Modulasi Jalur Inflamasi oleh Ko-kemoterapi Kurkumin dan Nanokurkumin terhadap Hepatotoksisitas Cisplatin pada Model Kanker Ovarium Tikus = Modulation of Inflammatory Pathway by Co-chemotherapy Curcumin and Nanocurcumin toward Cisplatin-induced Hepatotoxicity in Ovarian Cancer Rat Model

Ekida Rehan Firmansyah, author

Abstrak

Salah satu obat antikanker yang sekarang paling efektif digunakan sebagai kemoterapi kanker ovarium adalah cisplatin. Namun, cisplatin memiliki banyak efek samping pada berbagai organ, salah satunya hepar. Hepatotoksisitas akibat cisplatin menyebabkan terbatasnya dosis kemoterapi cisplatin. Salah satu faktor kunci patofisiologi kerusakan akut hepar adalah inflamasi. Kurkumin merupakan senyawa alami yang memiliki sifat antiinflamasi tetapi bioavailabilitasnya rendah. Untuk itu, diformulasikan nanokurkumin untuk meningkatkan bioavailabilitasnya. Meskipun begitu, efek kurkumin dan nanokurkumin dalam memodulasi jalur inflamasi hepatotoksisitas akibat cisplatin pada kanker ovarium belum diamati. Penelitian ini bertujuan untuk membandingkan pengaruh kurkumin dan nanokurkumin sebagai ko-kemoterapi terhadap hepatotoksisitas cisplatin dalam jalur inflamasi. Penelitian in vivo dilakukan pada tikus Wistar betina yang diinduksi DMBA untuk mendapatkan model kanker ovarium. Kemudian, tikus-tikus diberi perlakuan terapi dengan cisplatin secara intraperitoneal (4 mg/kgBB/minggu) dan kombinasinya dengan kurkumin (100 mg/kgBB/hari) dan nanokurkumin (100 mg/kgBB/hari) per oral. Tikus-tikus tersebut dibagi menjadi kelompok: tikus normal, model kanker ovarium saja, terapi cisplatin, terapi cisplatin + kurkumin, dan terapi cisplatin + nanokurkumin. Setelah 1 bulan, tikus di-sacrifice dan organ hepar disimpan beku. Ekspresi mRNA relatif NF-ÎºB dan IL-1Î² serta kadar protein IL-6 diukur dengan metode qt RT-PCR dan ELISA secara berurutan. Data hasil pengukuran IL-6 dan data hasil transformasi logaritma NF-ÎºB dan IL-1Î² dianalisis menggunakan uji one-way ANOVA, menggunakan perangkat lunak SPSS20. Tidak terdapat perbedaan signifikan secara statistik antar kelompok perlakuan dalam mRNA NF-ÎºB (p=0,503), mRNA IL-1Î² (p=0,237), dan protein IL-6 (p=0,157). Tidak ada perbedaan yang signifikan antara kurkumin dan nanokurkumin dalam memodulasi jalur inflamasi hepatotoksisitas cisplatin pada model kanker ovarium tikus.

.....

Up to now, one of the most effective anticancer drug as ovarian cancer chemotherapy is cisplatin. Nevertheless, cisplatin has many side effects on several organs, one of which is liver. Cisplatin-induced hepatotoxicity causes limited cisplatin chemotherapy dose. One of the pathophysiological key factor of acute liver injury is inflamation. Curcumin is natural compound which has antiinflamation properties but the bioavailability is low. To overcome it, nanocurcumin is made to increase its bioavailability. Nonetheless, curcumin and nanocurcumin effect on modulating inflammatory pathway toward cisplatin-induced hepatotoxicity in ovarian cancer rat model has not been observed. This study aims to compare the effect of curcumin and nanocurcumin as co-chemotherapy toward cisplatin-induced hepatotoxicity in inflammatory pathway. An in vivo study was done on female Wistar rats induced by DMBA to achieve ovarian cancer model. Then, rats was treated with cisplatin intraperitoneally (4 mg/kgBW/week) and the combination with

per oral curcumin (100 mg/kgBW/day) and nanocurcumin (100 mg/kgBW/day). Those rats were divided into groups, which are normal rat, only ovarian cancer model, cisplatin therapy, cisplatin + curcumin therapy, and cisplatin + nanocurcumin therapy. After 1 month, rats are sacrificed and liver organs are stored frozen. mRNA relative expression of NF-ÎºB and IL-1Î² as well as protein level of IL-6 was measured using qt RT-PCR and ELISA method, respectively. The result data from the measurement of IL-6 and the data from logarithmic transformation of NF-ÎºB and IL-1Î² was analysed using one-way ANOVA test using SPSS20 software. There is no significant differences between groups in mRNA NF-ÎºB (p=0.503), mRNA IL-1Î² (p=0.237), and protein IL-6 (p=0.157). There is no significant differences between curcumin and nanocurcumin in modulating inflammatory pathway of cisplatin-induced hepatotoxicity in ovarian cancer rat model.