

XXXII.18 Bone Marrow Stem Cell Injections: Can They Be a Treatment for Critical Ischemia and How Do They Work?

Berthold Amann, MD, Claas Luedemann, Jan A. Schmidt-Lucke Berlin, Germany

Approximately one-third of limbs with critical limb ischemia (CLI) may not be candidates for percutaneous or surgical revascularization. Amputation rates in these patients are high, and mortality approaches 25%. Because autologous bone marrow mononuclear cells (BMNCs) are a potent source of angiogenic cyto- and chemokines and contain pluripotent stem cells as well as endothelial progenitor cells, BMNC-induced angiogenesis theoretically has advantages over angiogenic gene therapy or single growth factor transfer. In contrast to growth factors such as VEGF or bFGF, which induce capillary growth, BMNCs enhance collateral artery growth and so can induce the development of conduit arteries, a process called arteriogenesis. Therefore, we tested if autologous BMNC transplantation is useful for limb salvage in CLI.

Methods

In 23 patients with CLI who had failed all standard treatments and faced major amputation, autologous BMNC transplantation in the ischemic leg was performed. The mean age of the patients was 65 ± 13 (SD) years (39-85), 74% were male, 60% had diabetes, 91% had ulcers, and the mean Wagner grade was 2 (1-4). In the first 12 patients, 450 to 500 mL of bone marrow were aspirated under general anesthesia from both iliac crests, and the mononuclear cell fraction was isolated via Ficoll gradient centrifugation. In 10 patients, 120 mL BM were aspirated under local anesthesia and separated with the Harvestech SmartPrep BM centrifuge. The resulting BMNC concentrate was injected deeply intramuscularly at 40 to 50 sites into the ischemic leg and foot. Clinical and apparative parameters of perfusion were assessed longitudinally.

Results

There were no serious procedure-related complications. The mean total number of reinjected BMNC was 1.1×10^9 cells with Ficoll and 1.9×10^9 with Harvest separation. In the mean follow-up time of 13 months (range 1-26), limb salvage was achieved in 16 of 23 (70%) patients, 7 of 23 (30%) underwent major amputation, and one death occurred. Transcutaneous oxygen tension is the first perfusion parameter that indicates improved perfusion.

Granulation of the ulcers started about 6 weeks after treatment. Angiography 6 months after treatment showed increased collaterals in one-third of patients.

Conclusion

Angiogenesis/arteriogenesis induced by autologous bone marrow transplantation is a feasible, secure, and simple therapy. From our preliminary results, autologous BMT for limb salvage in CLI can help avoid amputations.

Results (Perfusion Parameters)

	Pre-t. (n = 23)	1 mo pt (n = 21)	2 mo post (ii = 21)	6 mo pt (n = 16)	P (ANOVA)
tcpO ₂	8 ± 13 mm Hg	12 ± 15	15 ± 15	23 ± 21	<.03 <.05
ABI	0.30 ± 0.2	0.37 ± 0.2	0.32 ± 0.2	0.48 ± 0.2	