Sexual dysfunction

Stem cell therapy for the treatment of erectile dysfunction in diabetes holds promise

Mike Cummings, Consultant Physician and Honorary Professor, Queen Alexandra Hospital, Portsmouth

The emergence of stem cell therapy (SCT) has offered an innovative approach to the treatment of a number of disease processes, in particular neurological and vascular disorders. The application of SCT to treat other pathologies has long been considered and erectile dysfunction (ED) is no exception.

Early hope that ED may respond to SCT came from the observation that stem cells modified with endothelial nitric oxide synthase – which promotes the production of nitric oxide, a chemical integral to the achievement of successful tumescence – injected into the corpus cavernosa of rats would improve erections (Bivalacqua et al, 2007). Bahk et al (2010; summarised alongside) tested this principle.

Human umbilical cord blood stem cells were injected into the corpus cavernosa of men with diabetes and organic ED. In the sample of seven, six men achieved improved rigidity and restoration of morning erections. There was no response in the control group.

There were also some interesting observations during the study. First, the use of human umbilical cells negated the need for immunosuppressive therapy, given the low potential for rejection. Second, the treatment protocol was relatively straightforward – a single injection into the corpus cavernosum is far easier than the insertion of penile implants. Third, morning erections were restored within a month of treatment initiation, which raises the possibility that humoral factors (i.e. paracrine, cytokine) were influencing tumescence before the anticipated differentiation of stem cells into the local target-cell population took place.

> ***"... stem cell technology offers hope for men with diabetes and erectile dysfunction. It may be the awaited alternative to long-term pharmacotherapy, or other more invasive therapies, to restore erections."***

Despite the small sample size of Bahk et al's study, uncertainties in the optimum "dosing" of stem cells and the precise mechanism of action, SCT offers hope for men with diabetes and ED. It may be the awaited alternative to long-term pharmacotherapy, or other more invasive therapies, to restore erections.

Bivalacqua TJ, Deng W, Kendirci M et al (2007) Mesenchymal stem cells alone or *ex vivo* gene modified with endothelial nitric oxide synthase reverse age-associated erectile dysfunction. *Am J Physiol Heart Circ Physiol* **292**: H1278–90

J SEXUAL MEDICINE

ED: Surrogate marker for future stroke

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors aimed to examine the association between erectile dysfunction (ED) and subsequent stroke by estimating the risk of stroke during a 5-year follow-up period after first treatment for ED using nationwide, population data in a retrospective case-controlled cohort.

2 The study cohort comprised 1501 men with a principal diagnosis of ED and 7505 randomly selected controls. Participants were tracked for 5 years from first visit to an episode of stroke.

3 After adjusting for confounders, including peripheral vascular disease, atrial fibrillation and hyperlipidemia, those with ED were more likely to experience a stroke during the 5-year follow-up period than controls (hazard ratio, 1.29; 95% confidence interval, 1.08–1.54; $P<0.01$).

4 The authors found ED to be a surrogate marker for future stroke.

Chung SD, Chen YK, Lin HC, Lin HC (2010) Increased risk of stroke among men with erectile dysfunction: a nationwide population-based study. *J Sex Med* [epub ahead of print]

EXPERIMENTAL & CLINICAL TRANSPLANTATION

Umbilical blood stem cell therapy improves ED in T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓✓

1 The authors investigated the effects of intracavernosal transplant of stem cells on erectile dysfunction (ED) in men with T2D.

2 Men (n=7; age range, 57–87 years) who had failed to achieve an erection in ≥6 months with pharmacotherapy, and who were awaiting penile prostheses, were recruited.

3 Human umbilical cord blood stem cells (1.5×10^7) were infused into the corpus cavernosum of each participant. No immunosuppression therapy was undertaken.

4 The International Index of Erectile Function-5, the Sexual Encounter Profile, Global Assessment Questions, erection diary, blood glucose diary and medication dosage were followed-up for 9 months.

5 Morning erections were restored in three participants within 1 month of therapy, and in six participants by the by the third month, and were maintained for >6 months.

6 The addition of a phosphodiesterase type-5 inhibitor before coitus resulted in two participants achieving penetration and experiencing orgasm (maintained for >6 months).

7 Two participants returned for prosthesis during follow-up; one participant maintained erection sufficient for coitus with medication until the eleventh month.

8 The authors concluded that stem cells and unknown humoral factors of human umbilical cord blood stem cells mediate mechanisms that positively effect ED in T2D.

Bahk JY, Jung JH, Han H et al (2010) Treatment of diabetic impotence with umbilical cord blood stem cell intracavernosal transplant: preliminary report of 7 cases. *Exp Clin Transplant* **8**: 150–60

INTERNATIONAL JOURNAL OF CLINICAL PRACTICE

Guidance for CAD risk reduction in men with ED

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓

1 The authors developed guidance on reducing vascular risk in men with erectile dysfunction (ED), with the aim of using the time interval between the onset of ED symptoms and the occurrence of coronary artery disease (CAD) symptoms and cardiovascular (CV) events (estimated at 2–3 years and 3–5 years, respectively) to achieve risk reduction.

2 The authors recommend that all men diagnosed with ED should undergo a thorough medical assessment including testosterone levels, fasting lipids, fasting glucose, blood pressure.

3 Based on assessment results, men should be stratified according future CV event risk. Those at high risk of CV disease (CVD) should be stress tested with selective use of computed tomography or coronary angiography.

4 Men with ED plus hypertension, T2D or hyperlipidaemia should be treated aggressively for those conditions.

5 Management of ED is secondary to stabilising CV function and controlling CV symptoms. Furthermore, improvement in CVD risk factors (e.g. weight loss, increased physical activity) improves erectile function.

6 The authors support the use of phosphodiesterase type-5 inhibitors as first-line therapy in men with CAD and ED, and those with ED and T2D.

7 Total testosterone and, selectively, free testosterone should be measured in all men with ED, particularly in those who fail to respond to phosphodiesterase type-5 inhibitors or have a chronic illness associated with low testosterone (e.g. T2D).

Jackson G, Boon N, Eardley I et al (2010) Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus. *Int J Clin Pract* **64**: 848–57

UROLOGY

Sildenafil improves ED in men who are unaware of their ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors sought to assess the efficacy of sildenafil citrate therapy in men who did not self-identify with, or were unsure about, ED but had ED based on their scores for the International Index of Erectile Function Erectile Function domain (IIEF-EF).

2 Men with an ED-associated comorbidity were asked, "Do you have ED?". Those who answered "no" or "unsure" and had an IIEF-EF score ≤25 were invited to participate.

3 Participants were randomised to sildenafil therapy (n=150) or placebo (n=155).

4 Both functional and psychosocial measures were improved in the sildenafil-treated men.

5 The authors concluded that men may not recognise that they have ED and sildenafil treatment improved sexual function and satisfaction in this group.

Shabsigh R, Kaufman J, Magee M et al (2010) A multicenter, double-blind, placebo-controlled trial to assess the efficacy of sildenafil citrate in men with unrecognized erectile dysfunction. *Urology* **76**: 373–9

J SEXUAL MEDICINE

New PDE-5 inhibitor safe and effective in treatment of ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The new phosphodiesterase type-5 (PDE-5) inhibitor mirodenafil was evaluated for efficacy, safety and tolerability in the treatment of erectile dysfunction (ED) in Korean men (n=112) with T2D in this multicenter, randomised, double-blind, placebo-controlled, parallel-group, fixed-dose study.

2 Participants received either placebo or mirodenafil (100 mg) on demand for 12 weeks.

3 Compared with the placebo group, the mirodenafil group showed significantly greater change in the International Index of ED domain score (9.3 vs 1.4; P<0.0001). By study end, normal erectile function domain scores (≥26) were achieved by 32.7% and 9.4% in the mirodenafil and placebo groups, respectively (P=0.0031).

4 Mirodenafil was found to be an effective and well-tolerated agent for the treatment of ED in men with T2D.

Park HJ, Choi HK, Ahn TY et al (2010) Efficacy and safety of oral mirodenafil in the treatment of erectile dysfunction in diabetic men in korea: a multicenter, randomized, double-blind, placebo-controlled clinical trial. *J Sex Med* [epub ahead of print]

J SEXUAL MEDICINE

Imatinib improves ED, vascular function

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The protein tyrosine kinase (PTK) inhibitor imatinib was investigated for its effects on erectile dysfunction (ED) and vascular function in rats with diabetes.

2 Male Sprague–Dawley rats were divided into six groups: (i) control; (ii) imatinib (50 mg/kg)-treated control; (iii) rats with diabetes; (iv) preventive imatinib (8 weeks); (v) reversal imatinib (4 weeks untreated diabetes and 4 weeks of treatment); and (vi) insulin (8 weeks)-treated rats with diabetes.

3 After 8 weeks, all groups underwent cavernosal nerve stimulation and measurements of intracavernosal pressure and mean arterial pressure.

4 Imatinib-treated rats with diabetes gained weight, improved blood glucose levels (P=NS) and displayed a decrease in intracavernosal pressure and mean arterial pressure.

5 Imatinib therapy was shown to improve diabetes-related ED and vascular function in rats.

Gur S, Kadowitz PJ, Hellstrom WJ (2010) A Protein tyrosine kinase inhibitor, imatinib mesylate (gleevec), improves erectile and vascular function secondary to a reduction of hyperglycemia in diabetic rats. *J Sex Med* [epub ahead of print]

"… men may not recognise that they have erectile dysfunction and sildenafil treatment improved sexual function and satisfaction in this group."