September 20th, 2023 17:30 - 18:30

PLENARY SESSION 3 - BENGT ROBERTSON AWARD

ID 562. THERAPY WITH A FRAGMENT OF RECOMBINANT SURFACTANT PROTEIN D DEMONSTRATES NO TOXICITY IN VENTILATED AND NON-VENTILATED TRANSLATIONAL MODELS.

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Introduction

Bronchopulmonary dysplasia (BPD) affects up to 40% of infants born <30 weeks gestational age, with inflammation playing a key role in its development. Surfactant Protein D (SP-D) has several immunomodulatory functions in the lung. We employed two translational models; a preterm lamb model of ventilator-associated lung injury and a non-ventilated mini-pig model to test the hypothesis that a recombinant fragment SP-D (rfhSP-D) is non-toxic when administered as intratracheal (IT) therapy whilst reducing inflammation and may have therapeutic potential in preterm infants.

Methods

The studies were funded by MRC and conducted with animal ethics approval. 16 mechanically ventilated preterm lambs and 18 non-ventilated mini pigs were randomised to either IT rfhSP-D or control (IT 0.9% saline). Lambs were treated with

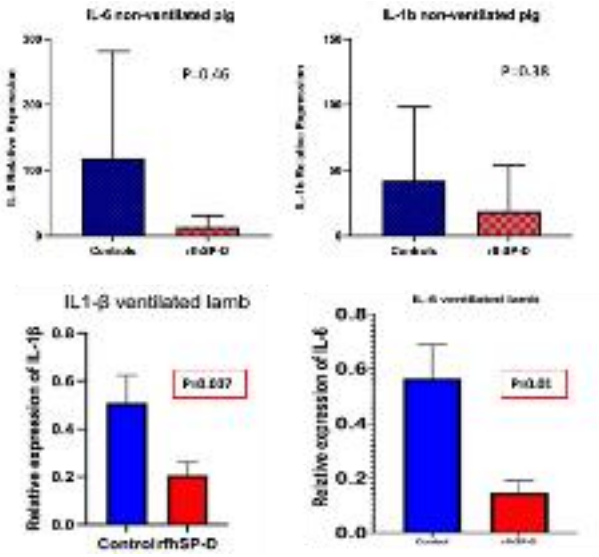
24mg of rfhSP-D administered at 20, 140 and 260 minutes. Mini-pigs were treated with 3 doses of 4mg/kg rfhSP-D at 0, 12 and 24 hours. SP-D levels and cell infiltrates were measured in terminal bronchoalveolar lavage, and PCR was used to analyse the expression of IL-1β, IL-6, IL-8 and TNF-α in homogenised lung tissue.

Results

IT administration of rfhSP-D in non-ventilated mini pigs was shown to be effective and was cleared from the BAL within 72 hours of administration. There was no increase in expression of pro-inflammatory cytokines, expression was lower in the treated animals but not statistically significant ($p>0.05$). There was no significant difference in the cell infiltrates between the treated and untreated groups. In ventilated preterm lambs expression of all pro-inflammatory cytokines was lower in the treated animals and expression of IL-1β and IL-6 was significantly lower in the IT rfhSP-D group ($p=0.007$ and $p=0.01$ respectively).

Conclusion

IT administration is effective in delivering rfhSP-D and there is good clearance from the lungs. IT rfhSP-D in these translational models showed no toxic effect on pro-inflammatory cytokines and in the ventilated model was shown to significantly reduce potent pro-inflammatory cytokines such as IL-1β and IL-6, which are known to have a role in the development of BPD. These results support that rfhSP-D is likely to have a therapeutic benefit in preterm infants at risk of BPD.



Expression of IL–1β and IL–6 in ventilated and non–ventilated models. Expression of pro–inflammatory cytokines was lower in the treated animals in both models. Mean+SD, compared using Mann–Whitney test, p<0.05=statistical significance.
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None Declared