Pioglitazone Ameliorates Peripheral Neuropathy in Rats: Evidence for Anti-Inflammatory and Antioxidant Mechanisms

Seema Thakur*, Neha Srivastava
Faculty of Pharmaceutical Sciences, PCTE Group of Institutes, Baddowal, Ludhiana, India
*Email: thakurseema1983@yahoo.co.in

OBJECTIVE

Neuropathic pain has been associated with local inflammation dur to peripheral nerve injury. Recently, we have shown protective role of peroxisome proliferator-activated receptor-gamma (PPAR-γ) activation in acute inflammatory and nociceptive conditions. In spite of this, its role in neuropathic pain is not known. Therefore, the aim of present study was to evaluate the effect of pioglitazone (PIO), a PPAR-γ agonist to define the role of PPAR-γ activation on peripheral neuropathy and to elucidate mechanisms in its beneficial actions.

MATERIALS AND METHODS

Chronic constriction injury (CCI) consisting of loosely ligating sciatic nerve of rat. Paw withdrawal latencies to noxious thermal and innocuous cold stimuli were measured to assess hyperalgesia and allodynia, respectively. The markers of inflammation: plasma extravasation in the paws and tumor necrosis factor (TNF)-α, and the markers of oxidative and nitrosative stress: lipid peroxidation, reduced glutathione, superoxide dismutase, and nitrite level in ipsilateral and contralateral sciatic nerve were estimated.

RESULTS

Thermal stimulus withdrawal latency on the ipsilateral paw of CCI rats was significantly increased four days after the start of PIO (10 or 30 mg/kg, i.p., 2h before and once daily continuously for 14 days) treatment, and thermal hyperalgesia was almost fully relieved. Similarly, the development of hypersensitivity to cold stimuli was also attenuated after PIO treatment. Our results showed that PIO attenuates the development of neuropathic pain by exerting anti-inflammatory effect evidenced by a decrease in plasma extravasation in paws and TNF-α in sciatic nerve of ipsilateral side. In addition, PIO showed antioxidant and antinitrosative effects demonstrated by a reduction of the markers of oxidative and nitrosative stress in ipsilateral sciatic nerve. These beneficial effects are abolished by pretreatment with BADGE, A PAPR-γ antagonist.

CONCLUSION

Our data suggest that PPAR-γ activation attenuate the development of neuropathic pain through pleiotropic effects including anti-inflammatory, antioxidative and antinitrative benefits in the mononeuropathic rat model, and strengthen that activation of PPAR-γ could be a promising therapeutic strategy for peripheral neuropathic pain.

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