The protective effects of sumatriptan on vincristine - induced peripheral neuropathy in a rat model

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Abstract

Introduction: Clinical use of vincristine (VCR), an effective chemotherapeutic agent- has been limited due to its peripheral neuropathy dose-dependent toxicity. Sumatriptan, which known an anti-migraine agent is a specific agonist for 5-hydroxytryptamine1B, 1D (5HT1B, 1D) receptors. Several studies have shown that sumatriptan exerts anti-inflammatory and im-munomodulatory properties. This study aimed to investigate the effects of sumatriptan on VCR-induced peripheral neuropathy in a rat model.

Material and method: Male Wistar rats were intraperitoneally injected with VCR and normal saline four times per week for 2 weeks. In the treatment group, sumatriptan (1 mg/kg) was administered intraperitoneally 30 min prior to VCR injection every day. Mortality rate, weight variations and histopathological changes were monitored. Hot plate, tail flick and motor nerve conduction velocity (MNCV) tests were used to evaluate sensory and motor neuropathy. Levels of tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β) and caspase-3 in the dorsal ganglion root were assessed by quantitative reverse transcription-PCR (qRT-PCR). Moreover, the protein levels of p65 nuclear factor kappa B (NF- < kappa > B) and phospho-p65 NF-< kappa > B were examined by Western blot analysis.

Results: Co-administration of sumatriptan with VCR significantly reversed alterations in the hot plate, tail flick threshold and sciatic MNCV induced by VCR and also prevented mixed sensory-motor neuropathy, as indicated by better general conditions, behavioral and electrophysiological results. In addition, sumatriptan improved the body weight loss caused by VCR. The mRNA levels of TNF-α, IL-1β and caspase-3 were significantly diminished in the treatment group. These findings were confirmed by histopathological analysis.

Conclusion: In conclusion, this study demonstrated that sumatriptan significantly attenuated VCR-induced neuropathy and could be considered as a neuroprotective agent to prevent the VCR-induced neuropathy