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Riluzole prevents morphine-induced apoptosis in rat cerebral cortex

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Abstract:
Neuronal apoptosis has been shown to be associated with the development of tolerance to morphine. In the present study, we investigated the effect of intracerebroventricular (*icv*) administration of an inhibitor of glutamate release, riluzole, on morphine-induced apoptosis in the rat cerebral cortex. Various groups of rats received either morphine (intraperitoneally, *ip*) and vehicle (*icv*) or morphine (*ip*) and different doses of riluzole (*icv*) once per day for 8 days. An *in situ* terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end-labeling (TUNEL) method was used as an apoptosis assay. Levels of the anti-apoptotic factors Bcl-2 and HSP70 and the pro-apoptotic agent caspase-3 were evaluated by immunoblotting. The glutamate concentration in the cerebral cortex was measured by high performance liquid chromatography (HPLC). The results showed that *icv* administration of riluzole decreased the number of apoptotic cells in the cerebral cortex compared with the control group, which was treated with morphine (*ip*) and 1% Tween 80 in 0.9% normal saline (*icv*). The levels of the anti-apoptotic proteins Bcl-2 and HSP70 were higher in the riluzole groups than in the control. Furthermore, co-administration of riluzole with morphine significantly decreased caspase-3 protein levels and glutamate content of the cerebral cortex compared with the control. In conclusion, we found that *icv* administration of riluzole attenuates morphine-induced apoptosis in the cerebral cortex after the development of morphine tolerance.

Key words:
apoptosis, cerebral cortex, glutamate, morphine, riluzole