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Commentary: Another iteration of cell-based therapy for acute ischemia-reperfusion injury, this time in the spine

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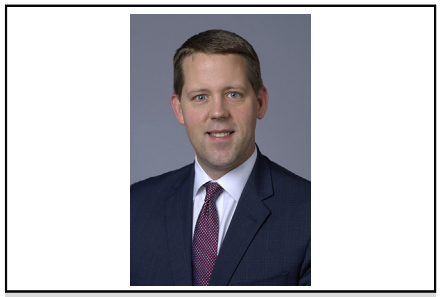

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CENTRAL MESSAGE

Cell-based therapies may hold potential for treating spinal cord ischemia–reperfusion injury.

Spinal cord injury is among the most feared complications of surgery for descending thoracic aortic pathology due to its devastating consequences and the mixed effectiveness of pharmacologic and lumbar drainage preventative and rescue therapies. Cell-based regenerative therapies (eg, stem cells or mesenchymal stromal cells [MSCs]) have received undulating attention over the past 15 years for the potential ability to protect against, or facilitate recovery from, ischemia–reperfusion injury in a variety of tissues. The literature is robust, with animal model-based studies while the translational leap to the clinical stage has been very limited and inconsistent.[1] This is largely due to the many confounding anatomical and physiological factors between bench and bedside.[2]

Cell-based therapies offer putative protective mechanisms of paracrine release of proangiogenic, anti-inflammatory, and antiapoptotic growth factors and cytokines. It is through these mechanisms that the authors speculate using the present observational data that human bone-marrow–derived MSCs may protect spinal cord motor neurons during episodes of acute ischemia and reperfusion in mice.[3] Their technically elegant surgical model involved inducing spinal cord ischemia at normothermia by crossclamping the aortic arch in 2 locations. Commercially available male human bone-marrow–derived MSCs (or control solution) were injected in standard doses into the tail veins of female mice 2 hours after reperfusion. This sex selection was intentional to allow for assaying graft cell localization and retention with chromosomal detection.

Hind limb function appeared to recover earlier in the MSCs group (as early as 8 hours after reperfusion) as well as recover to baseline or near-baseline up to 28 days after surgery. Histologically, there appeared to be more motor neuron preservation in the lumbar spinal cord, and donor MSCs were identified in areas of spinal cord, lung, spleen, and kidney. Reverse transcription polymerase chain reaction analysis of mRNA expression in spinal cord tissue showed a more anti-inflammatory, proangiogenic profile in the MSCs group. The authors conclude that MSC administration did not affect overall survival but could reduce the degree of spinal cord injury and paraplegia after temporary interruption of aortic flow at normothermia.

There are several important limitations of this study, most of which are acknowledged in the article. The sample sizes are very small, and the mortality rate in both groups appeared to be very high (although typical for this model). Because cardiovascular outcomes and MSCs function may differ between men and female women, it would have been helpful to account for such variations using opposite combinations of groups.[4] Finally, these observations are purely descriptive because specific mechanisms were not evaluated.

However, the main strength of this study is the novel application of MSCs for treating acute spinal cord ischemia–reperfusion injury, whereas the vast majority of prior work has focused on traumatic injury.[5-7] The potential of this work to directly assess benefits of cell-based therapy for acute spinal cord ischemia-reperfusion injury in a model that mimics aortic surgery should capture the attention of cardiovascular surgeons. Unfortunately, as with many other small animal, basic science models, we are left with a question: What is next?

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