Peran kurkumin sebagai ko-kemoterapi cisplatin pada model kanker ovarium tikus yang diinduksi 7,12-dimethylbenz[a]anthracene (DMBA) melalui mekanisme endothelin-1 (et-1) = The role of curcumin as co-chemotherapy of cisplatin in ovarian cancer rats model-induced by 7,12-dimethylbenze[a]anthracene (DMBA) through endothelin-1 (et-1) mechanism.

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Abstrak

Pendahuluan: Hampir 85% kasus karsinoma ovarium terjadi overekspresi endothelin-1 (ET-1) yang memodulasi persinyalan tumorigenesis dan metastasis. Disisi lain, cisplatin sebagai kemoterapi kanker ovarium menimbulkan efek samping dan resistensi terapi. Berbagai penelitian menunjukkan kurkumin berpotensi sebagai antikanker yang meningkatkan efikasi cisplatin dan menekan overekspresi ET-1 pada lini sel nonkanker. Namun, belum banyak penelitian yang mengidentifikasi penekanan ekspresi ET-1 oleh kurkumin dalam regimen terapi bersama cisplatin di kanker ovarium. Oleh karena itu, penelitian ini bertujuan melihat efek ko-kemoterapi kurkumin bersama cisplatin pada kanker ovarium terkait ekspresi relatif mRNA ET-1.

Metode: Jaringan ovarium tersimpan dari 24 tikus betina galur Wistar dibagi kedalam 4 kelompok: tikus yang hanya dibedah dan diberi aquadest (sham), tikus yang diimplantasi DMBA tanpa intervensi terapi, tikus yang diimplantasi DMBA dan diberi terapi tunggal cisplatin intraperitoneal 4 mg/kgBB/minggu, tikus yang diimplantasi DMBA dengan diberi terapi cisplatin 4 mg/kgBB/minggu dan kurkumin oral 100 mg/kgBB/hari. Implantasi DMBA dilakukan selama 28 minggu dan intervensi pada hewan coba selama 4 minggu. Setelah itu, jaringan ovarium tersimpan dianalisis ekspresi relatif mRNA ET-1 dengan mesin qRT-PCR menggunakan metode Livak-Schmittgen (2(-Ct)).

Hasil: Didapatkan rerata ekspresi relatif mRNA ET-1 [p=0,021] pada kelompok sham (0,349±0,24), kelompok DMBA (3,117±1,532), kelompok DMBA+cisplatin (0,993±0,651), dan kelompok DMBA+kurkumin+cisplatin (0,117±0,081). Ketiga kelompok tidak memiliki perbedaan bermakna dibandingkan sham. Meski demikian, terdapat perbedaan bermakna pada kelompok kombinasi cisplatin serta ko-kemoterapi kurkumin dengan kelompok tanpa intervensi terapi [p=0,019].

Kesimpulan: Terjadi penurunan ekspresi relatif mRNA endothelin-1 di jaringan ovarium model tikus yang diinduksi DMBA setelah pemberian kombinasi cisplatin dan ko-kemoterapi kurkumin.
.....Introduction: Endothelin-1 overexpression happens in 85% ovarian carcinoma cases that modulate metastatic and tumorigenesis. Meanwhile, cisplatin as ovarian cancer chemotherapy cause side effects and therapy resistances. Prior studies show potential effect of curcumin as an anticancer could enhance cisplatin efficacy and attenuate ET-1 overexpression in non-cancer cell lines. However, not many studies have identified suppression effect of ET-1 expression by curcumin with cisplatin in ovarian cancer. Therefore, this study is conducted to identify the effect of curcumin with cisplatin in ovarian cancer treatment

especially its relation to relative expression of ET-1 mRNA.

Methods: Frozen ovarian tissue samples from 24 female Wistar rats were divided into 4 groups: a group that only operated on and treated with distilled-water (sham), group with DMBA-implantation, group with DMBA-implantation and intraperitoneal cisplatin 4mg/kgBW/week, group with DMBA-implantation and cisplatin with same dose as before plus oral curcumin 100mg/kgBW/day. After 28 weeks of DMBA-implantation and 4 weeks of intervention, frozen ovarian tissue samples were taken to measure its relative expression of ET-1 mRNA level with qRT-PCR machine.

Results: The mean of relative expression of ET-1 mRNA level [p=0,021] in frozen tissue sample of sham group (0,349±0,24), DMBA-implantation group (3,117±1,532), DMBA+cisplatin-treated group (0,993±0,651), and DMBA+curcumin+cisplatin-treated group (0,117±0,081). This study shows those 3 groups did not have significant difference compared with sham. But among group with cisplatin+curcumin-treated compared to DMBA-implantation shows a significant difference (p=0,019).

Conclusion: The relative expression of ET-1 mRNA in ovarian tissue of DMBA-induced rats model decreases after given by a combination of cisplatin+curcumin co-chemotherapy.