511 FESOTERODINE reduces autonomic dysreflexia in individuals with spinal cord injury suffering from neurogenic detrusor overactivity

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Introduction

- Neurogenic detrusor overactivity (NDO), a leading cause of urinary incontinence (UI), can elicit a life-threatening hypertensive crisis known as autonomic dysreflexia (AD) in individuals with spinal cord injury (SCI)[1]
- Both UI and AD-related symptoms place a tremendous burden on individuals with spinal cord injury (SCI)[2]
- Although lower urinary tract (LUT) function can be improved by treating NDO in this population using muscarinic antagonists, no study has ever quantitatively assessed the capacity of antimuscarinics to ameliorate AD

Objectives

To investigate the efficacy of FESOTERODINE to ameliorate AD while improving LUT function and quality of life (QoL) in individuals with SCI

Methods

- Currently, 7 individuals (6 males, 1 female, mean age 40±10 years (yrs.), mean time post-SCI 22±13 yrs.) with chronic (>1 yr.) SCI (5x AIS[3] A, 1x AIS B, 1x AIS D) at or above T6 have completed this prospective, open-label phase II study
- AD was defined as an increase in systolic blood pressure (SBP) of ≥20mmHg from baseline[4]
- Participants underwent a 12-week treatment period of FESOTERODINE (extended release), starting with 4mg (1x/day) with the option to increase to max. 8mg (1x/day)
- Pre- and during treatment assessments:
  - ✓ Severity of AD using standardized urodynamic investigation (UDI)[1] and 24-hour ambulatory-blood-pressure-monitoring (ABPM)[5]
  - ✓ AD-related clinical symptoms and incontinence-related QoL were assessed using validated, standardized questionnaires, i.e. AD Health-Related QoL (AD HR QoL)[5] and Incontinence QoL (I-QOL)[6]
  - ✓ Cognitive and bowel function, which could be negatively affected by FESOTERODINE, were monitored with the Montreal Cognitive Assessment (MoCA)[7] Scale and neurogenic bowel dysfunction score[8]

Results

FESOTERODINE's effect on LUT function and frequency and severity of AD (during UDI and 24-h ABPM)

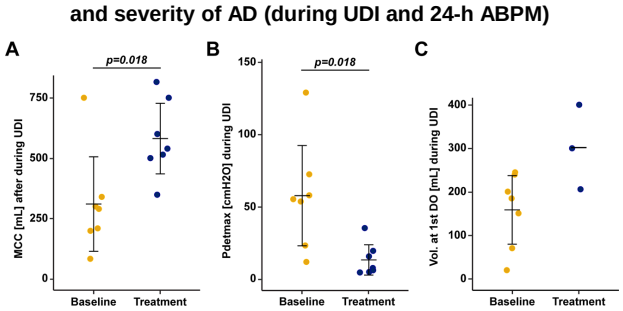

Figure 1. FESOTERODINE objectively improved lower urinary tract (LUT) function, i.e. **[A]** increased maximum cystometric capacity (MCC) 311±211 vs. 581±158mL **[B]** decreased maximum detrusor pressure (Pdetmax) during bladder filling 58±37 vs. 13±11cmH_2O and **[C]** increased volume at first detrusor overactivity (DO) 159±85 vs. 302±98mL. In addition, DO was eliminated by FESOTERODINE in four (57%) individuals.

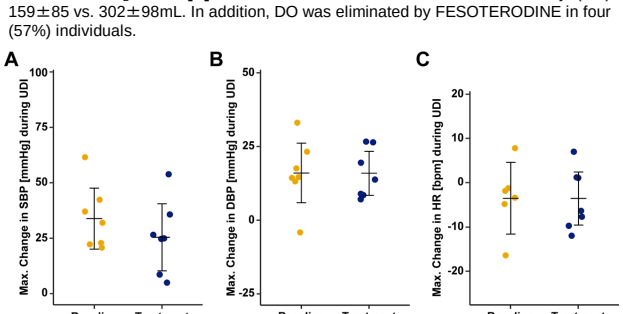

Figure 2. FESOTERODINE objectively improved cardiovascular responses during urodynamic investigation (UDI), i.e. **[A]** decreased maximum change in systolic blood pressure (SBP) 34±15 vs. 25±16mmHg. In addition, AD was eliminated by FESOTERODINE in two (29%) individuals. However, it did not affect maximum change in **[B]** diastolic blood pressure (DBP) 16±11 vs. 16±8mmHg or **[C]** heart rate (HR) -4±8 vs. -4±7bpm.

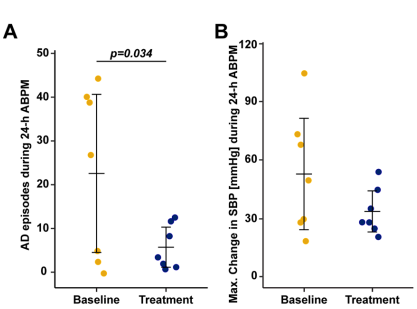

Figure 3. FESOTERODINE objectively improved cardiovascular function during the 24 hour ambulatory blood pressure measurement (24-h ABPM), i.e. **[A]** reduction in AD episodes 23±20 vs. 6±5, decreased maximum change in **[B]** systolic blood pressure (SBP) 53±31 vs. 34±11mmHg.

FESOTERODINE's effect on incontinence-related QoL and AD symptoms (during daily life and bladder specific)

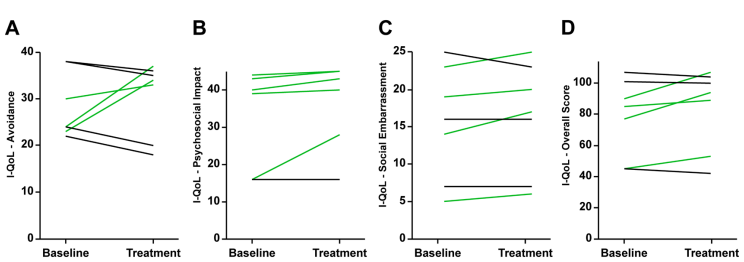

Figure 4. FESOTERODINE subjectively improved incontinence-related quality of life (I-QoL), i.e. **[A]** avoidance (score 0 [worst] to 40 [best]) in three (43%) individuals (group: 28±7 vs. 30±8), **[B]** psychosocial impact (score 0 to 45) in six (86%) individuals (35±13 vs. 37±11) in four (57%) individuals, **[C]** social embarrassment (score 0 to 25) in four (43%) individuals (16±8 vs. 16±7) and **[D]** overall score (score 0 to 110) in four (57%) individuals (79±25 vs. 84±26). (Each line represents one subject, i.e. green = improved and black = not improved compared to baseline).

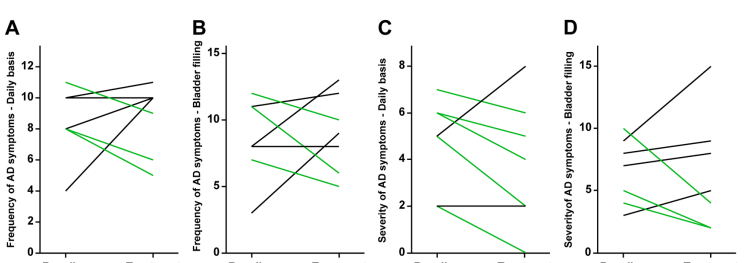

Figure 5. FESOTERODINE subjectively decreased the frequency of AD symptoms during **[A]** daily life (scale 0 [no symptoms] to 24 [max. possible symptoms]) in three (43%) individuals and **[B]** bladder filling (scale 0 to 27) in three (43%) individuals as well as the severity AD symptoms during **[C]** daily life (scale 0 to 24) in five (71%) individuals and **[D]** bladder filling (scale 0 to 27) in three (43%) individuals. (Each line represents one subject, i.e. green = improved and black = not improved compared to baseline).

FESOTERODINE's side effects

Five individuals (71%) reported adverse events (AE's, all grade 1, i.e. minor) judged as related or possibly related to FESOTERODINE. Cognitive (MoCA, 28±3 vs. 29±1) and bowel (neurogenic bowel dysfunction score, 10±4 vs. 10±5) function did not deteriorate during treatment period.

Conclusion

FESOTERODINE can ameliorate AD while improving LUT function and incontinence-related QoL without affecting cognitive or bowel function negatively

References:
1 – EAU Guidelines on Neuro-Urology 2018
2 – Anderson, J Neurotrauma. 2004
3 – Kirshblum et al, J Spinal Cord Med. 2011
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5 – Hubli et al., Am J Hypertens. 2015
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