The Intensive Care Society

Churchill House, 35 Red Lion Square, London WC1R 4SG
Tel: +44 (0)20 7280 4350 Fax: +44 (0)20 7280 4369
E-mail: admin@ics.ac.uk www.ics.ac.uk

Patron: HRH The Princess Royal

Young Investigator Award Winner

Investigation of the protective effects of aspirin in an inhaled endotoxemic model of acute lung injury in healthy volunteers

Dr Murali Shyamsundar, The Queen's University of Belfast

Acute lung injury (ALI) has an incidence of 79/100,000 patient years with high mortality of up to 65%. Inhalation of lipopolysaccharide (endotoxin) results in a local inflammatory response in the alveolar compartment of healthy humans, with neutrophilic infiltration and an increase in inflammatory cytokines in bronchoalveolar lavage (BAL) fluid, without causing adverse events and is a useful *in vivo* model of lung injury.

Depletion of platelets has been shown to decrease neutrophil sequestration in the lungs in models of ALI. Platelets can interact with activated endothelial cells which is followed by platelet–neutrophil and platelet-macrophage interaction through cell surface molecules. Thromboxane A_2 (TXA_2) which is released by activated platelets can also act on endothelial cells.

Aspirin has been shown to be beneficial in murine models of transfusion related ALI (TRALI) and acid-induced ALI. Apart from inhibiting the production of TXA_2, aspirin can decrease the expression of TNF-α via NFκB inhibition. Aspirin treatment can also increase production of lipoxins which have anti-inflammatory effects.

The hypothesis is that treatment with a clinically relevant dose of aspirin will reduce pulmonary inflammation induced by LPS inhalation in humans.

The aims of this study are to provide insight into the biology and pathogenesis of lung injury and assess the ability of aspirin to attenuate lung injury by measuring

1) alveolar and plasma inflammatory response
2) alveolar matrix metalloproteinase activity
3) alveolar and systemic prostaglandin and lipoxin level
4) intracellular signalling and transcription factor activation in the alveolar space

alveolar epithelial and endothelial function and injury