Efek protektif kurkumin terhadap nefrotoksisitas cisplatin pada tikus

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Abstrak

Ruang lingkup dan cara penelitian : Cisplatin merupakan obat golongan platinum yang sering dipakai pada terapi kanker, seperti kanker testis, kepala, leher, kandung kemih dll. Sayangnya, efek samping berupa gagal ginjal akut atau kronis seringkali membatasi pemberian dosis cisplatin. Sejauh ini, mekanisme nefrotoksisitas cisplatin belum sepenuhnya diketahui. Radikal bebas diperkirakan berperan penting dalam terjadinya nefrotoksisitas cisplatin. Hal ini ditandai dengan peningkatan peroksidasi lipid dan penurunan enzim-enzim antioksidan setelah pemberian cisplatin. Kurkumin telah banyak diteliti sebagai antioksidan dan bersifat protektif terhadap kerusakan di beberapa organ atau sel yang terkena paparan radikal bebas. Penelitian ini bertujuan untuk mengetahui efek proteksi kurkumin terhadap nefrotoksisitas cisplatin pada tikus dan mengetahui apakah efek proteksi ini diperantarai oleh efek antioksidan kurkumin. Untuk melihat peranan antoksidan, efeknya dibandingkan dengan N-asetil sistein (NAC). Tiga puluh ekor tikus jantan galur Sprague Dawley dibagi secara acak menjadi 5 kelompok. Kelompok cisplatin (Csp) diberi pelarut kurkumin (CMC 1%) per oral selama 7 hari berturut-turut dan pada hari ke-5 diberi injeksi cisplatin 5 mg/kg BB intraperitoneal. Kelompok Csp-Curl0 dan Csp-Cur50 masing-masing diberikan kurkumin 10 mg/kg BB dan 50 mg/kg BB per oral selama 7 hari berturut-turut dan pada hari ke-5 diberi injeksi cisplatin 5 mg/kg B13 intraperitoneal. Kelompok Csp-NAC mendapatkan NAC 500 mg/kg BB per oral selama 7 hari berturut-turut dan pada hari ke-5 diberi injeksi cisplatin 5 mg/kg BB intraperitoneal. Kelompok kantrol diberi CMC 1% per oral selama 7 hari berturut-turut dan pada hari ke-5 diberi injeksi salin 0,9% intraperitoneal. Pada hari ke-8, fungsi ginjal diukur dengan parameter ureum dan kreatinin serum, sedangkan adanya peroksidasi lipid diukur dengan parameter kadar malondialdehid (MDA) dalam plasma dan ginjal.
Hasil dan Kesimpulan : Kadar ureum dan kreatinin serum meningkat berturut-turut sebesar 318% dan 275% dibandingkan kelompok kontrol negatif. Hal ini menunjukkan bahwa cisplatin menyebabkan gangguan fungsi ginjal yang bermakna. Pemberian cisplatin juga menyebabkan peningkatan kadar MDA plasma (165%) dan ginjal (146%), meskipun tidak mencapai kemaknaan statistik. Pemberian kurkumin 10 mg/kg BB sedikit menurunkan kadar ureum, kreatinin dan MDA plasma dibandingkan kelompok Csp namun tidak bermakna secara statistik, sedangkan kadar MDA ginjal menurun secara bermakna sampai kadar normal. Peningkatan dosis kurkumin menjadi 50 mg/kg BB tidak menurunkan kadar ureum dan kreatinin dibandingkan kelompok Csp. Kadar MDA plasma menurun secara bermakna ($p<0,05$) sampai kadar normal dan kadar MDA ginjal sedikit menurun dibandingkan kelompok Csp tetapi secara statistik tidak berbeda bermakna. Pemberian NAC 500 mg/kg BB sedikit menurunkan kadar ureum, kreatinin dan MDA, namun secara statistik tidak bermakna. Dari hasil penelitian tersebut, dapat disimpulkan bahwa pemberian kurkumin sebelum dan sesudah pemakaian cisplatin tidak mengurangi nefrotoksisitas cisplatin secara bermakna. Pengurangan stres oksidatif oleh kurkumin tidak mampu mencegah nefrotoksisitas cisplatin.
.....Scope of Study and Methods: Cisplatin is a platinum group of chemotherapeutic agent, frequently used for treatment of testicular, head, neck, bladder cancer, etc. Unfortunately, the use of cisplatin is limited by the high rate of acute or chronic renal failure. The mechanism of cisplatin-induced nephrotoxicity is not

fully understood. However, free radicals are suggested to play an important role in cisplatin nephrotoxicity. Administration of cisplatin increases lipid peroxidation and reduces the activity of antioxidant enzymes. Curcumin has been reported to be a potent antioxidant agent and has protective effects on several organs or cells from free radical-induced injury. The present study was aimed to investigate the protective effects of curcumin on cisplatin-induced nephrotoxicity in rats and to find out whether these protective effects were mediated by the antioxidant effects of curcumin. The antioxidant effects of curcumin were compared to N-acetyl cysteine (NAC). Thirty male Sprague Dawley rats were randomly devided into 5 groups of 6 rats. Cisplatin group (Csp) received solvent of curcumin (CMC 1%) by gavage for 7 consecutive days, and on day 5, intra peritoneal injection of cisplatin 5 mg/kg BW was given. Csp-Cur10 and Csp-Cur50 groups received curcumin 10 mg/kg BW and 50 mg/kg BW, respectively, by gavages for 7 consecutive days, and on day 5, intra peritoneal injection of cisplatin 5 mg/kg BW was given. The NAC group received NAC 500 mg/kg BW by gavage for 7 consecutive days, and on day 5, intra peritoneal injection of cisplatin 5 mg/kg BW was given. The control group received the solvent of curcumin (CMC 1%) by gavage for 7 consecutive days, and on day 5, intra peritoneal injection of saline 0,9% was given. On day 8, serum ureum and creatinin were measured as parameters of renal function. MDA was assayed from plasma and renal homogenate and taken as the parameter of oxidative stress.

Results and Conclusion: Serum ureum and creatinin were increased by 318% and 275%, respectively in the cisplatin treated animals compared to the negative control. Administration of cisplatin increased MDA levels in plasma (165%) and kidney (146%), although it was not statistically significant. Curcumin administration at the dose of 10 mg/kg BW slightly, but not significantly reduced ureum, creatinin and plasma MDA levels compared to the Csp group. Whereas the renal MDA level was significantly reduced approaching normal level. The increase of curcumin dose to 50 mg/kg BW did not decrease ureum and creatinin levels compared to the Csp group. In contrast to renal MDA level, the administration of curcumin 50 mg/kg BW significantly decreased MDA level in plasma. Administration of NAC 500 mg/kg 13W slightly reduced ureum, creatinin, and NIDA levels; however, no statistical significance was observed. From this study we concluded that curcumin administration before and after cisplatin injection did not significantly decrease the nephrotoxicity effects of cisplatin. The reduced oxidative stress by curcumin may not prevent cisplatininduced nephrotoxicity.