INTISARI

Latar Belakang: Pencegahan kanker payudara masih perlu ditingkatkan. Restriksi kalori diduga dapat mencegah terjadinya kanker payudara melalui peningkatan autofagi dan penurunan sintesis lipid. Tepung garut mengandung tinggi serat sehingga berpotensi untuk restriksi kalori.

Tujuan Penelitian: Penelitian ini bertujuan melihat efek restriksi kalori menggunakan tepung garut dalam diet terhadap tumorigenesis payudara tikus yang diinduksi DMBA dan mekanismenya yang berkaitan dengan metabolisme lipid dan autofagi.

Metode: Sebanyak 25 ekor tikus SD dirandomisasi menjadi 5 kelompok yaitu 1) kontrol pakan standar AIN93 *ad libitum* tanpa DMBA, 2) pakan standar *ad libitum* dengan DMBA 20mg/kgBB 2 kali seminggu selama 5 minggu, 3) DMBA dengan pakan tepung garut 30%, 4) DMBA garut 45% dan 5) DMBA garut 60%. Pemeriksaan adanya nodul, dilakukan setiap 7 hari sekali selama 22 minggu. Pengukuran berat badan dilakukan setiap 2 minggu sekali. Pada minggu ke_29, darah diambil dari orbita untuk pemeriksaan kadar glukosa darah dan profil lipid. Jaringan payudara/tumor dilakukan pemeriksaan histologi untuk mengetahui *grading* dan tipe tumor dengan pewarnaan HE. Pemeriksaan penanda proliferasi (Ki67), invasif (p63), ekspresi protein ER, PR, HER2, dan autofagi (Beclin1, LC3B, p62) dengan imunohistokimia, dan pemeriksaan kuantitatif *Real Time* PCR untuk ekspresi mRNA SREBP1 dan HMGCR.

Hasil: Pemberian diet tepung garut pada tikus yang diinduksi DMBA dibandingkan dengan DMBA pakan standar menunjukkan: berat badan di awal dan selama perlakuan tidak berbeda namun diakhir perlakuan berat badan kelompok garut 60% lebih baik dibanding DMBA pakan standar. Kadar glukosa dan profil lipid tidak ada perbedaan, namun terdapat penurunan insiden dan multiplisiti tumorigenesis payudara yaitu 4 ekor tikus dari kelompok DMBA pakan standar, 2 ekor pada DMBA garut 30% dan 1 ekor pada DMBA garut 45% terdapat kanker. Pada kelompok garut gambaran histopatologi lebih baik, ekspresi p63 lebih tinggi, ekspresi protein Ki67 lebih rendah, ekspresi ER lebih tinggi, PR lebih tinggi, dan HER2 lebih rendah namun tidak signifikan. Ekspresi protein autofagi yaitu Beclin1 signifikan lebih tinggi, tetapi LC3B dan p62 tidak berbeda signifikan. Ekspresi mRNA HMGCR lebih tinggi namun eskpresi SREBP1 tidak ada perbedaan.

Kesimpulan: Pemberian tepung garut 60% dalam diet berpotensi mencegah tumorigenesis payudara melalui mekanisme peningkatan protein inisiator autofagi.

Kata kunci: Restriksi kalori, Kanker payudara, DMBA, Autofagi, SREBP1, HMGCR, *Maranta arundinacea L*

ABSTRACT

Background: Breast cancer prevention still needs to be improved. Caloric restriction is thought to prevent breast cancer by increasing autophagy and decreasing fatty acid synthesis. Arrowroot flour contains high fiber therefore it has the potential for calorie restriction.

Objectives: This study aimed to examine the effect of calorie restriction using arrowroot flour in the diet on DMBA-induced rat breast tumorigenesis and its mechanisms related to lipid metabolism, and autophagy.

Methods: A total of 25 SD rats were randomized into five groups: 1) control standard feed AIN93 ad libitum without DMBA, 2) standard feed ad libitum with DMBA 20mg/kg BW 2 times a week for five weeks, 3) DMBA with 30% arrowroot flour feed, 4) DMBA-arrowroot 45% and 5) DMBA-arrowroot 60%. The examination of nodules was conducted every seven days for 22 weeks. Body weight was measured every two weeks. Blood was taken for measuring lipid profiles and glucose levels on week 29. The breast tissue/tumor was stained Hematoxylin-Eosin to determine the type and grading of histopathology. The proliferative markers (Ki67), invasive marker (p63), expression of ER, PR, HER2, and autophagy (Beclin1, LC3B, p62) were conducted by immunohistochemistry. A Quantitative Real-Time PCR assay was carried out for SREBP1 and HMGCR mRNA expression.

Results: The administration of the arrowroot flour diet in DMBA-induced rats compared with the DMBA standard diet showed body weight at the beginning and during the treatment was not different. However, at the end of the treatment, the bodyweight of the 60% arrowroot group was higher than DMBA standard diet. There was no difference in lipid profiles and glucose levels, but there was a decrease in the incidence and multiplicity of breast tumorigenesis. Four rats from the standard diet DMBA group, two rats of arrowroot DMBA 30%, and one rat of arrowroot DMBA 45% had cancer. In the arrowroot group, the histopathology was better, p63 expression was higher, Ki67 protein expression was lower, ER expression was higher, PR was higher, and HER2 was lower but not significant. The autophagy protein expression of Beclin1 was significantly higher, but LC3B and p62 were not different significantly. HMGCR mRNA expression was higher but there was no difference in SREBP1 expression.

Conclusion: The administration of 60% arrowroot flour in the diet has the potential to prevent breast tumorigenesis through the mechanism of increasing autophagy initiator protein.

Keywords: Calorie restriction, Breast cancer, DMBA, Autophagy, SREBP1, HMGCR, *Maranta arundinacea* L