SEXUAL DYSFUNCTION

Rodent models of diabetic ED

Erectile dysfunction (ED) is commonly reported in men with diabetes. Diabetic ED occurs at an earlier age than in the general population and is often refractory to treatment with phosphodiesterase type 5 inhibitors. This lack of response is thought to be due to either a more severe form of endothelial dysfunction observed in diabetic men compared with nondiabetic patients or via overactivation of the ROCK/RhoA signalling pathway. Treatment is currently focused on symptomatic relief and not cure. However, two recent studies published in the *Journal of Sexual Medicine* have investigated alternative therapeutic strategies and mechanisms for diabetic ED using rodent models, and one may possibly offer hope of a cure for diabetic ED using stromal vascular fraction (SVF) as a source of stem cells.

The first study investigated the effect of freshly isolated SVF on cavernous endothelial regeneration and erectile function in streptozotocin (STZ)-induced diabetic mice. SVF is a source of easily harvested multipotent stem cells and can promote neovascularization via differentiation into vascular endothelial cells or by secretion of angiogenic factors. SVF can be used as an alternative to adipose-tissue-derived stem cells (ADSC), which have been shown in previous studies to restore erectile function in rat models of diabetic ED.

STZ-induced diabetic mice were treated with a single intracavernous injection of SVF isolated from mouse epididymal tissue. Erectile function was measured 2 weeks after injection by cavernous nerve stimulation and penile tissue was studied for expression of endothelial markers and markers of cell proliferation. At this timepoint, diabetic mice treated with SVF at concentrations of 1×10^5 cells/20 μ l and 2×10^5 cells/20 μ l showed a significant improvement in erectile response to cavernous nerve stimulation compared with control mice (both diabetic mice treated with vehicle and nondiabetic mice). This effect was also seen at just 1 week after a single injection. Furthermore, cavernous endothelial and smooth muscle content, which were significantly lower in untreated and PBS-treated mice than control mice, were completely restored with SVF treatment. Immunohistochemical assessment using antibodies to CD31 showed that SVF differentiated into endothelial cells. These data illustrate the restoration of cavernous endothelial content by SVF via enhanced endothelial proliferation and support the further investigation of SVF as a curative therapy for diabetic ED.

The second study used a rat model to investigate the effect of NADPH oxidase inhibitor apocynin on STZ-diabetes-related ED. Rats were given either saline or apocynin (16 mg/kg) by gavage for 4 weeks. Erectile function was once again assessed using cavernous nerve stimulation and cavernosum tissue was analysed for expression of RhoA pathway constituents and reactive oxygen species (ROS). Erectile function was decreased in diabetic rats compared with controls, but was significantly improved by apocynin treatment. Expression of RhoA and ROCK—which were higher in diabetic rats than controls—were significantly reduced by apocynin treatment, and ROS, also higher in STZ-diabetic rats than controls, were also reduced. Thus, the data suggest that apocynin can also ameliorate diabetic ED, in this case by reducing ROS production and inhibiting the RhoA signalling pathway, which is overactive in diabetic rats. Apocynin is thought to inhibit NADPH oxidase by reducing expression of the NADPH oxidase protein subunits, thus reducing ROS production. The mechanism of apocynin's effect on the RhoA pathway remains unclear.

It is hoped that these data will lead onto clinical studies and the eventual development of therapies for not just relief, but potentially cure, of diabetic ED.

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Original articles Ryu, J. K. et al. Intracavernous delivery of freshly isolated stromal vascular fraction rescues erectile function by enhancing endothelial regeneration in the streptozotocin-induced diabetic mouse. *J. Sex. Med.* doi:10.1111/j.1743-6109.2012.02962.x | Lim, M. et al. Apocynin improves erectile function in diabetic rats through regulation of NADPH oxidase expression. *J. Sex. Med.* doi:10.1111/j.1743-6109.2012.02960.x