NEONATAL PULMONARY RESEARCH

Mesenchymal stromal cells are more effective than the MSC secretome in diminishing injury and enhancing recovery following Ventilator-induced lung injury

Background

The therapeutic potential of mesenchymal stromal cells (MSCs) for lung diseases like acute respiratory distress syndrome (ARDS) has been demonstrated in several models of ARDS. Furthermore, several studies have reported that MSCs act via a paracrine mechanism – either by its secreted factors alone or together with direct cell-to-cell contact. MSCs secrete factors, which enhance lung repair and regeneration at 48 hours following ventilation-induced lung injury (VILI), but the timing of benefit is unknown. In this study, the authors determined the potential for MSC therapy in Sprague-Dawley rats in the early recovery phase following VILI by comparing the beneficial effect of: I) 10 million MSCs or fibroblasts/kg, II) 500µl MSC-conditioned medium (CM) or phosphate buffered saline four hours following VILI induction (n=8-9).

Summary of results

The results showed that MSCs administered four hours following ventilation-induced lung injury have lung protective effects. MSCs improved arterial oxygenation and lung compliance and decreased lung oedema. Additionally, they modulated the inflammatory response by decreasing inflammatory cell counts (e.g. neutrophils) in BAL fluid or by decreasing the alveolar concentration of the pro-inflammatory cytokines IL-1ß and IL-6. Furthermore, the lung structure was improved by decreased alveolar thickening and increased recovery of airspace volume. In contrast to these observations, MSC-CM alone had no significant effects on alveolar oxygenation, lung compliance and lung oedema but had at least a partial effect on reducing inflammatory cell infiltration.

Strength

Finding the earliest time-point at which MSCs exert their benefits after lung injury allows determining the optimal timing of MSC administration. In contrast to many other studies, the authors analysed the beneficial effect of MSCs as early as four hours after inducing the lung injury. They could show that there are lung-protective effects after MSC administration but no (or less) effects after administration of MSC-CM alone.

Limitations

As the authors mentioned, the analysis of rodent models limits the extrapolation to the clinical situation and they do not provide data of the effects of MSCs on protectively ventilated or unventilated lungs, or on lungs where the MSC were given at the time of ventilation. A comparison of these results could help to determine the optimal time-point for MSC administration. There could be also lung-protective effects of MSC-CM at other application time-points. The authors do not give any information about oxygen concentrations in the MSC and MSC-CM culture atmosphere. That information could be important, because there is evidence that MSC characteristics, e.g. their secretion profile, change with their oxygen environment.

Practical conclusion

The observation that mesenchymal stromal cells in combination with their secretome rather than their secretome alone generate the most efficient lung protective effects and that these effects also exist in the early recovery phase following ventilation-induced lung injury are helpful hints for clinical MSC-therapy designs in lung diseases.

Hayes et al., Mesenchymal stromal cells are more effective than the MSC secretome in diminishing injury and enhancing recovery following Ventilator-induced lung injury. *Intensive Care Medicine Experimental,* (2015) 3:29

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