SELENIUM-BASED COMPOUND 7-CHLORO-4-(PHENYLSELANYL) QUINOLINE ATTENUATES OXALIPLATIN-INDUCED NEUROTOXICITY IN AGED RATS

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INTRODUCTION: Chemotherapy-induced neurotoxicity, including cognitive impairment and anxiety-like behavior, poses a significant challenge in oncology, especially among elderly patients, who are more vulnerable due to age-related neural decline. Oxaliplatin (OXA), a platinum-based chemotherapeutic agent commonly used in colorectal cancer treatment, induces neurotoxicity through oxidative stress, neuroinflammation, and neurochemical imbalances. Recent findings demonstrated that 7-chloro-4-(phenylselanyl)quinoline (4-PSQ) exerts antinociceptive effects and reduces OXA-induced neuropathic pain. OBJECTIVE: In view of our continued interest in the pharmacology of this compound, this study evaluated the effect of 4-PSQ, a selenium-based antioxidant, in mitigating OXA-induced neurotoxicity in aged rat models. MATERIALS AND METHODS: Aged Wistar rats received intraperitoneal injections of either OXA (2 mg kg^{-1}) or a 5% glucose solution (10 mL kg^{-1}) for five consecutive days. Starting on day 5, 30 minutes after the last OXA administration, animals were treated daily via intragastric route with 4-PSQ (5 mg kg^{-1}) or vehicle (10 mL kg^{-1}) until day 14. Behavioral tests were conducted on days 9, 10, and 12. On day 15, the animals were sacrificed, and tissues were collected for ex vivo analyses. Key assessments included Na^+,K^+-ATPase activity, brain-derived neurotrophic factor (BDNF) expression, and selenium levels in the nervous system. RESULTS AND CONCLUSION: Notably, this study demonstrated the beneficial effects of 4-PSQ on OXA-induced neurotoxicity in aged rats. Our results indicated that OXA administration exacerbated anxiety-like behavior and cognitive decline typically associated with aging. This exacerbation was primarily linked to the modulation of BDNF expression and inhibition of Na^+,K^+-ATPase activity. Notably, 4-PSQ treatment restored Na^+,K^+-ATPase activity and effectively modulated BDNF expression levels. Through these mechanisms, 4-PSQ reversed OXA-induced and age-related anxiety-like behaviors and cognitive deficits. Additionally, we observed for the first time that 4-PSQ treatment increased selenium concentrations in both the peripheral and central nervous systems (PNS and CNS) of aged rats treated with OXA. This study highlights the neuroprotective potential of 4-PSQ in addressing OXA-induced neurotoxicity, offering a promising therapeutic strategy to improve the quality of life of elderly cancer patients undergoing OXA treatment.

Keywords: Chemotherapy-induced neurotoxicity; Aging; Oxaliplatin; 4-PSQ; Selenium

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