

## The anti-convulsant effect of pioglitazone in the intra-venous (i.v.) pentylenetetrazole-induced clonic seizures in male mice through nitric oxide system

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**Background and Aims:** Pioglitazone, peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ) delayed the development of seizure responses and shortened the duration of convulsion of genetically epileptic EL mice. The anti-epileptic effect of pioglitazone was attributed partly through the reduction of inflammatory responses and preventing apoptosis. There are also some reports showing that some pioglitazone effects mediate through nitric oxide. The present study was designed to investigate the anti-convulsant effect of pioglitazone, a peroxisome proliferator-activated receptor gamma (PPAR $\gamma$ ), in the i.v. pentylenetetrazole-induced clonic seizure in male mice through nitric oxide system.

**Methods:** Different doses of pioglitazone were administered orally for 10 days in different groups of male mice. L-NAME, a non selective inhibitor of nitric oxide synthase, aminoguanidine, a selective inhibitor of inducible nitric oxide synthase, or L-arginine, a nitric oxide donor, was administered acutely or sub-chronically to evaluate the role of nitric oxide in pioglitazone anti-seizure effects. Minimal dose of PTZ (mg/kg of mice weight) needed to induce clonic seizure, was considered as an index of seizure threshold.

**Results:** We demonstrated that sub-chronic administration of pioglitazone exerted anti-convulsant effects in intra-venous pentylenetetrazole-induced clonic seizure. Acute and sub-chronic pre-administration of L-NAME prevented the anti-convulsant effect of pioglitazone. Aminoguanidine did not alter the anti-convulsant effect of pioglitazone. Acute administration of L-arginine with a non-effective dose of pioglitazone enhanced the seizure clonic latency.

**Conclusions:** sub-chronic pioglitazone treatment exerts anti-convulsant effects in intra-venous pentylenetetrazole-induced seizures in mice probably through induction of constitutive nitric oxide synthase.

**Keywords:** Pioglitazone; Anti-convulsant; Nitric oxide