Mannitol boosts effectiveness of potential cord blood treatment for cerebral palsy in lab animals

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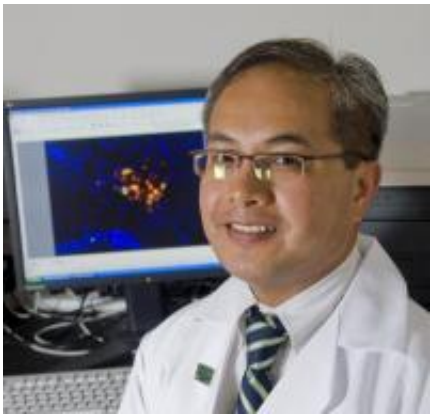

Cesar Borlongan, Ph.D., of the University of South Florida's Department of Neurosurgery and Brain Repair, led the study. Credit: © University of South Florida

The sugar-alcohol compound mannitol improved the therapeutic effectiveness of human umbilical cord blood cells injected into neonatal rat models of cerebral palsy, reports a new international study led by the University of South Florida. The mannitol opened the blood-brain barrier by temporarily shrinking the tight endothelial cells that make up the barrier.

Intravenously-delivered human umbilical cord blood (HUCB) may offer therapeutic benefits to those suffering from cerebral palsy if the blood

cells can get past the blood-brain barrier to the site of injury, the research team suggests. Their findings were recently published online in the *Journal of Cellular and Molecular Medicine* (14:4).

There is supportive treatment, but no cure for cerebral palsy, a group of neurological disorders caused by brain damage before birth or during infancy and characterized by impaired muscle coordination.

"The combination of mannitol and human umbilical cord blood treatment increased central nervous system levels of at least three neurotrophic factors -- glial cell line-derived neurotrophic factor, nerve growth factor and brain-derived neurotrophic factor," said Dr. Cesar Borlongan, the study's lead author and a professor in the University of South Florida College of Medicine's Department of Neurosurgery and Brain Repair.

The mannitol treatment did not increase the survival of human umbilical cord blood (HUCB) grafts, but by elevating the trophic factors HUBC combined with mannitol "could mediate robust functional improvement," according to Dr. Borlongan and his co-authors.

"Intravenous delivery of human umbilical cord blood alone promoted behavioral recovery in neonatal animal models of cerebral palsy, but their functional improvement was more pronounced when human umbilical cord blood transplantation was combined with mannitol," commented Dr. Borlongan.

He noted that the lab animals were administered a variety of post-treatment movement tests and that those receiving the combination treatment instead of HUCB alone or mannitol alone demonstrated the most motor improvement.

"Our results indicate a pivotal role played by mannitol permeabilization

of the blood-brain barrier," Dr. Borlongan explained.

Since the neonatal study animals receiving the combined HUCB cells and mannitol exhibited the most robust neurotrophic factor up-regulation, the study also suggests that even the immature blood-brain barrier needs to be permeabilized to facilitate entry by HUCB and to promote trophic factor effects, added Dr. Borlongan. The long-held view is that young animals display immature, not fully developed blood-brain barriers. However, the researchers demonstrated that manipulating the immature barrier is still required to gain improved access of therapeutic substances from peripheral circulation to the brain.

"Also, the therapeutic effects were achieved without immunosuppression, which is often accompanied by harmful side effects," said Dr. Borlongan.

Previous work by the research team demonstrated that grafted cells need not cross the blood-brain barrier to rescue the injured brain in adult stroke-modeled animals. In those studies mannitol helped facilitate the entry of growth factors secreted by the grafted cells.

"Our present findings extend the usefulness of blood-brain barrier permeabilization in facilitating cell therapy for treating neonatal brain injury and potentially cerebral palsy," concluded Dr. Borlongan.

Provided by University of South Florida