麩醯胺或精胺酸添加對發炎反應引發免疫黏著分子表現及白血球遷移之影響

Effects of glutamine or arginine on inflammatory-induced adhesion molecule expression and leukocyte migration

中文摘要

本研究分成動物實驗及細胞培養兩部分，動物實驗主要觀察以 glutamine (GLN) 或 arginine (Arg)介入對敗血症黏著分子及發炎反應相關介質的影響。細胞培養實驗將人類臍帶靜脈內皮細胞(human umbilical vein endothelial cells, HUVECs)及中性多形核白血球(polymorphonuclear neutrophils, PMNs)培養於不同濃度的 GLN 或 Arg 中，以腹部手術病人的血漿及腹腔沖洗液(peritoneal drain fluid, PDF)刺激後，觀察細胞上黏著分子、細胞激素及接受器的表現，並觀察 PMNs 穿過 HUVEC 轉移的情形。在 GLN 介入的動物實驗結果顯示，與控制組比較，GLN 組降低循環血中的 intercellular adhesion molecule (ICAM)-1 濃度，器官中 myeoloperoxidase (MPO)的活性及肝外器官中 interleukin (IL)-6 的表現，淋巴球內 interferon (IFN)-γ 濃度較高而 IL-4 則較低，此結果顯示 GLN 使敗血症時發炎反應趨緩，體內 Th1/Th2 平衡趨向 Th1。細胞培養實驗結果顯示 HUVEC 及 PMNs 上的免疫黏著分子及整合素會被腹部手術病人的血漿及 PDF 刺激而表現。與低濃度(300uM)相較，GLN 在接近人類正常生理濃度(600μM)及高於生理濃度(1000μM)時，會降低因病人體液刺激所表現的免疫黏著分子、整合素、IL-8 濃度及 PMNs 轉移的數目。在 Arg 介入的動物實驗結果顯示，與控制組比較，Arg 組增加循環血中的 ICAM-1 濃度，器官中
MPO 的活性及肝外器官中 IL-6 的表現，淋巴球內 IFN-γ 濃度較低而 IL-4 則較高，此結果顯示 Arg 使敗血症時發炎反應增加，體內 Th1/Th2 平衡較趨向於 Th2。細胞培養實驗結果顯示與低濃度(50uM)相較，Arg 在接近人類正常生理濃度(100μM)時，會降低因病人體液刺激所表現的免疫黏著分子、整合素、IL-8 濃度及 PMNs 轉移的數目，在高於生理濃度(1000μM)時降低的情況更為明顯。在給予 NO synthase 抑制劑(LNMMA)後，則 100uM 及 1000 uM 在黏著分子表現及 PMNs 遷移的結果均與 50 uM 相同。此結果顯示 NO 在 HUVEC 及 PMNs 受到刺激時對黏著分子表現及 PMNs 發生轉移的作用扮演非常重要的調節角色。

英文摘要

There were two parts in this study. The animal studies investigated the effects of glutamine (GLN) or arginine (Arg) on plasma intracellular adhesion molecule (ICAM)-1 levels and leukocyte integrin expressions in gut-derived sepsis. Myeloperoxidase (MPO) activities in organs were also analyzed to identify the extent

of tissue injury resulting from neutrophil infiltration. The in vitro studies investigated the effect of different GLN or Arg concentrations on surface molecule expression on endothelial cells (ECs) and leukocytes and the transendothelial migration of polymorphonuclear neutrophils (PMNs) through ECs stimulated by plasma or peritoneal drain fluid (PDF) from a surgical patient. The results of GLN intervention in septic mice showed that, GLN administration may enhance lymphocyte function, reduced interleukin (IL)-6 levels in organs, attenuate the PMN-endothelium interactions and may consequently decrease neutrophil infiltration into tissues. The GLN in vitro study suggests that ECs and PMNs were activated after patient's plasma or PDF stimulation. A low GLN concentration comparable to catabolic conditions (300 uM) resulted in higher adhesion molecule expression and greater transendothelial migration of neutrophils. GLN administration at levels similar to (600 uM) or higher than physiologic concentrations (1000 uM) reduced IL-8 and adhesion molecule expression, and PMN transmigration was also decreased after stimulation with plasma or PDF from a surgical patient. The results of Arg intervention in septic mice showed that, Arg administration increased CAM expression, enhanced MPO activities in organs and aggravated the PMN-endothelium interactions in septic condition. The Arg in vitro study suggests that a low Arg concentration comparable to catabolic conditions (50 uM) resulted in higher adhesion molecule expression and greater transendothelial migration of neutrophils. Arg administration at levels similar to physiologic concentrations (100 uM) reduced IL-8 and adhesion molecule expression, and PMN transmigration was also decreased. High Arg concentration (1000 uM) had greater reduction effect on CAM expression and PMNs migration after stimulation with body fluid from a surgical patient. There were no differences in CAM and IL-8 expressions in groups incubated with different Arg concentration when nitric oxide (NO) synthase inhibitor (LNMMA) was added in the medium. This result suggests that NO plays an important role in modulating CAM expression and PMNs transmigration.