2 Anti-Nogo-A antibodies: Promising treatment for neurogenic lower urinary tract dysfunction after spinal cord injury

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Schneider M.P. [1], Sartori M. [2], Schwab E. [3], Kessler M. [2]

[1]Inselspital, Dept. of Urology, Bern, Switzerland, [2]University of Zürich, Balgrist University Hospital, Dept. of Neuro-Urology, Spinal Cord Injury Center & Research, Zurich, Switzerland, [3]University of Zürich, Brain Research Institute, Dept. of Health Sciences and Technology, Zurich, Switzerland

Introduction & Objectives: Neurogenic detrusor overactivity (NDO) combined with detrusor sphincter dyssynergia (DSD) due to spinal cord injury (SCI) may lead to high intravesical pressure causing structural damage to the lower and upper urinary tract with a relevant risk for life-threatening end-stage renal failure. Currently, no causal therapy is available to treat this dangerous condition. We therefore investigate if antibodies against the nerve fiber growth inhibitory central nervous system protein Nogo-A applied to the injured spinal cord in rats could prevent the development of neurogenic lower urinary tract dysfunction, in particular DSD.

Materials & Methods: Lower urinary tract function of 86 female Lewis rats with no injury (n=17), complete (n=28) or incomplete (n=41) SCI at thoracic level 8 was assessed using our novel urodynamic model (Schneider MP et al., BJUI 2015) allowing repetitive longitudinal measurements of both bladder and external urethral sphincter function in the same animal under fully awake conditions.

Results: Four weeks after large but incomplete thoracic SCI, DSD had developed in all untreated or control antibody infused animals. In contrast, 2 weeks of intrathecal anti-Nogo-A antibody treatment lead to a significantly reduced maximum detrusor pressure during voiding and a reduction of electromyographic high frequency activity in the external urethral sphincter. Importantly, no effect of anti-Nogo-A therapy on lower urinary tract function was observed in animals with a complete SCI. Four weeks after incomplete SCI, animals treated with control antibodies showed a significant decrease in CRF-innervation in lamina X compared to non-injured animals. In contrast, the density of CRF fibers and terminals in this region in the injured anti-Nogo-A antibody treated rats was not different from that of intact rats but was significantly higher than that of the control antibody SCI animals.

Conclusions: Our findings indicate that anti-Nogo-A antibody treatment has beneficial effects on the lower urinary tract in rats re-establishing a physiological status and preventing DSD after incomplete SCI, presumably by influencing the neuronal wiring of descending micturition circuits. Thus, anti-Nogo-A immunotherapy, which currently enters clinical trials, could become a unique causal treatment option for lower urinary tract dysfunction in patients with SCI.