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# Letters

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## Long Lasting, Grade IV, Orthostatic Hypotension after a Single Cycle Combination Chemotherapy with Paclitaxel and Cisplatin

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CISPLATIN AND paclitaxel are very active agents in ovarian cancer and their combination is perhaps the first choice chemotherapy in advanced stages of this disease [1]. Both drugs act on microtubules: cisplatin inhibits tubulin polymerisation [2] and paclitaxel induces that polymerisation *in vitro* [3]. Neurotoxicity occurs with both drugs, so a possible synergistic neurotoxic effect is anticipated when the two drugs are combined.

In fact, autonomic neuropathy in 2 patients after paclitaxel administration at doses of 170–250/m$^2$ [4] and orthostatic hypotension and transient paralytic ileus in 2 diabetic patients after paclitaxel administration at a dose of 250 mg/m$^2$ [5] have been reported. Paclitaxel has been found to alter sympathetic control of blood pressure [6]. Syncopal or near-syncope episodes with orthostatic symptoms immediately after paclitaxel alone or in combination with cisplatin have also been reported [7]. Slowly reversible grade 3–4 orthostatic hypotension has been described in 6 patients after combination chemotherapy with cisplatin (100 mg/m$^2$) and paclitaxel (200–250 mg/m$^2$), even with a single cycle [8]. However, severe incapacitating orthostatic hypotension after a single course of conventional treatment with cisplatin and paclitaxel has not yet been reported.

We attended a 60 year old women who presented a long lasting orthostatic hypotension after a sole course of cisplatin/paclitaxel combination chemotherapy and at lower than the above described doses of each drug. She had had successful debulking surgery for a stage IIIc ovarian carcinoma, was not diabetic nor an alcohol abuser and was asymptomatic with an unremarkable physical examination prior to chemotherapy. She received paclitaxel (135 mg/m$^2$) as a 3 h infusion on day 1 and cisplatin (75 mg/m$^2$) as a short infusion on day 2. Appropriate hydration was administered and the water/electrolyte balance was maintained. On day 3 she experienced a near-syncope episode while standing. Blood pressure was 130/80 mm Hg while supine and 55/40 mm Hg while upright. A similar episode occurred on day 4. A generalised weakness and a slight decrease of deep tendon reflexes were the only physical findings. Her central venous pressure was normal and as her electrocardiograph, except for the disappearance of the normal heart rate variation with respiration. No abnormalities in cortisol rhythm, adrenocorticotropic hormone (ACTH), epinephrine, nor-epinephrine, free triiodothyronine ($FT_3$), free thyroxine ($FT_4$), thyroid-stimulating hormone (TSH), luteinising hormone (LH), follicle-stimulating hormone (FSH), vanilylmandelic acid (VMA), antidiuretic hormone (ADH) or brain magnetic resonance imaging scan were detected. It was apparent that the patient had developed a drug-induced autonomic nervous system dysfunction. Oral administration of etilephine hydrochloride and dihydroergotamine proved ineffective. A third near-syncope episode occurred on day 25 and morbid orthostatic hypotension kept the patient bedridden for 8 weeks. Paclitaxel/cisplatin was stopped and replaced with a cyclophosphamide/doxorubicin combination. The patient recovered slowly and remained with orthostatic hypotension for 3 months after discharge.

Paclitaxel/cisplatin combination chemotherapy can induce long lasting and morbid orthostatic hypotension after a single course; although rare, this side-effect may deprive patients of a very active treatment.

1. McGuire WP, Hoskins WJ, Brady MF, *et al.* Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and IV ovarian cancer. *N Engl J Med* 1996, **334**, 1–6.
2. Peyot V, Briand C, Crevat A, *et al.* Action of hydrolyzed cisplatin and same analogs on microtubule protein polymerization *in vitro*. *Cancer Treat Rep* 1983, **67**(7–8), 641–646.
3. Schiff PB, Fant J, Horwitz SB. Promotion of microtubule assembly *in vitro* by Taxol. *Nature* 1979, **277**, 655–667.
4. Jerian SM, Sarosy GA, Lind CJ, *et al.* Incapacitating autonomic neuropathy precipitated by Taxol. *Gynecol Oncol* 1993, **51**(2), 277–280.
5. Wiernik PH, Swatz EL, Eizing A, *et al.* Phase I trial of Taxol given as 24 hour infusion every 21 days: responses observed in metastatic melanoma. *J Clin Oncol* 1987, **5**(8), 1232–1239.
6. Ekholm E, Rantanen V, Antila K, Salminen E. Paclitaxel changes sympathetic control of blood pressure. *Eur J Cancer* 1997, **33**(9), 1419–1424.
7. Rowinsky EK, McGuire WP, Guarnieri T, *et al.* Cardiac disturbances during the administration of Taxol. *J Clin Oncol* 1991, **9**(9), 1704–1712.
8. Hnauske AR, Scilling T, Heinrich B, *et al.* Clinical phase I study of paclitaxel followed by cisplatin in advanced head and neck squamous cell carcinoma. *Semin Oncol* 1995, **22**(6 Suppl. 14), 35–39.

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