INVESTIGATION OF AGING EFFECTS ON NERVE DAMAGE IN AN ANIMAL MODEL OF PACLITAXEL-INDUCED PERIPHERAL NEUROPATHY.

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Chemotherapy-induced peripheral neurotoxicity (CIPN) is one of the most common dose-limiting side-effects of paclitaxel (PTX) treatment. Nevertheless, the mechanisms underlying the pathogenesis of such complication are still not clear. Numerous alterations related to aging have been hypothesized to underlie age-related susceptibility to damage or impaired regeneration/repair after nerve injury. However, the results of these studies are inconclusive and other targets, which might be used as potential biomarkers of nerve impairment, deserve to be investigated.

Twelve young (2 months of age) and twelve adult (9 months of age) Wistar male rats were randomized to either paclitaxel treatment (10 mg/kg i.v. 1 time/week for 4 weeks) or saline administration. Neurophysiological and behavioral tests were performed to investigate nerve damage. Skin biopsies from sacrificed animals were examined for intraepidermal nerve fiber (IENF) density assessment. Blood samples were collected before and after chemotherapy completion.

At the end of treatment, the neurophysiological studies revealed a reduction in sensory nerve action potential (SNAP) amplitude ($p<0.05$) in the caudal nerve of young treated animals, and in both the digital nerve and the caudal nerve of old treated animals. Nerve conduction velocity (NCV) did not significantly differ between treated animals and controls in both young and old rats after the last PTX-administration. Behavioral tests revealed a significant decrease in the mechanical threshold in young treated animals ($p < 0.001$), indicating the development of mechanical allodynia, differently from old treated rats. Concerning IENF assessment, both young and old PTX-rats presented reduced IENF density ($p<0.0001$), which persisted at the 4th follow-up week.

Our study suggests that age might be a potential risk factor for more severe CIPN, and should be considered in future studies in order to tailor chemotherapy regimen and dosage on individual susceptibility of older cancer patients.