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Intratracheal administration of clinical-grade mesenchymal stem-cell-derived extracellular vesicles reduces lung injury in a rat model of Bronchopulmonary Dysplasia

Andrea Porzionato[1], Patrizia Zaramella[2], Arben Dedja[3], Diego Guidolin[1], Kelly Van Wemmel[4], Veronica Macchi[1], Marcin Jurga[4], Giorgio Perilongo[5], Eugenio Baraldi[2], Maurizio Muraca[6] and Raffaele De Caro[1]

[1] Sezione di Anatomia Umana, Dipartimento di Neuroscienze, Università degli Studi di Padova, Padova, Italia
[2] Unità di Terapia Intensiva Neonatale, Dipartimento della Salute della Donna e del Bambino, Università degli Studi di Padova, Padova, Italia
[3] Dipartimento di Scienze Cardiache, Toraciche e Vascolari, Università degli Studi di Padova, Padova, Italia
[4] The Cell Factory BVBA, (Esperite NV), Niel, Belgio
[5] Clinica Pediatrica, Dipartimento della Salute della Donna e del Bambino, Università degli Studi di Padova, Padova, Italia
[6] Laboratorio di Cellule Staminali e Medicina Rigenerativa, Dipartimento della Salute della Donna e del Bambino, Università degli Studi di Padova, Padova, Italia

Mesenchymal stem cells (MSCs) prevent the onset of bronchopulmonary dysplasia (BPD) in animal models, an effect that seems to be mediated by their secreted extracellular vesicles (EVs). The aim of this study was to compare the protective effects of intratracheally (IT)-administered MSCs vs. MSC-EVs in a hyperoxia-induced rat model of BPD.

At birth, rats were distributed as follows: animals raised in ambient air for 2 weeks (n=10); and animals exposed to 60% oxygen for 2 weeks and treated with IT-administered physiological solution (n=10), MSCs (n=10), or MSC-EVs (n=10) on postnatal days 3, 7, and 10.

The sham-treated hyperoxia-exposed animals showed reductions in total surface area of alveolar air spaces, and total number of alveoli (Nalv), and an increased mean alveolar volume (Valv). EVs prompted a significant increase in Nalv ($P<0.01$), and a significant decrease in Valv ($P<0.05$) compared with sham-treated animals, while MSCs only significantly improved Nalv ($P<0.05$). Small pulmonary vessels of the sham-treated hyperoxia-exposed rats also showed an increase in medial thickness, which only EVs succeeded in preventing significantly ($P<0.05$).

In conclusion, both EVs and MSCs reduce hyperoxia-induced damage, with EVs obtaining better results in terms of alveolarization and lung vascularization parameters. This suggests that IT-administered EVs could be an effective approach to BPD treatment.