BMC Pharmacology



Poster presentation



# Inhaled NO and the guanylate cyclase stimulator Bay 41-2272 in oleic acid induced acute lung injury in rabbits

Andreas Weidenbach*[1], Johannes-Peter Stasch[2], Hossein Ardeschir Ghofrani[1], Norbert Weissmann[1], Friedrich Grimminger[1], Werner Seeger[1] and Ralph Theo Schermuly[1]

Address: [1]Center for Internal Medicine, Medical Clinic II, University Hospital of the Justus-Liebig-University Giessen, Klinikstrasse 36, 35392 Giessen, Germany and [2]Institute of Cardiovascular Research, Bayer HealthCare, Aprather Weg 18a, 42096 Wuppertal, Germany

Email: Andreas Weidenbach* - Andreas.Weidenbach@innere.med.uni-giessen.de

* Corresponding author

*from* 2nd International Conference of cGMP Generators, Effectors and Therapeutic Implications
Potsdam, Germany, 10–12 June, 2005

Published: 16 June 2005

*BMC Pharmacology* 2005, **5**(Suppl 1):P61 doi:10.1186/1471-2210-5-S1-P61

## Background

Pulmonary hypertension (PH) due to vasoconstriction and occlusion of the pulmonary microvasculature is a characteristic feature of the acute respiratory distress syndrome (ARDS). Inhaled nitric oxide (NO) selectively dilates the pulmonary vasculature by activating soluble guanylate cylase (sGC). Bay 41-2272 a novel sGC stimulator not only activates sGC NO independently, but also leads to synergistic effects when combined with NO. Because contradictory results of a number of experimental studies dealing with the effects of iNO in acute lung injury and the uncertain efficacy of iNO in the treatment of ARDS, we evaluated the effects of iNO and BAY 41-2272 in a model of acute lung injury. METHODS: Acute lung injury (ALI) was induced by i.v. injection of oleic acid (OA). In the first treatment group iNO (2 ppm) was administered continuously after ALI. In the second group, BAY 41-2272 (100 μg/kg) was infused for 10 min directly after injection of OA. In the third group, iNO and BAY 41-2272 were combined.

## Results

iNO was not able to improve OA induced lung injury. The intravenous administration of BAY 41-2272 alone slightly decreased pulmonary artery pressure (PAP) with no systemic hemodynamic effects but failed to improve gas exchange. The combined administration of iNO and BAY 41-2272 clearly lowered PAP again without affecting systemic arterial pressures but improved arterial oxygenation and intrapulmonary shunting.

## Conclusion

This study showed that combined administration of BAY 41-2272 with iNO leads to selective pulmonary vasodilatation which is associated with an improvement of gas exchange. Due to the known mechanism of action of the two substances, this effect is probably mediated by an increase of local cGMP concentrations in well ventilated lung regions.