

BEHAVIOURAL AND MORPHOLOGICAL DESCRIPTION OF BORTEZOMIB-INDUCED PAINFUL NEUROPATHY IN RATS

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Bortezomib is a proteasome inhibitor that shows a high antineoplastic effects mainly in the treatment of a multiple myeloma. Painful bortezomib-induced peripheral neuropathy represents the dose-limiting factors in its use in clinical practice. To reproduce the clinical pain symptoms, we have established an animal model of bortezomib-induced nociceptive sensory neuropathy. This study was performed by repeated administration of bortezomib in Wistar rats at doses of 0.15-0.20 mg/kg [3q7d] for eight weeks, followed-up by an observation period of 4 weeks. Bortezomib-treated rats had a reduced weight gain at the end of treatment if compared to controls, that recovered after the follow-up period.

A significant decrease in the nerve conduction velocity in both doses group was observed after the treatment period. The sensory behavioural assessment, demonstrated the onset of mechanical allodynia after the eight weeks of treatment. Sciatic nerve and DRG specimens, collected at the end of treatment and after the follow-up period, were processed for light and electron microscope analysis to evaluated any pathological alteration on fibers and on dorsal root ganglions (DRG). Morphological evaluation described a dose-dependent axonopathy in treated rats' sciatic nerves vs. control rats, involving also the unmyelinated fibers. No pathological alteration in most of DRG satellite cells or neurons was observed. This model can be useful for the study on the neurotoxicity and pain onset mechanisms related to the treatment with bortezomib.

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