

## Inhaled lipopolysaccharide-induced bronchial neutrophilia in anaesthetized pigs: inhibition by fluticasone propionate

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The pig has previously been shown to be a suitable species in which to investigate allergic inflammation of the airways (Fornham et al 1995). In this study, we have investigated an acute inflammatory response in the lung of the pig following inhalation of aerosolised lipopolysaccharide (LPS). In addition, the effects of fluticasone propionate (FP) administered directly into the lungs as a dry powder was investigated on the LPS-induced inflammatory response.

Pigs of either sex, weighing 25-35kg, were anaesthetised, ventilated and surgically prepared to allow measurement of blood pressure and heart rate via a carotid artery, and tracheal inflation pressure. Following an equilibration period of approximately 30 minutes, an aerosol of saline or LPS (10-1000µg/ml) was administered for 10 minutes via a tracheal cannula. Two to six hours later, the lungs were lavaged and the cellular content of the bronchoalveolar lavage fluid (BALF) was determined.

Inhaled LPS caused a dose- and time- dependent lung neutrophilia in the anaesthetised pig (tables 1 and 2).

Table 1. Lung neutrophilia in response to increasing doses of LPS. Data are mean neutrophil numbers  $\times 10^5/\text{ml}$  BALF (+/-SEM) from 3 – 4 experiments.

|       | Saline       | LPS (µg/ml)  |              |              |
|-------|--------------|--------------|--------------|--------------|
|       |              | 10           | 100          | 1000         |
| Neuts | 0.9<br>(0.4) | 1.7<br>(0.4) | 6.4<br>(1.2) | 9.9<br>(4.5) |

Table 2. Time course of lung neutrophilia in response to LPS (100µg/ml). Data are mean neutrophil numbers  $\times 10^5/\text{ml}$  BALF (+/-SEM) from 3 – 4 experiments.

|       | Saline (4h)  | Time (hours) |              |              |
|-------|--------------|--------------|--------------|--------------|
|       |              | 2            | 4            | 6            |
| neuts | 0.9<br>(0.4) | 2.0<br>(0.8) | 6.4<br>(1.2) | 5.5<br>(1.3) |

For subsequent studies, 100µg/ml LPS was administered over 10 minutes, followed by bronchoalveolar lavage four hours later.

FP in dry powder form was administered directly into the lungs one hour prior to LPS aerosol, and caused a dose-dependent inhibition of the neutrophilia. The doses of FP used were 1%, 2%, 5% and 10% in lactose (~ 20mg of dry powder administered), which caused 17.1%, 48.2%, 72.4% and 94.5% inhibition of the LPS-induced neutrophilia, respectively.

In conclusion, inhaled LPS caused a dose- and time-dependent influx of neutrophils into the lungs of anaesthetised pigs. Furthermore, pre-treatment with inhaled FP inhibited this acute lung neutrophilia.

Fornham, C. et al (1995) *Eur. Respir. J.* 8: 1100-1109