Editorial Commentary

Stem cell therapy in diabetic men with erectile dysfunction: a step closer to safe and effective regenerative technology

Eric Chung[1,2]

[1]AndroUrology Centre, Brisbane, QLD, Australia; [2]University of Queensland, Princess Alexandra Hospital, Brisbane, QLD, Australia; [3]Macquarie University Hospital, Sydney, NSW, Australia

Correspondence to: Eric Chung. Associate Professor, AndroUrology Centre, St Andrew's War Memorial Hospital, Boundary St, Brisbane, QLD 4000, Australia. Email: ericchg@hotmail.com.

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I would like to congratulate the authors on an interesting paper exploring the clinical outcomes of bone marrow-derived mesenchymal stem cells (BM-MSC) injections in diabetic men with erectile dysfunction (ED) (1). This prospective pilot, open-label single arm study showed an improvement in penile erection following 2 separate intracavernous injections of BM-MSC given 30 days apart, with sustained effect up to 12 months as evident by the IIEF-5 and EHS scores.

Preclinical research into various animal models of ED has highlighted many pathophysiologic mechanisms contributing to ED such as cavernous nerve injury and diabetic models (2) and over the past decade, there has been considerable interest in stem cell (SC) therapy in the treatment of ED. The MSC is by far the most frequently used cell types in the field of urology and the most popular method of SC delivery in ED treatment is intracavernosal injection given its ease of administration and has proven success in both preclinical and clinical trials (3-5). The regenerative effects of SC are likely achieved by secretion of various growth factors into the blood stream and/or migration of these factors to major pelvic ganglia in addition to cell contact, paracrine signalling system and cellular differentiation (6,7).

The first reported clinical trial of SC therapy in diabetic men with ED showed a reasonable increase in penile rigidity after a single intracavernous injection of umbilical cord blood SC (5). While penile rigidity was maintained for more than 6 months, the erection was not hard for sexual penetration, suggesting that the amount and a single administration of SC were likely insufficient for adequate penile rigidity. In a different study on the use of SC in men with ED following radical prostatectomy, Yiou (4) showed that intracavernous injection of bone marrow mononuclear cells appeared to be safe and improved the erectile function for a period of 6 months. However, the decline in erectile function over time suggests a need to assess for repeated intracavernous injections.

It is important to understand that ED is common in diabetic men and proposed pathogenesis is likely multifactorial with vascular, neurological and hormonal alterations. Dysfunctions of the endothelium-dependent and neurogenic relaxations in corpus cavernosum, a lack of nitric oxide production with a significant increase in nitric oxide (NO) synthase binding sites in penile tissues, coupled by advanced glycation end-products, change in androgen level as well as alterations in various neuro-humoral mediators such as vascular endothelial growth factor and endothelin-1, all play a role in the development and progression of ED. Furthermore, the differential gene expression for various growth factors in penile tissues and the alterations in the neural pathway and autonomic nerve fibers can contribute to ED pathogenesis too (8). Some of these changes may not be adequately addressed with SC therapy alone.

The rapid advances of SC clinical trials for a broad spectrum of urological conditions have promised to establish various clinical pathways for a new emergent medicine that may one day replace conventional medical and surgical interventions. However, the initial optimism regarding the rapid translation of SC therapy to clinical evidence-based practice has slowed down recently due to several concerns and lack of clear longer-term effect in humans. The intracavernous injection of SC to treat ED appears straightforward and logical with proposed regenerative effect is achieved by either secreting growth factors locally via a paracrine mechanism or by migration to the major pelvic ganglia, to promote the propagation and differentiation of resident progenitor cells and encourage the recovery of injured tissue via the production of antiapoptotic and proangiogenic factors, rather than transdifferentiation into different cell types (6,7). Adult SC has the advantage of avoiding the ethical issues of ESC and in addition, published literature shows a very low probability of malignant transformation and tumour formation (6). While data is slowly accruing and proving that SC appears to be safe and effective in the shorter terms, possible genomic or epigenetic changes in the longer term, and infection (including zoonotic infections with virus integration), as well as potential immune reactions, cannot be ignored when such technology is introduced in humans and need to be identified in more stringent clinical trials. Therefore, it is useful for future SC trials to include histology confirmation and larger multicentre trials with various study protocols to compare various treatment templates including dose, duration and numbers of SC injections.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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