

## Neuroprotective effect of minocycline against morphine-induced apoptosis in rat brain cortex and spinal cord: A possible mechanism involves in attenuating morphine tolerance

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**Background and Aims:** Tolerance to the chronic administration of opioids such as morphine reduces the utility of these drugs in pain management. Despite significant investigation, the precise cellular mechanisms underlying opioid tolerance and dependence remain elusive. It has been indicated that tolerance to the analgesic effect of morphine is associated with apoptosis in the central nervous system. The aim of this study was to examine the effects of the intracerebroventricular (icv) administration of minocycline (a second-generation tetracycline) on morphine-induced apoptosis in the cerebral cortex and lumbar spinal cord of rats after morphine-induced tolerance.

**Methods:** Different groups of rats received either morphine (ip) and distilled water (icv) or morphine and different doses of minocycline (icv) or minocycline alone once per day. The terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) method was used to analyze apoptosis. The anti-apoptotic factors, Bcl-2 and HSP 70 and the pro-apoptotic element caspase-3 were evaluated by immunoblotting.

**Results:** The results indicated that minocycline attenuated the number of apoptotic cells in both the cerebral cortex and lumbar spinal cord. Immunoblotting findings showed that the amounts of anti-apoptotic agents (Bcl-2 and HSP 70) were greater in the treatment groups than in the controls in both regions. **Conclusions:** In conclusion, minocycline decreased the number of TUNEL-positive cells and increased the amount of anti-apoptotic factors (Bcl-2 and HSP 70), but did not change the caspase-3 content.

**Keywords:** Apoptosis; Intracerebroventricular; Minocycline; Morphine; Tolerance