

INFLUENCE OF MUSCARINIC ANTAGONISTS ON THE MICTURITION PATTERN OF MALE RATS

Hypothesis / aims of study

Pathological conditions of the urinary bladder, such as cystitis, can induce changes in both the afferent and the efferent nervous pathway. Since bladder contraction is mainly under the control of the parasympathetic nervous system, i.e. muscarinic receptors, several studies have examined the effect of antimuscarinic drugs on the function of both the normal and the pathological bladder. This study set out to investigate how the micturition patterns of both healthy male rats and those affected by cyclophosphamide-induced cystitis, mimicking interstitial cystitis in man, are influenced by muscarinic antagonists.

Study design, materials and methods

Male Sprague-Dawley rats were pre-treated with either saline (1mL/kg i.p; serving as controls) or cyclophosphamide (CYP; 100mg/kg i.p; in order to induce cystitis). 60h after pre-treatment the rats were injected with either saline (1mL/kg i.p; control) or 4-diphenylacetoxo-*N*-methylpiperidine (4-DAMP; 1-1000µg/kg i.p) and placed for 24h in a metabolic cage with free access to water. Micturition pattern was recorded by a sensor detecting each drop of urine, and a cup gathered the urine in order to measure the total voided volume. Together this yielded the possibility to calculate the mean volume per micturition. Water intake was also recorded. After the experiment, bladders from CYP-pretreated rats were excised in order to establish an inflammatory state.

Results

The volume per micturition was significantly smaller in CYP-pretreated rats compared to control rats (0.77 ± 0.07 and 0.96 ± 0.06 mL/micturition, respectively; $n = 20$; $p = 0.0096$). The micturition pattern was not altered in a consistent matter by any dose of 4-DAMP in normal or CYP-pretreated rats. Water intake was similar in all groups, as was the total voided volume.

Interpretation of results

Cyclophosphamide has previously shown to yield cystitis in rats, with a peak inflammatory state at 60h post injection [1]. The cyclophosphamide induced cystitis shows resemblance to interstitial cystitis in man, being a non-infectious inflammatory condition yielding urgency and frequency. It is therefore not surprising that we find a smaller volume per micturition among rats with cystitis. However, one would expect to find a larger volume per micturition in 4-DAMP treated rats compared to control rats. This we could not see in any of the treatment groups. Similar observations have been made in man, i.e. indicating that antimuscarinic drugs may not significantly alleviate urgency or frequency [2].

Concluding message

Cystitis increases the urgency and frequency in conscious male rats. Antimuscarinic treatment (4-DAMP; 1-1000 µg/kg i.p) does not alter the micturition pattern in neither normal nor CYP-pretreated rats. This strengthens the proposed idea that antimuscarinic drugs may not necessarily be the most effective treatment for overactive bladder.

References

- [1] *Auton Neurosci* 2005, **122**, 9-20
 [2] *Br J Obstet Gynaecol* 1997, **104**, 988-93

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Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	The Ethical Committee of the University of Gothenburg, Sweden