PACLITAXEL AND ANASTROZOLE CAUSE NEUROPATHIC AND MUSCULOSKELETAL PAIN SYMPTOMS IN MICE

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Introduction: Breast cancer patients often report pain resulting from the tumour itself or from antineoplastic treatment. Paclitaxel, a chemotherapeutic agent used widely to treat solid tumours, can induce both acute and chronic peripheral neuropathic pain symptoms. Anastrozole, an antineoplastic drug used in the treatment of hormone receptor-positive breast cancer, is associated with musculoskeletal pain symptoms. Patients previously treated with paclitaxel appear to be more susceptible to adverse effects induced by anastrozole. **Objective:** Investigate whether paclitaxel and anastrozole induce nociceptive behaviours alone or in combination in a mouse model. **Materials and methods:** Male C57BL/6 mice (Ethical approval 4400060223) were assessed for nociceptive parameters (mechanical and cold allodynia, and pain affective-motivational behaviour) following a single (1 mg/kg, intraperitoneal) or repeated (4 x 1 mg/kg, intraperitoneal) administrations of paclitaxel. The pain-like symptoms (mechanical allodynia, muscle strength, and pain affective-motivational behaviour) induced by a single administration of anastrozole (0.05, 0.1 and 0.2 mg/kg, oral) were also evaluated. At 21 days after the first of four doses of paclitaxel (0.001, 0.001, 0.001 plus 0.001 mg/kg, intraperitoneal), it was assessed whether anastrozole (0.1 mg/kg, oral) could exacerbate pain-related symptoms induced by paclitaxel. **Results and conclusion:** A single dose of paclitaxel induced mechanical and cold allodynia and increased pain affective-motivational behaviour, but not heat hyperalgesia. In the chronic paclitaxel-induced neuropathic pain model, mice developed mechanical, cold, and heat hypersensitivity along with increased emotional pain responses. Anastrozole caused dose- and time-dependent mechanical allodynia, increased affective motivational behaviour, and reduced muscle strength. When associated, anastrozole enhanced paclitaxel-induced mechanical allodynia. These results provide a valuable experimental model for future research into the nociceptive mechanisms and antinociceptive drugs to alleviate pain caused by antineoplastic paclitaxel and anastrozole agents alone or in combination.

Keywords: Antineoplastic therapy; Taxanes; Aromatase inhibitors

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