幹細胞静脈内投与の期待されるベネフィット (Abstract 1232)

心不全における幹細胞注入は健康状態を改善したが心機能は改善しなかった

Infused stem cells in heart failure improved health status but not cardiac function

慢性非虚血性心筋症患者に対する間葉系幹細胞の静脈内単回投与は、器質的または機能的に有意な改善をもたらさなかったが、いくつかの臨床的に有意な改善をもたらした、との第II相ランダム化トライアルの結果が2016年ESC Congressで発表された。特に、プラセボに比べ、itMSC療法は、臨床概要および注入後90日の機能状態スコアに加え、6分間歩行試験（p=0.02）においても大きな改善を示した。過去の研究は、専ら幹細胞を直接心臓に注入する侵襲的なアプローチに焦点を当てていた。

Full Text

A single dose of mesenchymal stem cells delivered intravenously to patients with chronic non-ischemic cardiomyopathy was not associated with significant cardiac structural or functional improvements, but did result in several clinically relevant benefits, according to results from a phase II-a randomized trial.

The study, presented in a Hot Line session as ESC Congress 2016, "demonstrated that a more convenient and less invasive infusion strategy is safe, well-tolerated and shows improvements in multiple measurements of patient health status," reported investigator Javed Butler MD, from Stony Brook University, Stony Brook, NY, USA.

Previous work in this field has focused almost exclusively on the more invasive approach of injecting stem cells directly into the heart.

Prof. Butler and his colleague used "ischemia tolerant" mesenchymal stem cells (itMSCs) that were grown under chronic hypoxic conditions, with the aim of enhancing their potential benefits.

"The premise was that stem cells may have immune modulatory properties, which are enhanced when grown under hypoxic conditions," he explained.

This potential immune modulation and anti-inflammatory effect also opens the door to new methods of delivery, he added.

"Virtually all previous studies of stem cell therapy for heart failure have centered on the concept that the cells must be injected directly into the heart to trigger new growth, but if stem cells have anti-inflammatory benefits, direct cardiac delivery may not be necessary to repair and stimulate the dysfunctional viable myocardium."

The single-blind, placebo-controlled, crossover, multicenter study randomized patients with non-ischemic cardiomyopathy and left ventricular ejection fraction (LVEF) ≤40% to receive intravenous itMSC therapy (n=10) or placebo (n=12) for 90 days and then cross over to the other treatment.

The stem cells were donated by a health volunteer and grown under hypoxic conditions from the moment of extraction.

At 90-days post itMSC infusion, there were no major differences in primary safety endpoints of all-cause mortality, all-cause hospitalization, and adverse events.

Secondary endpoints of cardiac remodeling (left ventricular ejection fraction and ventricular volumes), assessed by cardiac magnetic resonance imaging, were also not different between groups at 90-days.

However, treatment with itMSCs resulted in improved health status and functional capacity – which were also prespecified secondary endpoints.

Specifically, compared to placebo, itMSC therapy resulted in statistically significant improvements in 6-minute walk test (an estimated 36m more than placebo, p=0·02) as well as greater improvements in Kansas City Cardiomyopathy Questionnaire scores (clinical summary score +5·22, p=0·02, and functional status scores +5·65, p=0·06) at 90-days post-infusion.

Additionally, itMSCs infusion resulted in significant alterations in several inflammatory cells, "supporting the immunomodulatory and anti-inflammatory mechanisms of itMSCs," noted Dr. Butler.

"To our knowledge, this trial represents the first experience with intravenously administered itMSCs in patients with any type of chronic cardiomyopathy," he concluded. "Further studies should explore the efficacy of serial dosing to produce more sustained immunomodulatory effects and thereby perhaps facilitate improvement in left ventricular structure and function, and in clinical outcomes."

The study was funded by Cardiocell LLC in San Diego, CA, USA.

Dr. Butler reports research support from the National Institutes of Health, PCORI and European Union; and is a consultant to Amgen, Bayer, Cardiocell, Novartis, Boehringer-Ingelheim, Relypsa, Z Pharma, PharmaIn, SC Pharma and Gilead.

Conference News