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Agmatine co-treatment attenuates allodynia and structural abnormalities in cisplatin-induced neuropathy in rats.

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Abstract

Cisplatin is a widely used antineoplastic agent in the treatment of various cancers. Peripheral neuropathy is a well-known side effect of cisplatin and has potential to result in limiting and/or reducing the dose, decreasing the quality of life. Thus, effective treatments are needed. Agmatine is an endogenous neuromodulator that has been shown to exert antiallodynic effects in various animal studies. The first aim of this study was to investigate the in vitro effects of agmatine on cisplatin-induced neurotoxicity. Primary cultures of dorsal root ganglia (DRG) which are the primary target of drug injury were prepared. DRG cells were incubated with cisplatin (100, 200, 500 μm). Then, agmatine (10, 100, 500 μm) was administered with the submaximal concentration of cisplatin. Cisplatin caused concentration-dependent neurotoxicity, and agmatine did not alter this effect. The second aim was to investigate the effects of agmatine on cisplatin-induced peripheral neuropathy in rats and the influence of nitric oxide synthase (NOS) inhibitor, L-NAME, in this effect. Female Sprague Dawley rats received intraperitoneal saline (control), cisplatin (3 mg/kg), cisplatin+agmatine (100 mg/kg), or cisplatin+agmatine+L-NAME (10 mg/kg) once a week for 5 weeks. The mechanical allodynia, hot plate, and tail clip tests were performed, and DRG cells and sciatic nerves were analyzed. Agmatine and agmatine+L-NAME combination attenuated CIS-induced mechanical allodynia and degeneration in DRG cells and sciatic nerves. However, L-NAME did not potentiate the antiallodynic or neuroprotective effect of agmatine. These findings indicate that agmatine co-administration ameliorates cisplatin-induced neuropathy and may be a therapeutic alternative.

KEYWORDS: L-NAME; agmatine; cisplatin; neuropathy; nitric oxide

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