

ABSTRACT SUBMISSION

TITLE

CHARACTERIZATION OF PERIPHERAL NEUROPATHY INDUCED BY CHRONIC CISPLATIN ADMINISTRATION IN SEVERAL MICE MODELS

AUTHORS AND AFFILIATION

Sala B.¹, Carozzi V.A.¹, Chiorazzi A.¹, Meregalli C.¹, Oggioni N.¹, Canta A.¹, Cavaletti G.¹.

¹ Department of Neuroscience and Biomedical Technologies, University of Milan Bicocca, via Cadore 48 – 20900 (MB) - Italy

ABSTRACT TEXT

The clinical use of cisplatin (CDDP) is often associated with a severe neurotoxicity that represents the dose-limiting factor in therapy. In the past, several rat models has been accomplished to study the mechanisms involved in peripheral neuropathy induced by chronic CDDP administration and they highlight its toxic effects particularly in the dorsal root ganglia (DRG) sensory neurons that are smaller in sizes.

Nevertheless, since only a limited number of cancer cell lines are able to induce the development of cancer in rat, we decided to use different murine models that allow a future combined study of the antineoplastic activity and the neurotoxic effects of CDDP.

To achieve this aim, we evaluated the neurophysiological, neuropathological and morphometrical alterations induced by chronic CDDP treatment in female Balb/c, CD1 and Hsd NuNu mice.

Balb/c mice were treated intraperitoneally with CDDP 4mg/Kg twice a week for 4 weeks, while CD1 and Hsd NuNu mice were treated with the same schedule followed by 2 weeks of follow-up.

The body weight was measured once a week while at the end of the treatment we evaluated the nerve conduction velocities (NCVs) in the caudal and digital nerves and we collected DRG for the morphological and morphometrical analysis.

We observed in all mice models a significant decrease in the body weight and a significant reduction in the caudal and digital NCV. This nerve functional damage was confirmed by morphological observations in DRG showing an increase in multinucleolated neurons and in nucleolar eccentricity and by the presence of nucleolar segregation.

Moreover the morphometrical analysis demonstrated that CDDP affects neurons through a significant decrease in the size of somatic and nucleolar area in Balb/c mice and also in nuclear size in CD1 mice while the Nu/Nu mice showed only a significant decrease in the nuclear area.

These results can confirm that the chosen schedule is able to induce peripheral neuropathy at rather different severity in the different mice strains. They could represent a useful guideline to future combined study of antineoplastic activity, neurotoxic effects of CDDP and eventually also for neuroprotection studies.

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