

Stem Cells for Ischemic Stroke: Hope or Panacea?

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Stem cells are defined as cells that retain the capability to replicate and differentiate into multiple cell lineages¹. These cells, which are present in variable proportions in the adult organs, could theoretically generate any living tissue of a particular organism. Although the concept of (fetal) stem cell transplantation is not new, considerable interest has arisen since the demonstration of such cells in the adult bone marrow, which could potentially provide enough cells for autologous transplantation². However, optimism that comes with any new therapy must be viewed with tempered caution.

In the issue of January/06 of the *Arquivos Brasileiros de Cardiologia* (Vol 86, pages 52-55), Mendonça et al report the first bone marrow-derived stem cell transplant in human ischemic stroke. Even though the results seem to suggest that the procedure was safe, feasible and produced an increase in perfusion and metabolism of the brain region affected by ischemia, analysis of this case report, by itself, cannot have a title that defines these attributes. Therefore, these terms should be suppressed from the title, as it was done on the electronic version of the *Arquivos Brasileiros de Cardiologia*. Mostly when we know that the analysis of the ischemic stroke in the acute phase can be challenging. As the authors correctly note, findings could be attributed to spontaneous recovery. In a local acute stroke case series, for example, 61% of patients experienced spontaneous recovery to complete independence (measured by a Rankin score of less than three)³. Additionally, in the case reported, a spontaneous recanalization of the middle cerebral artery was noted on transcranial Doppler, which is a known predictor of good outcome^{4,5}.

Neuroimaging surrogate endpoints for stroke outcome are also presented in the case report, including MRI, SPECT and PET. These should also be interpreted in the context of the natural history of stroke on neuroimaging. The most frequent pattern in acute stroke patients is that of an area of necrosis ("core") surrounded by an area of hypoperfusion that is ischemic but still viable ("penumbra")⁶. This pattern usually persists for 24 hours, where cells located in the penumbra progressively die and the core expands approximately to the area of the initial hypoperfusion⁶. Improvement in the initial hypoperfusion is expected in most stroke patients over time, and even diffusion abnormalities have been shown to recover in select cases^{7,8}. Regional improvement in metabolism by PET was suggested in this report, but some spontaneous improvement is expected in stroke patients, and the lack of quantitative data somewhat limits the conclusions.

Stem cell research is an exciting new avenue in neurological diseases. Much is still needed: basic science studies should clarify the exact mechanisms by which stem cells improve stroke-related deficits; and clinical studies with control groups should compare natural history with treatment groups. Safety also requires more thorough evaluation, as risk of thrombosis at the site of injection and long-term epilepsy are still concerns as more patients are studied. The authors are to be congratulated for their pioneering experience as well as for their realistic comments. Future comparative data from their phase I study is anxiously awaited. Stem cells will probably not be a panacea for neurological diseases, but hope should foster sound scientific research. Our patients deserve it.

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