AB088. Inhibition of prongf pathway restores erectile function through dual angiogenic and neurotrophic effects in the diabetic mouse

Nguyen Nhat Minh, Kang-Moon Song, Min-Ji Choi, Kalyan Ghatak, Mi-Hye Kwon, Guo Nan Yin, Ji-Kan Ryu, Jun-Kyu Suh

National Research Center for Sexual Medicine, Department of Urology, Inha University School of Medicine, Incheon, Korea

Background: Patients with diabetic erectile dysfunction (ED) usually respond poorly to oral phosphodiesterase-5 inhibitors due to a lack of bioavailable nitric oxide from severe endothelial and neural dysfunction. ProNGF and its receptor $p75^{NTR}$ are known to be up-regulated in diabetic condition and to play important role in triggering neuronal survival and vascular cells apoptosis. The aim of this study was to investigate the role of proNGF/$p75^{NTR}$ signal pathway and the effectiveness of proNGF neutralizing antibody (proNGF-Ab) in restoring erectile function in streptozotocin-induced diabetic mouse.

Methods: Diabetes mellitus was induced by intraperitoneal injection of streptozotocin (50 mg/kg) into 8-week-old C57BL/6 male mice for 5 consecutive days. At 8 weeks after the induction of diabetes mellitus, the animals were distributed into 3 groups: controls, streptozotocin-induced diabetic mice receiving repeated intracavernous injections of saline (days –3 and 0; 20 µL) or proNGF-Ab (days –3 and 0; 20 µg in 20 µL of saline). We measured erectile function by electrical stimulation of the cavernous nerve at 2 weeks after treatment. The penis then was harvested for histological and biochemical studies. We also examined the effect of proNGF-Ab and $p75^{NTR}$ siRNA in primary cultured mouse cavernous endothelial cells, pericytes and major pelvic ganglion.

Results: The cavernous expression of proNGF and $p75^{NTR}$ was up-regulated in diabetic patients and STZ-induced diabetic mouse. Intracavernous injection of proNGF-Ab successfully restored erectile function in diabetic mice, which reach up to 90–100% of control values. ProNGF-Ab significantly increased cavernous endothelial cell content, pericytes content and endothelial cell-cell junction proteins; and restored neuronal cell content in the cavernous tissue of diabetic mice. Under the high glucose condition, proNGF-Ab and $p75^{NTR}$ siRNA also promoted tube formation in mouse cavernous endothelial cells and pericytes; decreased the apoptosis of endothelial cells and pericytes; and enhanced neurite sprouting in major pelvic ganglion culture.

Conclusions: Our findings suggest that inhibition of proNGF/$p75^{NTR}$ signal pathway is a promising therapeutic strategy for diabetic ED.

Keywords: Erectile dysfunction (ED); diabetes, proNGF; $p75^{NTR}$

doi: 10.21037/tau.2018.AB088

Cite this abstract as: Minh NN, Song KM, Choi MJ, Ghatak K, Kwon MH, Yin GN, Ryu JK, Suh JK. Inhibition of proNGF pathway restores erectile function through dual angiogenic and neurotrophic effects in the diabetic mouse. Transl Androl Urol 2018;7(Suppl 5):AB088. doi: 10.21037/tau.2018.AB088

