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• 中文摘要

當供給腦組織養分的血管阻塞或破裂，導致腦細胞無法維持正常生理活性的情況，稱爲「腦中風」(stroke)。腦中風依其產生的病理機轉分爲缺血性(ischemic)與出血性(hemorrhagic)中風。因爲血塊阻塞血流所引起的中風爲缺血性中風，發生率約佔所有腦中風病人的七至八成，缺血性中風的潛在因子之一爲血管壁脂質不正常堆積，也稱爲動脈粥狀硬化(atherosclerosis)，依其發生部位的不同可能進一步引起血栓性(thrombotic)或栓塞性(embolic)的缺血性中風。脆弱的腦血管破裂所引起的出血性中風，可能由動脈瘤(aneurysm)或是血管畸形(arteriovenous malformation)所引發。針對缺血性中風所引起的腦組織傷害，已有許多藥物進行動物實驗或是臨床研究，包括鈉、鉀、鈣離子阻斷劑(sodium, potassium, calcium channel blockers)、NMDA 拮抗劑(NMDA antagonists)、AMPA 拮抗劑(AMPA antagonists)、鎂鹽(magnesium)、GABA 刺激劑 (？R-aminobutyric acid agonist)、自由基清除劑(free radical scavengers)、吸附分子拮抗劑(anti-adhesion molecule agents)、基質金屬蛋白酵素抑制劑(matrix metallo-proteinase inhibitors)等。 TMPZ (2, 3, 5, 6-tetramethyl-pyrazine)爲中藥常用活血化瘀藥「川芎」的成分，已被證實具有抑制血小板凝集、促使血管擴張 (vasodilation) 的作用。本篇論文探討 TMPZ 對缺血與再灌流 (ischemia-reperfusion) 大鼠腦中風實驗模式所引起傷害的保護作用根據腦組織切片染色的實驗結果顯示 TMPZ 隨劑量關係 (10 與 20 mg/kg) 可減少腦中風引起之腦組織傷害，尤其在高劑量 (20 mg/kg) 時更有意義的減少腦部中大腦動脈 (middle cerebral artery) 引起梗塞區域神經細胞的傷害，但對大鼠神經缺損等級無明顯之影響。此外，從組織免疫染色 (immunohistochemical staining) 結果顯示 TMPZ 在劑量爲 20 mg/kg 即可抑制大鼠腦內過氧化亞硝酸之堆積，尤其對腦組織異常 iNOS (inducible nitric oxide synthase) 表現也有減低之效果。綜合實驗的結果，TMPZ 可以保護活體大鼠缺血性腦中風所引起的傷害，至於 TMPZ 在腦組織不同細胞層面詳細的作用與機轉，尚待進一步的探討。

- 英文摘要

Stroke is the state of ischemia that localized tissue is unable to maintain physiological condition due to obstruction or rupture of blood vessels in the brain. According to the pathological mechanisms, stroke is classified into two main types, ischemic and hemorrhagic stroke. Ischemic strokes are caused by blood clots that form and obstruct a blood vessel. Ischemic strokes are caused in part by atherosclerosis which is the process of abnormal lipid deposit around the vessel wall. Ischemic strokes are subtyped to thrombotic and embolic strokes according to where the blood clot forms and where it causes obstruction. Hemorrhagic stroke is defined as the rupturing of cranial blood vessels caused in part by aneurysm or arteriovenous malformation. Various drugs have been intensively researched in many animal experiments and clinical trials for the treatment of stroke including sodium, potassium and calcium channel blockers, NMDA (N-methyl-D-aspartate), and AMPA (? H ? H-amino-3-hydroxy-5-methyl-4-isoxazole) anta-gonists, magnesium, ? HR-aminobutyric acid agonist, free radical scavengers, anti-adhesion molecule therapy, matrix metalloproteinase inhibitors and therapeutic hypothermia. TMPZ (2, 3, 5, 6-tetramethylpyrazine) is extracted from the root of Ligusticum wallichii, a common herb used in traditional Chinese medicine. TMPZ has antiplatelet and vasodilation activity. It is shown to improve changes in microcirculation of patients with acute cerebral thrombosis. In this study we evaluated the protective effects of TMPZ in a cerebral ischemia-reperfusion injury model in rats. Volumes of cerebral infarct decreased when rats were pretreated with 20 mg/kg TMPZ. However, the neurological deficits didn ? H ? Ht change after drug treatment. Moreover, immunohistochemical staining showed that the accumulation of peroxynitrite in cerebrum with infarct was reduced by TMPZ pretreatment. According to the findings, TMPZ have protective effects against cerebral infarction. However, the exact mechanisms of their protective effects at cellular level need to be clarified in the future.