

Efficacy and safety of high-dose cisplatin and cyclophosphamide with glutathione protection in the treatment of bulky advanced epithelial ovarian cancer.

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Source

Cancer Chemother Pharmacol. 1990;25(5):355-60.

Abstract

Recent efforts to improve the response rates in advanced ovarian cancer with the use of high-dose cisplatin have been limited by unacceptable toxicity. Based on experimental and clinical studies indicating that reduced glutathione (GSH) is a protective agent against cisplatin-induced toxicity, a new high-dose regimen including GSH as a chemoprotector was designed in an attempt to improve the efficacy and therapeutic index of cisplatin. A total of 40 consecutive patients with stage III (bulky) and IV ovarian carcinoma were treated with cisplatin (40 mg/m² daily for 4 consecutive days) and cyclophosphamide (600 mg/m² i.v. on day 4). The treatment was repeated every 3-4 weeks for five courses unless progression or severe toxicity occurred. Before each cisplatin administration, patients received GSH (1,500 mg/m²) i.v. over 15 min, with a standard i.v. hydration (2,000 ml fluid) without diuretics. Debulking surgery was initially attempted in 18 patients and, after 2-3 courses, in 16 patients; it could not be carried out in 6 patients. Three patients were not evaluable for response because they prematurely discontinued their treatment. In all, 23 patients (62%) achieved complete clinical remission (negative second-look laparotomy in 16), with an overall (complete + partial) response rate of 86%; 2 patients achieved disease-free status following second surgery. Nausea/vomiting was the most severe acute toxic effect; myelosuppression was acceptable. Renal impairment was effectively prevented by GSH. Neurotoxicity that was not associated with motor dysfunction was the most significant cumulative toxicity in patients (24/32) receiving 4-5 courses. The results of this study indicate that the use of GSH is a safe new method for high-dose cisplatin administration. This regimen is well-tolerated and very effective in ovarian cancer patients with bulky disease and warrants further evaluation.

