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IMPROVEMENT BY PLANT EXTRACTS OF LOSS OF MUSCARINIC RECEPTORS IN BLADDER OF RATS WITH CYCLOPHOSPHAMIDE-INDUCED CYSTITIS

Hypothesis / aims of study

Interstitial cystitis (IC) is a chronic, abacterial inflammatory disease of the bladder characterized by urinary frequency, urgency and suprapubic pain associated with bladder filling and relieved by voiding, but its exact etiology and pathogenesis remain unclear and effective treatment is not established. Currently, there are increasing evidences to suggest the idea that the abnormality of muscarinic receptors in the bladder is implicated in the development of cystitis in rats. [1-3] The present study was aimed to characterize the pharmacologically relevant receptor in the pathophysiology of IC and the effects of plant extracts (Saw palmetto extract: SPE, Gosha jinki gan: GJG, Eviprostat: EVI, Green tea extract: GTE), by measuring muscarinic receptors in the bladder and submaxillary gland of rats with cystitis induced by cyclophosphamide (CYP).

Study design, materials and methods

Cystitis model was induced by injecting CYP (150 mg/kg, i.p.) in female Sprague-Dawley rats (9 weeks old). Rats were divided into sham group, CYP-treated group, CYP+plant extract-treated group. SPE (60 mg/kg), GJG (1000 mg/kg), EVI (18 mg/kg) and GTE (400 mg/kg) were administered orally for 7 days. On the last day of treatment, the tissue muscarinic receptor was measured by radioligand binding assay using [^{3}H]*N*-methyl-scopolamine ([^{3}H]NMS), a selective radioligand of muscarinic receptors, and binding parameters of apparent dissociation constant (K_d) and maximal number of binding sites (B_{max}) were estimated by nonlinear regression analysis using Graph Pad Prism.

Results

As shown in Table 1, the B_{max} for specific [^{3}H]NMS binding was significantly decreased in the bladder of CYP treated rats compared with sham rats. Thus, CYP treatment was shown to cause down-regulation of muscarinic receptors in the bladder of rats. There was significant increase in the Bmax for [^{3}H]NMS in the bladder of rats treated with CYP+SPE, CYP+GJG, CYP+EVI, and CYP+GTE, compared with CYP-treated rat bladder. On the other hand, the B_{max} for [^{3}H]NMS in the submaxillary gland was not altered by the CYP treatment.

Interpretation of results

The present results revealed down-regulation of muscarinic receptors in the bladder of rats with chemically induced cystitis, suggesting significant involvement of muscarinic receptors in the pathophysiology of cystitis. Moreover, the alteration of pharmacologically relevant receptors in CYP-treated rats was attenuated by the treatment with plant extracts such as SPE, GJG, EVI and GTE at pharmacological doses.

Concluding message

Bladder muscarinic receptors may be partly involved in the pathophysiology of cystitis. Plant extracts such as SPE, GJG, EVI and GTE may be useful in the pharmacological therapy of cystitis.

Table 1 K_d and B_{max} for specific [^{3}H]NMS binding in the bladder and submaxillary gland of sham, CYP, CYP + SPE and CYP+GJG-treated rats.

	K_d	B_{max}
	(pM)	(fmol/mg protein)
Bladder		
Sham	296±26	246±21
CYP-treated rats	274±12	158±11*
CYP + SPE-treated rats	324±13	228±17†
Sham	265±9	224±15
CYP-treated rats	234±15	147±8**
CYP + GJG-treated rats	240±10	211±19†
Submaxillary gland		
Sham	228±12	198±10
CYP-treated rats	255±19	197±17
CYP + SPE-treated rats	242±15	208±10
Sham	190±12	143±7
CYP-treated rats	182±4	149±8
CYP + GJG-treated rats	167±7	132±7

Values are expressed as mean±S.E. (n=7–9). Asterisk shows the significant difference from the values in sham, *P<0.05, **P<0.01. Dagger shows the significant difference from the values in CYP-treated rats, †P<0.05.

References

1. 1 Am J Physiol Renal Physiol, 287: F1084-1091 (2004).
2. 2 Auton Neurosci, 122: 9-20 (2005).
3. 3 Neurosci Lett, 436: 81-84 (2008).

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