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Chemotherapeutic agents: effects and biochemical changes occurring following prolonged exposure from animal studies and comparison of different compounds in alleviating chemotherapy-induced neuropathy

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Abstract

Chemotherapeutic agents (cisplatin, paclitaxel and vincristine) are used for the treatment of different types of cancer such as breast, prostate, lung, and many others. The development of animal models using chemotherapeutic agent has advanced our understanding about improving analgesic treatment for patients. Clinical studies have demonstrated that morphine, gabapentin and antidepressants alleviate pain in cancer patient although with certain limitations regarding inadequate pain relief and/or side-effects. Morphine, gabapentin and antidepressants can also alleviate one of the major toxicities induced by chemotherapeutic treatment which is the development of painful neuropathy. However, the side effects of these chemotherapeutic treatments are less investigated and new combination of compounds need to be evaluated to improve pain management in patient as well as reducing neuropathies induced by chemotherapeutic agents. Indeed, combination of reference compounds with structurally distinct compounds such as inhibitors of endocannabinoid degradation (URB597, URB937 and JZL184) will provide a comparison in alleviating pain from conventional to new alternative and combined approach. These observations suggest the presence of antinociceptive synergism between mechanistically distinct treatments for neuropathic pain. Moreover, adjunctive therapy combining reference compounds with inhibitor of endocannabinoid deactivation (URB597, URB937 and JZL184) is therapeutically advantageous to alleviate neuropathic pain in comparison to conventional treatment administered alone. An overview of the mechanism of action of these chemotherapeutic agents will be evaluated with data from tissue collection determining interesting biochemistry changes in different enzymes, eicosanoids and protein levels. Although our understanding of chemotherapeutic agents inducing neuropathy and other side effects has evolved throughout the years, chemotherapy treatment could lead to adaptive changes that preclude the actual treatment to be completely effective. Multimodal approaches are leading the way to better alleviate pain clinically by simultaneously giving different class of compounds (for example, opioids, antidepressant, anticonvulsivant, cannabinoids) since it is known that a single compound can't solely alleviate pain.

Biography

Josée Guindon has completed her DVM in 2000 and her Ph.D in 2007 from Université de Montréal. She has pursued her postdoctoral studies at University of Georgia which was granted a substantial FRQS fellowship. She is now a Scientist/Research Faculty at Indiana University. She has won several awards. She has published more than 22 manuscripts in reputed journals and 4 book chapters. Two of the book chapters are published in: the Handbook of Neuroscience by John H. Wiley & Sons and in: the IASP Press. She is also reviewing for 16 prestigious journals as well as serving on the editorial board member of reputable journal. She is also the Chair of the upcoming Gordon Research Seminar: Cannabinoid Function in the CNS.