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Cell-based therapy for hypoxic-ischemic injury in the preterm brain

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Background and aims: Preterm infants are at risk for hypoxic-ischemic encephalopathy. Unfortunately, no therapy exists to treat the brain injury in this patient population. The aims of this translational study were to assess the neuroprotective effect of exogenous administration of mesenchymal stem cells (MSC) and the mobilization of endogenous hematopoietic stem cells in the preterm brain after global hypoxia-ischemia.

Methods: Instrumented preterm sheep were subjected to global hypoxia-ischemia by 25 minutes of umbilical cord occlusion at a gestational age of 104 (term is 150) days. During a 7 day reperfusion period all vital parameters, including (amplitude-integrated) electroencephalogram, were recorded. At the end of the experiment, the preterm brain was assessed using histology and magnetic resonance imaging (diffusion tensor imaging (DTI)). In two separate experimental set-ups, exogenous MSCs or granulocyte-colony stimulating factor (G-CSF) were administered intravenously with the appropriate control groups.

Results: Administration of exogenous MSCs reduced cerebral inflammation and white matter injury. MSCs induced T-cell tolerance, which was paralleled with diminished mobilization and invasion of these cells in the preterm brain. In addition, MSCs established functional improvement, as shown by decreased number of seizures after global hypoxia-ischemia. Similarly, mobilization of endogenous stem cells using systemic granulocyte-colony stimulating factor (G-CSF) reduced cerebral inflammation and white matter injury. However, G-CSF did not reduce the number of seizures after global hypoxia-ischemia.

Conclusion: We have shown for the first time in a translational animal model that cell-based therapy is effective in protecting the preterm brain against the cerebral and peripheral inflammatory responses which are involved in the etiology of white matter injury in the preterm brain after global hypoxia-ischemia. Our studies form the basis for future clinical trials studying feasibility of cell-based therapy in preterm infants with hypoxic-ischemic encephalopathy.

Biography

Boris W Kramer has completed his MD at the University of Tübingen/ Germany, and his PhD at the University of Maastricht. He performed Postdoctoral studies at the Cincinnati Children's Hospital/Ohio/USA. He is a neonatologist and the director of pediatric research. He has published more than 165 papers in reputed journals and serving as an editorial board member of international journals.

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