

Prevention of neurogenic detrusor overactivity in spinal cord transected rats with early anticholinergic treatment

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ABSTRACT

After spinal cord injury (SCI), detrusor overactivity (DO) leads to incontinence affecting patient's quality of life and jeopardizes kidney function. Currently, the only recognized method preventing DO is electrical neuromodulation implemented immediately after SCI. However, this technique is expensive and not widely available. Therefore, the aim of this experiment was to assess the urodynamic effects of early fesoterodine fumarate (FF) administration in preventing DO in a spinal cord transected (SCT) rat model and investigate whether observed effects were due to alternations in expression patterns of bladder muscarinic receptors.

METHODS

33 Sprague-Dawley rats were allocated to 6 groups:

- Group 1:** 3 normal controls;
- Group 2:** 6 SCT controls;
- Group 3:** 6 SCT rats + FF 0.18 mg/kg/d;
- Group 4:** 6 SCT rats + FF 0.12 mg/kg/d;
- Group 5:** 6 SCT rats + FF 0.18 mg/kg/d + 72-h wash-out period;
- Group 6:** 6 SCT rats + FF 0.12 mg/kg/d + 72-h wash-out period.

SCT was performed at T10 and FF was administered subcutaneously from post-op day 1 by osmotic pump in peri-device space. The pump was implanted at the time of SCT. Cystometry was undertaken 6 weeks after SCT in awaked rats right before the animals were sacrificed.

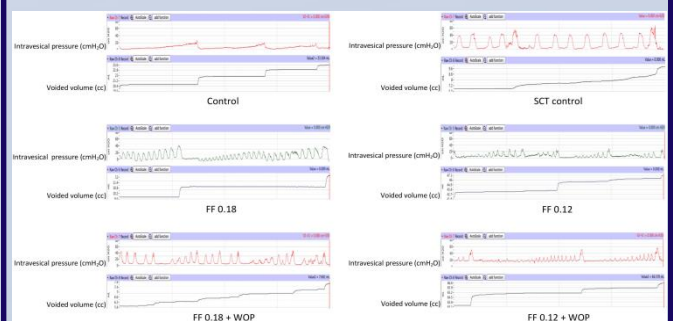
Then, the bladders were collected. Changes of bladders layers were assessed by hematoxylin/eosin and Masson's trichrome staining. Distribution of the receptors was investigated by immunofluorescence staining against muscarinic receptors (M1 to M5). Their prevalence was analyzed by Western blots. Comparisons were conducted using Kruskal-Wallis test (post-hoc Dunn test).

CONCLUSIONS

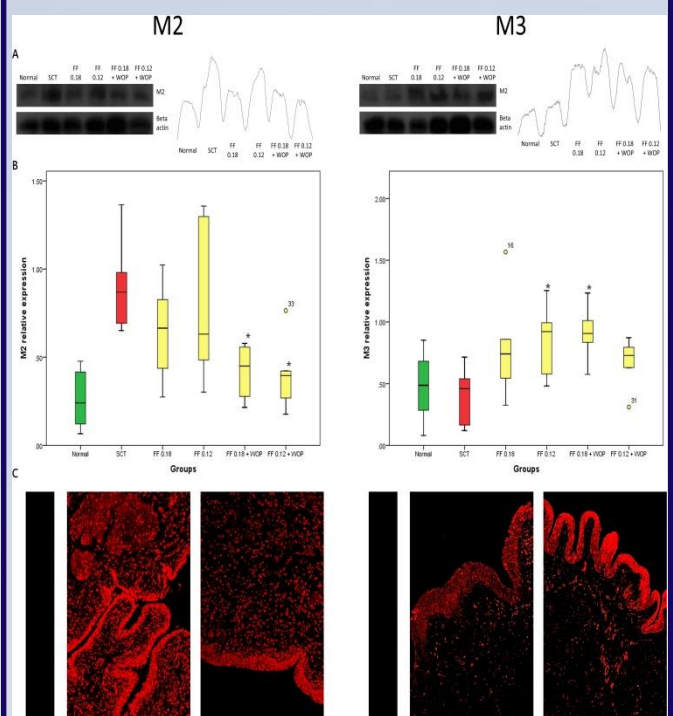
Early FF administration at the time of transection modulates bladder overactivity and modifies profile of bladder muscarinic receptors. The treatment effect is sustained after a wash-out period. The evidence is strong enough to support clinical trials analyzing long-term prevention of DO in patients after SCI with the presented approach.

RESULTS

Urodynamic data: 6 weeks after SCT, intermicturition pressure was lower in low dose treated group (Group 4) compared to SCT controls ($p < 0.05$). Maximum pressure was lower in most of the SCT treated rats (Groups 3–5) ($p < 0.01$). Threshold pressure was lower in full time treated rats (Group 3–4) ($p < 0.05$).



Morphological data: No changes were observed within the bladders layers in terms of degree of fibrosis and muscle hypertrophy. Expression of M2 receptors was lower in groups with wash-out period (Groups 5 and 6) ($p < 0.01$) whereas expression of M3 receptors was higher in Groups 4 and 5 ($p < 0.01$).



DISCLOSURE

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