DOI: 10.16016/j.1000-5404.1998.01.022

hypobaric hypoxia in rats. Methods: Adult Wistar rats were randomized into 6 groups: 1) sea level group (SL); 2) 1-day-hypoxic group (H1); 3) 7-day-hypoxic group (H2); 4) 14-day-hypoxic group (H14); 5) 21-day-hypoxic group (H21); 6) 30-day-hypoxic group (H30). Erythrocyte filtration index (IF), the ATPase activities and ATP content were determined. Results: 1) IF was significantly lower in SL than in each hypoxic group ($P < 0.05$ or 0.01). It reached its peak in H7 and then gradually decreased. There was no evident difference between H21 and H30. 2) Erythrocyte ATP content was significantly lower in H1 and H7 than in SL and negatively correlated to their IF ($r = -0.6358$, $P < 0.01$; $r = -0.7044$, $P < 0.01$). 3) Na-K-ATPase and Ca-ATPase activities were significantly lower in hypoxic groups than in SL but Mg-ATPase activity reduced only in H30. Conclusion: Hypoxia can destroy erythrocyte deformability, but it was not progressive. Erythrocyte deformability might be improved in the second hypoxic week and then decreased to reach hemostasis in the third or fourth week. 2) The decrement of erythrocyte ATP contents in the early hypoxic period and ATPase activity in the whole hypoxic course play an important role in erythrocyte deformability damages during hypobaric hypoxia.

Key words erythrocyte devormability; ATPase activity; ATP; hypoxia; rat

烟雾吸入性肺损伤大鼠 SPA表达异常机制研究

A study on the mechanisms of SPA down- regulation in a rat model of smoke inhalation injury

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我所既往研究发现吸入伤后 SPA mRNA表达下降,然而其机理尚不清楚,本研究旨在探讨吸入伤后 SPA mRNA表达下降机理。

反式作用因子与基因顺式元件相互作用,对基因转录具有关键性作用,活性氧作为基因调控信号传导分子,通过对反式作用因子活性调节,调控多种基因转录过程。故本研究从 SPA反式作用因子(TTF$_1$)与 SPA顺式元件环节,探讨吸入伤后活性氧对 SPA基因调控机制。拟从以下三方面进行研究:① 动物体内实验:研究吸入伤后肺脏氧化应激与 SPA mRNA表达及其关系;② 体外实验:a.从 SPA顺式元件与 TTF$_1$分子结合水平,研究活性氧及氧化还原状态对其结合活性的影响;b.从 SPA体外转录水平,研究活性氧及氧化还原状态对 TTF$_1$启动 SPA体外转录的影响;③ 以 NAC清除吸入伤肺脏氧化应激,研究氧化应激解除后,SPA mRNA表达情况。

本研究还采用动物实验研究了 NAC对吸入伤 SPA相关功能及对吸入性肺损伤保护作用,为 NAC用于吸入伤临床治疗提供依据,也是本研究另一目的。

结果与结论:(1)体内实验发现:① 吸入伤后肺脏 MDA含量显著增加;总抗氧化能力(TAO)显著降低;还原性谷胱甘肽显著消耗。② 吸入伤后 SPA mRNA表达明显降低。提示:吸入伤后肺脏活性氧大量产生、肺脏氧化还原电势(GSSG/GSH)增高,可能是吸入伤后 SPA mRNA表达下降的原因。

(2)体外实验发现:① 活性氧(H_2O_2)及 GSH氧化产物 GSSG,可抑制 TTF$_1$与 SPA顺式件结合,GSH可解除上述抑制作用;② 活性氧介质(H_2O_2)及 GSSG可抑制 TTF$_1$与 SPA体外转录,GSH可解除上述抑制作用。表明:吸入伤后 TTF$_1$"置身"于高活性氧及高氧化还原电势环境,TTF$_1$与 SPA顺式元件结合受抑制可能是吸入伤后 SPA mRNA表达下降的分子病理基础。

(3)以 NAC清除吸入伤肺脏氧化应激、提高 GSH含量,发现吸入伤后 SPA mRNA表达增强。证实了上述推论及结论。

(4) NAC对吸入伤治疗保护实验发现:① NAC治疗可改善 SPA相关功能:a. NAC治疗后可使反映静态肺顺应性的参数 C2.94 C0.49 EI;及反映肺表面活性物质特性的参数 STmin Ha RI SI恢复至正常水平;b. NAC治疗后肺Ⅱ型细胞板层体恢复至正常形态。② NAC治疗可保护肺损伤:a. NAC治疗后反映肺损伤的 BALF中 AKP LDH酶活性;及反映肺微血管损伤的 BALF中白蛋白含量恢复至正常水平。b. NAC治疗后 BALF中白细胞总数及中性粒细胞百分数皆恢复至正常水平;c. NAC治疗后肺脏病理形态异常明显减轻。表明: NAC对吸入性肺损伤具有治疗、保护作用。

关键词 肺损伤; SPA; TTF;顺式元件;反式因子;氧化还原

中图法分类号 R644

(收稿: 1997-12-05;修回: 1998-01-06)

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