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Commentary: Nanobubbles—A promising technology or another therapy stuck in the laboratory?

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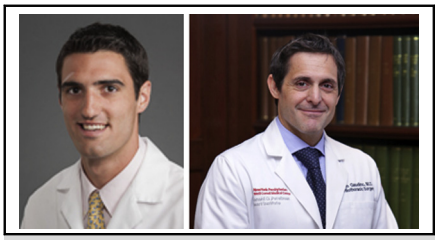

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CENTRAL MESSAGE

Nanobubble technology to treat spinal cord ischemic injury shows promising results that must be interpreted within the limits of a preclinical animal study.

In the current issue of the *Journal*, Naganuma and colleagues[1] report their results using a novel nanobubble technology to prevent ischemic spinal cord injury in an animal model. As demonstrated in previous publications, there is evidence that spinal cord ischemia can be attenuated by greater cerebrospinal fluid (CSF) oxygen content.[2,3] In this report, the authors build on their previous findings by investigating subcellular mechanisms. By demonstrating improved clinical and histopathologic scoring as well as suppression of the inflammatory response, they conclude that the administration of intrathecal oxygenated nanobubbles through artificial CSF attenuates ischemia–reperfusion injury following transient spinal cord occlusion. The authors are to be congratulated for their work.

Spinal cord injury and resultant paraplegia or paraparesis remains one of the most significant complications following both open and endovascular repair of thoracic aortic aneurysms, with an overall rate of 4.5% (5.7% following open repair and 3.9% following endovascular repair).[4] As the authors highlight, a number of strategies have been used to decrease the incidence of spinal cord ischemia in the intra- and postoperative settings. While their results offer an attractive addition to the arsenal, their results must be interpreted in the context of several limitations unique to preclinical animal studies.

One of the most pertinent critiques of many studies that use animal models involve the methodology. In this analysis, authors included a total of 20 animals in their final analysis (n = 5 in each experimental group). While a post-hoc power analysis was performed, a formal sample size calculation was missing in the experimental protocol. A review by Pound and colleagues[5] identified small experimental groups with inadequate power and failure to follow intention to treat principles as central methodologic problems with experiments involving animals.

Perhaps the most important question in preclinical animal studies is how they will translate into the clinical setting. In a previous analysis, our group demonstrated that less than one quarter of more than 400 studies published between 2007 and 2008 involving animal models were cited in a subsequent human/clinical trial over a 10-year period, despite a majority (83.5%) reporting positive findings.[6] To their credit, the authors acknowledge several barriers to clinical translation, including the need for a double-lumen catheter to limit increased intrathecal pressure, the use of which is not feasible in a small animal model, as well as the unknown effects of continuous replacement of native CSF with an artificial oxygenated CSF. Before these issues can be evaluated, the clinical translation of this technology appears to be limited. In the absence of additional data demonstrating safety, this analysis is at risk of the fate of many preclinical animal studies—never leaving the laboratory.

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