Research Highlight

Research highlights on stem cell therapy for the treatment of Peyronie's disease

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Abstract: New treatment modalities have been developed to improve the treatment outcomes of Peyronie's disease (PD). Stem cells are undifferentiated cell populations that are capable of self-renewal and of differentiation into various kinds of cells or new tissues. In addition, stem cells also have antiapoptotic, antifibrotic, and immunomodulatory properties. The results from preclinical studies support the potential role of adipose-derived stem cells (ADSCs) therapy for both the prevention and treatment of PD. However, there are several limitations of the animal model used in the studies. Further animal and clinical studies are still needed to validate the therapeutic effects and clinical application of ADSCs for the treatment of PD.

Keywords: Peyronie's disease; penile curvature; stem cell; adipose-derived stem cells (ADSCs)

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Peyronie's disease (PD) is characterized by plaque formation in the tunica albuginea (TA). Novel treatments are currently being developed to improve the treatment outcomes. In recent years, researchers in the field of male sexual dysfunction have studied stem cell therapy. Stem cells are undifferentiated cell populations with antifibrotic properties that are capable of self-renewal and of differentiation into various kind of cells or tissues (1). A number of animal studies documented the therapeutic effects of stem cells in the kidney, liver, and pulmonary fibrosis (2-4). This is promising for the treatment of PD because of the potency to prevent or repair PD plaque and to decrease the penile curvature.

In 2013, a proof-of-principle study reported that adipose-derived stem cells (ADSCs) injection improved erectile function and decreased expression of elastin and collagen type I in a rat model of TA fibrosis (5). The TA fibrosis was induced by a transforming growth factor β1 (TGF-β1) injection. This animal model is generally accepted and widely used in PD research. The rats were treated with ADSCs injection 1 day after TGF-β1 injection (early phase of PD). The result is promising; however, there is some concern about the use of the xenogenic cell source. The researchers injected ADSCs obtained from female subjects into immunocompetent rats without the use of immunosuppressants. The authors maintained that the beneficial effects of ADSCs injection are mediated in paracrine fashion without cell engraftment (6). These cells have antiapoptotic, antifibrotic, and immunomodulatory properties.

While the previous study focused on the early phase of PD to prevent TA fibrosis, Gokce *et al*. documented the beneficial effects of ADSCs injection in both the prevention and treatment groups (7). Autologous ADSCs were injected on the same day (prevention group) and 30 days (treatment group) following TGF-β1 injection. A local injection of ADSCs resulted in significant improvement of erectile function in both groups and were able to prevent or reduce Peyronie's-like changes by decreasing the expression of tissue inhibitors of metalloproteinases (TIMPs), and by stimulating expression and activity of matrix metalloproteinases (MMPs). Because most PD patients presented in the chronic phase, the results of this study indicated that local injection of ADSCs might benefit most PD patients. Furthermore, this study used autologous ADSCs, which eliminated the concern regarding immune responses of the recipients.

Table 1 Summary of stem cell-based studies in Peyronie's-like conditions

Study	Year	Animal model	Type of stem cells	Results
Castiglione *et al*. (5)	2013	TA fibrosis (Prevention)	Human ADSCs	- Improve erectile function - Prevent upregulation of collagen type III and elastin
Gokce *et al*. (7)	2014	TA fibrosis (Prevention and treatment)	Rat ADSCs	- Improve erectile function - Prevent and/or reduce Peyronie's-like changes
Gokce *et al*. (11)	2015	TA fibrosis (Prevention and treatment)	Rat ADSCs with interferon α-2b	- Improve erectile function - Reduce Peyronie's-like changes
Ma *et al*. (12)	2012	TA incisions	Rat ADSCs seeded SIS	- Improve erectile function - Increase expression of endothelial NOS and neuronal NOS

ADSCs, adipose-derived stem cells.

Intralesional interferon α-2b is an alternative treatment option for PD patients. This drug class has the ability to regulate fibroblast function, reduce the production of extracellular collagen, and stimulate collagenase activity (8,9). The significant improvement in penile curvature, plaque size, and pain resolution were documented in the placebo-controlled study (10). Intratunical injections of genetically modified ADSCs with human interferon α-2b (ADSCs-IFN) were also evaluated in the rat model of TA fibrosis. In this study, there was a significant improvement in erectile response in the ADSCs-IFN group compared to ADSCs alone and also the placebo group (11). It appears that all available animal studies support the potential role of local ADSCs administration for the treatment of PD (*Table 1*). Further animal and clinical studies are needed to support these findings.

For surgical treatment of PD, allografts and xenografts (e.g., processed pericardium from a bovine or human source, porcine intestinal submucosa, and porcine skin) have been widely used for partial incision/excision and grafting. In this regard, ADSCs seeded small intestinal submucosa (ADSCs-SIS) was evaluated for TA reconstruction in a rat model of bilateral TA incision (12). Rats in the autologous ADSCs-SIS group maintained better erectile function compared to rats grafted with SIS alone. There was a significant increase in the expression of endothelial nitric oxide synthase (NOS) and neuronal NOS, and a reduced expression of inducible NOS in the cavernosal tissue of the ADSCs-SIS group. These findings suggest that ADSCs improve the recovery of TA and erectile function by enhancing angiogenesis and decreasing fibrosis.

Conclusions

The results from preclinical studies support the potential role of ADSCs therapy for both prevention and treatment of PD. Because of the limitations of the animal model used, most studies have focused on the treatment of PD-associated erectile dysfunction. Currently, no studies report the significant improvement of plaque size or penile curvature, which is considered the main objective of PD treatment. Further animal and clinical studies are needed to validate the therapeutic benefits of ADSCs for the treatment of PD.

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Footnote

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

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