1/5). Histopathological examination showed that nodules in DMBA S, and DMBA S-E were encapsulated inflammatory cells infiltrates, with CD3-. Hyperplastic epithelial and hyperchromatic nucleus were observed in the nodules of mice with DMBA O, DMBA S and DMBA S-E. However, breast cancer nodule was found in DMBA O-E indicating malignant type of adenocarcinoma subtype ER+/PR-. In general, expression of estrogen receptor and progesterone receptor in abdominal mammary gland of treatment group was higher compared to control group.
Conclusion. The combination of subkutaneous DMBA induction with estrogens in mice was able to produce the first nodules more rapidly, with larger diameter of nodule, and higher numbers of nodules/head compared to others. Combination of oral DMBA and estrogen induction in BALB/c produced mammary cancer, solid adenocarcinoma with ER+/PR- subtype.
Keywords: Mammary cancer, DMBA, estrogen, BALB/c