中国药理学与毒理学杂志 2012 26 (3): 305-309 ISSN: 1000-3002 CN: 11-1115/R

论著

吡格列酮对脂多糖诱导星形胶质细胞诱导型一氧化氮合酶表达的抑制作用

刘卓[1], 金英[1], 隋海娟[1], 闫恩志[1], 刘婉珠[2]
1. 辽宁医学院, 药理学教研室, 辽宁 锦州 121001;
2. 辽宁医学院, 机能实验中心, 辽宁 锦州 121001

收稿日期 2011-9-5 修回日期 2011-12-6 网络版发布日期 2012-7-19 接受日期

摘要 目的 研究吡格列酮(Pio)对脂多糖 (LPS) 诱导星形胶质细胞(AC)诱导型一氧化氮合酶(iNOS)的抑制作用及其作用机制。方法 AC分别加入Pio 0.1, 1.0和10.0 μmol·L^{-1}, c-Jun氨基端激酶(JNK)抑制剂SP600125 20.0 μmol·L^{-1}, p38丝裂原活化蛋白激酶(p38MAPK)抑制剂SB203580 20.0 μmol·L^{-1}或过氧化物酶体增殖物激活受体γ(PPARγ)抑制剂GW9662 10.0 μmol·L^{-1}, 1 h以后加入LPS 10.0 mg·L^{-1}, 继续作用24 h。Griess法测定培养AC上清液中一氧化氮(NO)含量。免疫印迹法和免疫荧光法检测iNOS的表达水平。结果 与正常对照组相比, LPS 10.0 mg·L^{-1}组iNOS表达水平和NO分泌水平均显著增高(P<0.01)。Pio 0.1, 1.0和10.0 μmol·L^{-1}可明显抑制LPS诱导的iNOS表达上调及NO分泌增加(P<0.05), Pio 10.0 μmol·L^{-1}组iNOS蛋白表达水平由LPS组1.711±0.283下降到0.157±0.082(P<0.01), NO分泌量由LPS组(16.63±2.25)μmol·L^{-1}下降到(6.92±1.30)μmol·L^{-1}(P<0.01)。GW9662 10.0 μmol·L^{-1}可抑制Pio 1.0 μmol·L^{-1}的上述作用, iNOS蛋白表达水平由Pio 1.0 μmol·L^{-1}组0.562±0.100增加到0.847±0.088(P<0.01), NO分泌量由(9.27±1.23)μmol·L^{-1}增加到(15.54±2.30)μmol·L^{-1}(P<0.01)。SB203580 20.0 μmol·L^{-1}和SP600125 20.0 μmol·L^{-1}的作用与Pio作用相似, 使iNOS蛋白表达水平降低到0.434±0.082和0.434±0.076, NO分泌量下降到(11.53±2.40)μmol·L^{-1}和(8.81±0.58)μmol·L^{-1};而单独应用SB203580 20.0 μmol·L^{-1}和SP600125 20.0 μmol·L^{-1}对AC的iNOS表达和NO分泌没有影响。结论 Pio能通过抑制LPS诱导的大鼠皮质AC的iNOS表达, 从而减少NO的分泌, 这种抑制作用可能与其激活PPARγ和阻断JNK和p38MARK信号转导通路有关。

关键词 吡格列酮 诱导型一氧化氮合酶 一氧化氮 过氧化物酶体增殖物激活受体γ c-Jun氨基端蛋白激酶 p38丝裂原活化蛋白激酶
分类号 R971 R966

Inhibitory effect of pioglitazone on the expression of inducible nitric oxide synthases induced by lipopolysaccharide in cultured astrocytes in rats

LIU Zhuo[1], JIN Ying[1], SUI Hai-juan[1], YAN En-zhi[1], LIU Wan-zhu[2]

1. Department of Pharmacology, Liaoning Medical University, Liaoning 121001, China;
2. Department of Functional Laboratroy, Liaoning Medical University, Liaoning 121001, China

Abstract

OBJECTIVE To investigate whether pioglitazone(Pio) can protect cortical astrocytes from lipopolysaccharide(LPS)-induced expressions of inducible nitric oxide synthases (iNOS) and release of NO, and their mechanisms. **METHODS** Pioglitazone 0.1, 1.0 or 10.0 μmol·L^{-1}, p38 mitogen-activated protein kinase (p38 MAPK) inhibitor SB203580 20.0 μmol·L^{-1}, c-Jun N-terminal protein kinase (JNK) inhibitor SP600125 20.0 μmol·L^{-1} or peroxisome proliferator-activated receptor γ (PPARγ) inhibitor GW9662 10.0 μmol·L^{-1} combined Pio 1.0 μmol·L^{-1} treated astrocyte(AC) cells for 1 h before LPS 10 mg·L^{-1} induced astrocytes. The supernatants of astrocytes were collected and analyzed

for NO generation. Western blotting and immunofluorescent technology were used to observe iNOS level in astrocytes in rats. **RESULTS** Compared with normal control group, expression of iNOS and the release of NO in cultured astrocytes in rats markedly increased when astrocytes were induced by LPS (P<0.01). Pio 0.1, 1.0 and 10.0 μmol • L^{-1} inhibited LPS-induced increase of iNOS expression and the release of NO in cultured astrocytes. iNOS expression decreased from 1.711±0.283 in LPS-treated group to 0.157±0.082 in Pio10.0 μmol • L^{-1} group and NO release decreased from (16.63±2.25) μmol • L^{-1} in LPS-treated group to (6.92±1.30)μmol • L^{-1} in Pio 10.0 μmol • L^{-1} group (P<0.01). GW9662 10.0 μmol • L^{-1} reversed the effects of Pio 1.0 μmol • L^{-1}, in which iNOS expression increased from 0.562±0.100 to 0.847±0.088 (P<0.01) and NO release increased from (9.27±1.23)μmol • L^{-1} to (15.54±2.30)μmol • L^{-1}(P<0.01). SP600125 or SB20358 significantly inhibited LPS-induced increase in