471

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CHARACTERIZATION OF BLADDER CONTRACTION DURING ACUTE INFLAMMATION IN RATS.

Aims of Study

Interstitial cystitis (IC) is a complicated chronic disease. Currently, there is no animal model that clearly demonstrates all the symptoms found in patients with IC. Most models use chemical irritation of the rat urinary bladder but it is unclear whether this provides a good model of IC. Among the various chemical irritants used to induce a bladder hyperactivity, dilute acetic acid is reported to produce a reduced intercontraction interval with no changes in contraction amplitude [1]. Bladder overactivity may be produced by mechanisms related to the peripheral sensory nerves, to spinal neural organization or to supraspinal controls or to combinations thereof [2]. In preparation for investigating these mechanisms, we have compared changes in bladder dimensions and the corresponding changes in wall tension during voiding under conditions of constant infusion of saline or irritant in the anesthetized rat.

Methods

Female Wistar rats were anesthetized with urethane. A saline-filled silastic cannula was sewn into the dome of the bladder, and Teflon-coated silver wires were placed in the pelvic floor musculature. Sonomicrometer crystals were glued onto the ventral surface of the bladder body. One pair was arranged longitudinally and the other pair was at right angles to the first. The abdominal incision was left open and the crystals and exposed bladder surface were covered by gel. A computer controlled the sonomicrometer tranceiver unit and accepted analog inputs of bladder pressure and emg activity. Sampling was carried out at 50Hz.

Reflex bladder contractions were elicited by continuous infusion at 0.05 or 0.1 ml/min over 3 hours. In some experiments, the infusion solution was switched from saline to 0.2% acetic acid at 1.5 hours. Intercontraction intervals were measured from the pressure trace. The contractions were assigned a complexity code ranging from 1 for a single contraction to values of 2-4 for closely-spaced multiple contractions. In some experiments, the fluid voided with each reflex contraction was collected. Input volume was estimated from the intercontraction interval and the infusion rate, and voiding efficiency was calculated. Bladder wall tension was calculated from the formula: tension = bladder pressure / (1/L + 1/C) where L=longitudinal length, C=circumferential length. The values of tension at threshold for bladder contraction were read from graphs of pressure and tension versus time.

Results

In 8 experiments, characteristics of voiding were compared between saline acetic acid infusions. Six others served as saline-only controls. Continuous saline infusion elicited repeated voiding episodes (intercontraction interval = 0.15ml) associated with fluid discharge at the meatus and with an EMG burst. It was evident visually that the voiding episodes did not empty the bladder. Intercontraction interval was not a reliable indicator of functional change after inflammation. The complexity of contraction events tended to be greater (saline 1.1, acetic acid 1.4), and voiding efficiency tended to be lower (saline 89%, acetic acid 75%) during acetic acid infusion but neither was significant by t-test.

The measurements of longitudinal and circumferential dimension changes revealed the following patterns of contraction. In Pattern A, the length increased gradually as the bladder distended. When micturition pressure rose, the length also underwent an abrupt increase, peaking at the same time as the pressure peak. The length then shortened during the fall in bladder pressure to a trough length shorter than the length just before the abrupt rise. It then began a gradual increase again. In Pattern B, the length increased gradually during bladder filling but shortened abruptly at the peak of bladder pressure to a trough for a short period. It then "popped" back to a length between the trough and the original length and began a gradual again. In Pattern C, the length showed little increase as the bladder filled. The length then increased, mirroring the pressure rise, and returned to the precontraction length but with no net shortening seen in any part of the trace. Patterns A and B were the most common but were not consistently related to orientation or to the presence or absence of inflammation.

During acetic acid infusion the mean bladder wall tension at the threshold for micturition contraction was lower by 10-50% compared to the value during saline infusion. This was a statistically significant drop in 5 of 6 evaluable experiments.

Conclusions

We conclude that acute bladder irritation by dilute acetic acid infusion produces a sensitization of peripheral afferent nerve terminals reflected in a reduced bladder wall tension at the threshold for micturition. The lack of changes in bladder wall length changes make it unlikely that the muscular process of developing a contraction was influenced by inflammation. However, the presence of trends toward increased contraction complexity and decreased efficiency may implicate central neural changes as well. This line of investigation is being pursued.

References

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