Tetramethylpyrazine suppresses HIF-1 alpha, TNF-alpha, and activated caspase-3 expression in middle cerebral artery occlusion-induced brain ischemia in rats

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摘要

Abstract

Aim: To examine the detailed mechanisms underlying the inhibitory effect of tetramethylpyrazine (TMPZ) in inflammatory and apoptotic responses induced by middle cerebral artery occlusion (MCAO) in rats. Methods: MCAO-induced focal cerebral ischemia in rats was used in this study. The hypoxia-inducible factor-1 α (HIF-1 α), activation of caspase-3, and TNF- α mRNA transcription in ischemic regions were detected by immunoblotting and RT-PCR, respectively. Anti-oxidative activity was investigated using a thiobarbituric acid-reactive substance (TBARS) test in rat brain homogenate preparations. Results: We showed the statistical results of the infarct areas of solvent- and TMPZ (20 mg/kg)-treated groups at various distances from the frontal pole in MCAO-induced focal cerebral ischemia in rats. Treatment with TMPZ (20 mg/kg) markedly reduced the infarct area in all regions, especially in the third to fifth sections. MCAO-induced focal cerebral ischemia was associated with increases in HIF-1 α and the activation of caspase-3, as well as TNF- α transcription in ischemic regions. These expressions were markedly inhibited by treatment with TMPZ (20 mg/kg). However, TMPZ (0.5-5 mmol/L) did not significantly inhibit TBARS reaction in rat brain homogenates. Conclusion: The neuroprotective effect of TMPZ may be mediated at least by a portion of the inhibition of HIF-1 α and TNF- α activations, followed by the inhibition of apoptosis formation (active caspase-3), resulting in a reduction in the infarct volume in ischemia-reperfusion brain injury. Thus, TMPZ treatment may represent an ideal

approach to lowering the risk of or improving function in ischemia-reperfusion brain injury-related disorders.