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Oxaliplatin-induced peripheral neurotoxicity: morphological characterization in different mouse strains

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Oxaliplatin is one of the most effective anticancer drug, particularly employed in the treatment of colorectal cancer, but one of the major limitation in its use is peripheral neurotoxicity. Oxaliplatin induced peripheral neurotoxicity (OIPN) has a high incidence and is frequently long lasting or permanent. Neuropathy is characterized by distal sensory impairment initially in the legs, then extending to the arms. A prominent manifestation of sensitive damage is ataxia. Besides chronic neurotoxicity, many patients experience an *acute*, rapidly developing cold-induced sensory neuropathy, usually resolving within one week. OIPN clinical manifestations reflect the involvement of dorsal root ganglia (DRG) as primary target of the drug toxicity. Although this assumption is largely accepted and some pathogenetic hypothesis have been proposed, mechanisms at the basis of OIPN need to be clearly defined. OIPN may vary in frequency and severity among different cancer patients despite equal treatment schedules. A genetic susceptibility for more severe oxaliplatin-induced peripheral neurotoxicity (OIPN) has been suggested but never confirmed. Therefore we designed a study to assess the phenotypic differences induced by oxaliplatin treatment in six different mice strains (Balb c, AJ, C57Bl6, FVB, DBA, CD1) aiming at identifying the more and less severely affected. Animals were treated with OHP 3.5 mg/Kg/iv twice weekly x 4 weeks and evaluated before and after treatment. In all strains we performed a multimodal characterization of its neurotoxicity through morphological and morphometrical assessment in caudal nerve and DRG at light and electron microscopy, intra-epidermal nerve fibers density quantification, evaluation of mechanical and cold allodynia/hypoaesteshesia, caudal and digital nerve conduction velocity, activity of wide dynamic range (WDR) neurons of the spinal dorsal horn. Our preliminary data suggest that all the strains show signs of OIPN but not the same modifications in the parameters examined. We will show these results with particular attention to morphological data. This study suggests that genetic variability might have a role in the type and severity of OHP-induced peripheral damage.

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References

[1] Cavaletti G, Alberti P, Marmiroli P (2011) Chemotherapy-induced peripheral neurotoxicity in the era of pharmacogenomics. Lancet Oncol 12(12): 1151-61

[2] Renn CL et al (2011) Multimodal assessment of painful peripheral neuropathy induced by chronic oxaliplatin-based chemotherapy in mice. Mol Pain 26:7-29.

Keywords

Peripheral neuropathy; oxaliplatin; mouse model.