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Original Contribution: Anorectal

Localized Administration of Mesenchymal Stem Cell–Derived Exosomes for the Treatment of Refractory Perianal Fistula in Patients With Crohn’s Disease: A Phase II Clinical Trial

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Abstract

BACKGROUND:

Crohn's disease perianal fistulas are often resistant to standard anti-tumor necrosis factor- α therapies. Mesenchymal stem cell-derived exosomes are extracellular vesicles with highly potent anti-inflammatory effects, and the previous phase of this study demonstrated their safety in the treatment of refractory perianal fistulas.

OBJECTIVE:

To evaluate the efficacy of mesenchymal stem cell-derived exosomes for the treatment of refractory perianal fistulas.

DESIGN:

Nonrandomized, nonblinded single-center phase II clinical trial.

SETTINGS:

Tertiary university hospital.

PATIENTS:

Twenty-three patients were enrolled, 20 of whom completed the study. Refractory perianal fistula was defined as resistance to at least 1 course of treatment with anti-tumor necrosis factor- α therapy.

INTERVENTIONS:

After clinical assessment and MRI, the patients received general anesthesia, and 5 mL of exosome solution was injected directly into the fistula tracts. The injections were repeated 3 times at 2-month intervals, and patients were followed monthly for 6 months after the last injection. Tissue samples from the tracts were obtained before each injection and subjected to immunohistopathological assessment. MRI data were obtained before and 6 months after the last injection.

MAIN OUTCOME MEASURES:

The primary outcome of this study was fistula tract closure on clinical examination and MRI. The secondary outcome was an improvement in the discharge from the tracts.

RESULTS:

Fistula tracts were fully closed in 12 patients (60%). Four patients showed clinical improvement, with some tracts remaining open, and 4 patients were completely resistant to treatment. A total of 43 fistula tracts were treated during the trial, 30 of which (69.7%) showed complete closure. Histopathological analysis revealed substantial reductions in local inflammation and signs of enhanced tissue regeneration. Immunohistochemical analysis of CD68, CD20, and CD31 reaffirmed these results.

CONCLUSIONS:

Mesenchymal stem cell-derived exosomes are safe and effective for treating refractory perianal fistulas in patients with Crohn's disease. See **Video Abstract**.