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).
- Both UI and AD-related symptoms place a tremendous burden on individuals with spinal cord injury (SCI).
- 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, mean time post-SCI 22 ± 13 yrs.) with chronic (>1 yr.) SCI (5x AIS 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 ≥20 mmHg from baseline.
- Participants underwent a 12-week treatment period of FESOTERODINE (extended release), starting with 4 mg (1×/day) with the option to increase to max. 8 mg (1×/day).
- Pre- and during treatment assessments:
  - Severity of AD using standardized urodynamic investigation (UDI) and 24-hour ambulatory-blood-pressure-monitoring (ABPM).
  - AD-related clinical symptoms and incontinence-related QoL were assessed using validated, standardized questionnaires, i.e. AD Health-Related QoL (AD HR QoL) and Incontinence QoL (I-QOL).
  - Cognitive and bowel function, which could be negatively affected by FESOTERODINE, were monitored with the Montreal Cognitive Assessment (MoCA) and Scale and neurogenic bowel dysfunction score.

Results

FESOTERODINE’s effect on LUT function and severity and severity of AD during daily life and bladder specific.

- FESOTERODINE objectively improved cardiovascular responses during urodynamic investigation (UDI), i.e. [A] increased maximum capacity (MCC) 31 ± 21 vs. 58 ± 15 mL, [B] decreased maximum detrusor pressure (Pdetmax) during bladder filling 58 ± 37 vs. 13 ± 11 mmHg, and [C] increased volume at first detrusor overactivity (DO) from 159 ± 33 to 302 ± 93 mL. In addition, DO was eliminated by FESOTERODINE in four (57%) individuals.
- FESOTERODINE objectively improved lower urinary tract (LUT) function, i.e. [A] increased maximum cystometric capacity (MCC) 31 ± 21 vs. 58 ± 15 mL, [B] decreased maximum detrusor pressure (Pdetmax) during bladder filling 58 ± 37 vs. 13 ± 11 mmHg, and [C] increased volume at first detrusor overactivity (DO) from 159 ± 33 to 302 ± 93 mL. In addition, DO was eliminated by FESOTERODINE in four (57%) individuals.

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

- FESOTERODINE subjectively decreased the frequency of AD symptoms during [A] daily life (scale 0 to 40) to 24 [max. possible symptoms] in three (43%) individuals and [B] bladder filling (scale 0 to 27) in three (43%) individuals and [C] overall score (score 0 to 110) in four (57%) individuals (79 ± 25 vs. 84 ± 26).”

Conclusion

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

References:
1. Matthies 1, Andrea L. Ramirez 1, Amanda H.X. Lee 1, Daniel Rapoport 1,2, Alex Kavanagh 1,2, and Andrei V. Krassioukov 1,3,4
2. International Collaboration on Repair Discoveries (ICORD), 2 Department of Urologic Sciences and 3 Division of Physical Medicine and Rehabilitation, Faculty of Medicine, University of British Columbia (UBC); 4 G.F. Strong Rehabilitation Centre, Vancouver, British Columbia, Canada.