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Lung alert

Inhibition of NKCC1 may be beneficial in sepsis

Mortality related to bacteraemic pneumonia remains high, and previous studies have shown that the Na⁺–K⁺–Cl cotransporter (NKCC1) may have an important role in causing acute lung injury secondary to compromise of the alveolar-capillary barrier. Under normal physiological conditions, NKCC1 plays a central role in salt transport and volume regulation in epithelial and non-epithelial cells. This study investigated the host response to *Klebsiella pneumoniae* infection in an experimental model of bacteraemia in congenic mice lacking NKCC1 expression (NKCC1^{–/–}) and control mice (NKCC1^{+/+}).

Mice were infected with *K pneumoniae* and bronchialveolar lavage fluid (BALF) was analysed 48 h later. NKCC1^{–/–} mice had significantly higher numbers of cells in BALF, in particular increased numbers of neutrophils and interleukin (IL)-10. There was also a 10-fold decrease in bacterial colony forming units (CFUs) in NKCC1^{–/–} mice compared with controls. Hypothermia was also significantly less in NKCC1^{–/–} mice 48 h after infection. Similar changes were noted in a model of acute inflammation after lipopolysaccharide stimulation, with significantly higher neutrophils, macrophages and IL-6 in NKCC1^{–/–} mice. However, these effects were observed primarily in the pneumonic model and not in the peritonitic model.

This study shows that NKCC1 contributes to changes in pulmonary vascular permeability during inflammation, and loss of NKCC1 expression shows a protective effect against hypothermic sepsis and bacteraemia. Inhibitors specific for NKCC1 might provide a novel means of limiting sepsis in individuals with bacterial pneumonia.

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