RINGKASAN

Salah satu penyebab kanker adalah bahan kimia. Benzopirene atau B (a) P adalah senyawa polisiklik aromatik hidrokarbon yang bersifat karsinogenik dan paling sering menyebabkan kanker di rongga mulut. Benzo(a)pyrene (B (a) P) sebagai salah satu penyebab KSSRM diketahui dapat mengekspresikan enzim siklooksigenase 2 (cox–2) yang diduga dapat mengkatalisis oksidasi dari B(a)P – 7,8- diol membentuk B(a)P – 7,8-diol - 9,10-oxide yang merupakan mutagenik karsinogen yang kuat dan reaktif. Nimesulide termasuk golongan OAINS terbaru yang mampu menghambat enzim cox - 2, sehingga dapat bekerja lebih efektif dengan efek samping yang sangat minimal terutama terhadap lambung, hepar dan jantung.

Tujuan penelitian ini adalah untuk dapat menjelaskan efek Nimesulide dalam menghambat pertumbuhan Karsinoma Sel Skuamosa Rongga Mulut (KSSRM) akibat paparan Benzopirene. Dengan meneliti perbedaan ekspresi dan mutasi p53, ras, cox 2 serta apoptosis dan proliferasi sel skuamosa rongga mulut antara kelompok mencit yang mendapat Nimesulide per oral dosis 50 mg/kg bb/hr, 100 mg/kg bb/hr, 200 mg/kg bb/hr dan kontrol.

Pemberian Benzopirene 10 mg/kg bb/hr dilakukan 2 kali seminggu selama 4 minggu dengan paparan di bagian bukal kanan mukosa rongga mulut mencit. Nimesulide diberikan per oral dimulai pada minggu ke 5 sampai minggu ke 12 satu kali setiap hari selama 60 hari. Setiap hari kondisi mencit dipantau. Pada akhir minggu ke 12 mencit dimatikan dan diambil jaringan mukosa rongga mulut dan jaringan yang mengalami perubahan berupa benjolan tumor sebagai spesimen biopsi, untuk dilakukan pewarnaan rutin HE dan pewarnaan imunohistokimia menggunakan antibodi monoklonal p53, ras dan cox 2 dengan teknik Avidin Biotin Complex produk Novo Castra Biotin System. Data penelitian dianalisis dengan Anava jika terdapat perbedaan yang bermakna dilanjutkan dengan uji HSD

Dari penelitian ini didapatkan hasil bahwa peningkatan dosis Nimesulide sebanding dengan peningkatan ekspresi p53 wild dan apoptosis serta berbanding terbalik dengan ekspresi ras mutan, cox 2 dan proliferasi KSSRM. Sehingga Nimesulide dapat digunakan untuk menghambat pertumbuhan Karsinoma Sel Skuamosa Rongga Mulut akibat paparan Benzopirene.

ANALISIS MUTASI GEN RAS DAN P53 PADA KARSINOMA SEL SKUAMOSA RONGGA MULUT AKIBAT BENZOPIRENE DENGAN HAMBATAN SIKLOOKSIGENASE (COX) 2 OLEH NIMESULIDE

SUMMARY

One of the cancer causes is a chemical substance. Benzopyrene or B (a) P constitutes an aromatic and polycyclic hydrocarbon compound which is carcinogenic and the most often causes cancer in oral cavity. Benzo(a)pyrene (B (a) P) as one of the Oral Cavity Squamous Cell Carcinoma (KSSRM) causes can express cycloocigenase enzyme 2 (cox-2) which is supposedly to be able to catalyze oxidation of B(a)P – 7,8-diol forming B(a)P-7,8-diol-9,10-oxide which is the strong and reactive mutagenic carcinogen. Nimesulide is the newest OAINS class that can inhibit cox-2 enzyme so that it can act more effectively with very minimal side effects on gastrointestinal tract, liver and heart.

The objective of the recent research was to explain the effect of Nimesulide in inhibiting the growth of Oral Cavity Squamous Cell Carcinoma induced by Benzopyrene exposure. By investigating a difference in expression and proliferation of p53 wild, ras and the oral cavity squamous cells between mice that received Nimesulide per oral dosage 50 mg/kg /day, 100 mg/kg/day and 200 mg/kg/day and the control group.

The administration of Benzopyrene 10 mg/kg/day was done twice a week for 4 weeks with exposure (im) in the right buccal mucosa of mice's oral cavity. Nimesulide was administered per oral 1 hour after Benzopyrene administration and done once a day for 30 days. The condition of the mice was monitored every day.

At the end of week 12 the mice were killed and their mucosal tissues of the oral cavity were taken for examination. Furthermore, the tissues that underwent a change in the form of tumor protrusion as the biopsy specimen were HE-stained and immunohistochemical-stained using monoclonal antibody p53 wild, ras with Avidin Biotin Complex Technique, the product of Novo Castra Biotin System. This was undertaken to strengthen the staining since they have been amplified. The data were analyzed using *multivariate analysis of variance* (Manova). When a significant difference emerged, this proceeded with Duncan test.

The results showed that an increase in Nimesulide dosage was directly correlated with the increased p53 wild and apoptosis expression and inversely related to ras and proliferation percentage of KSSRM. Thus, Nimesulide can be used to inhibit the growth of Oral Cavity Squamous Cell Carcinoma induced by Benzopyrene exposure.

Keywords: Nimesulide, Benzopyrene, Oral Cavity Squamous Cell Carcinoma