Aims: We investigated the in vitro effects of local anesthetics on the contractility of the human bladder. Methods: By measuring the in vitro isometric contractions of human bladder strips, we determined the effects of tetracaine, bupivacaine, lidocaine, and ropivacaine on the basal spontaneous contractions and contractions induced by various stimuli, namely, KCl (60 mM), carbachol (CCh), and electrical field stimulation (EFS). The effect of local anesthetic agents on Ca\(^{2+}\)-independent sustained tonic contraction (SuTC) of the detrusor was also investigated. Results: Local anesthetics increased phasic and tonic spontaneous contractile activity dose dependently in the concentration range 1–500 \(\mu\)M, but abolished phasic activity at higher concentrations. Local anesthetic agents inhibited nerve-mediated contraction (EFS, 0.8 msec) in a concentration-dependent manner (ropivacaine > tetracaine = bupivacaine > lidocaine), and inhibited non-nerve mediated contractions induced by KCl, long pulse EFS (direct muscle stimulation, 100 msec), and CCh. Inhibitory potency on non-nerve mediated contraction was for long pulse EFS: ropivacaine = tetracaine > bupivacaine = lidocaine and for KCl- and CCh-induced contractions: ropivacaine > tetracaine > bupivacaine = lidocaine. Higher concentrations of local anesthetics were needed to inhibit non-nerve-mediated bladder contraction than nerve-mediated contraction. SuTC was suppressed by all local anesthetics concentration dependently. Conclusions: Our study demonstrates that local anesthetics have inhibitory effects on the contraction of human bladder as induced by different stimulants and concentrations. Their effects and differences suggest that they may be considered potentially useful as diagnostic and therapeutic agents for bladder dysfunction. Neurourol. Urodynam. 24:288–294, 2005. © 2005 Wiley-Liss, Inc.

Key words: bladder; local anesthetics; muscle contraction; smooth muscle

INTRODUCTION

Local anesthetic agents have been used for topical analgesia intravesically, with or without an electromotive drug administration in the case of painful procedures, to produce mucosal anesthesia for bladder biopsy [Holmang et al., 1994] or instillation of irritative substances including capsaicin [Dasgupta et al., 1998].

In addition to their analgesic purposes, local anesthetic agents have been used as a diagnostic tool for certain pathological conditions or a preoperative prognostic indicator before a surgical procedure in urge incontinence. Yokoyama et al. [1997, 2000] suggested that intravesical administration of local anesthetic agent is useful in differentiating detrusor hyperactivity caused by lesions of spinal cord versus those of the brain, as well as, in identifying the overactive bladder attributable to spinal or other lesions. Westney et al. [2002] suggested that preoperative positive response to subtrigonally injected bupivacaine prior to detrusor denervation procedure might be useful to predict long-term improvement of symptoms after the procedure in patients with intractable urge incontinence.

Moreover, local anesthetic drugs have been administered therapeutically in interstitial cystitis [Giannakopoulos and Champilomatos, 1992; Gurpinar et al., 1996; Henry et al., 2001] and even in female urge incontinence [Gassner and Briel, 1988]. More recently, Lapointe et al. [2001] observed that intravesical lidocaine instillation lead to an improvement in bladder capacity and compliance and decrease in the number of uninhibited contractions in children with neurogenic bladder caused by meningomyelocele [Lapointe et al., 2001]. This may imply that the effects of local anesthetics can alter the bladder contractility as well as viscoelastic properties of the neurogenic bladder. These findings suggest that the effects of local anesthetics may not be confined to the already well-known submucosal sensory nerve fibers, but that they may simultaneously involve intrinsic motor nerves and even the detrusor muscle.

Despite many clinical trials, the basic theoretical background of the mechanistic action of local anesthetics remains insufficiently defined. Our previous study in the rat revealed that the primary action of local anesthetics was to inhibit both intrinsic...
motor nerves and bladder smooth muscle [Oh et al., 2001]. However, the effect of local anesthetics on human bladder contraction induced by various external stimuli has not been studied. We have thus investigated the effects of local anesthetics that are in common clinical use in the human bladder.

MATERIALS AND METHODS

Tissue Preparation

Human bladder tissue was obtained from 23 patients undergoing radical cystectomy for bladder malignancy. Subjects with any history of neurological abnormality, diabetes, or obstructive symptom were excluded. After excision of the bladder, whole layer bladder tissue macroscopically distant from any apparent tumor or inflammation was excised from the bladder anterior wall. Longitudinal detrusor muscle strips (thickness × width × length = 0.7 mm × 1.1 mm × 5.7 mm) were prepared. Multiple strips were obtained from each patient, but each strip was only used to investigate the action of one local anesthetic on a single type of external stimulus. Six vertical chambers of 20 ml capacity were used for the experiment. Within a vertical chamber, one end of a muscle strip was tied to a glass hook fixed to muscle holder and the other end was connected to a force transducer (FT03, Grass, Quincy, MA). The analog signal from a fitted force transducer was amplified (P-122, Grass) and digitized (Polyview, Grass) at a sampling rate of 5 Hz. Data was stored on a personal computer in ASCII format. The muscle strips were stretched to approximately 200% of their resting lengths (the length determined in preliminary experiments that resulted in a maximal contractile response to stimuli) and then equilibrated in the bath solution for 50 min prior to the application of the agents. Each strip was exposed to only one local anesthetic agent and then discarded.

Effect of Local Anesthetic Agents on Spontaneous Bladder Contractions

Basal spontaneous contractions were observed after equilibration, without any treatment or manipulation. After the baseline tone and spontaneous contractile activities had stabilized, local anesthetic agents were added cumulatively up to a bath concentration of 5 mM.

Effects of Local Anesthetic Agents on Nerve-Mediated Bladder Contraction

A train of short-pulse electrical field stimulation (EFS) (70 V/cm²; 50 Hz, 0.8 msec pulse duration, and 2.5 sec train duration) was applied every 2 min to activate the intrinsic nerves. This stimulation induced a transient contraction of the muscle strip. A preliminary study revealed that maximal contraction was induced at a frequency of 50 Hz. After confirming the reproducibility of the contractile amplitudes induced by each train of EFS, local anesthetic agents were applied cumulatively. EFS-induced contraction was completely abolished by treatment with tetrodotoxin (TTX, 0.3 μM), indicating that the short-pulse EFS induced contractions were mediated exclusively by the release of transmitters from intrinsic neurons.

Effects of Local Anesthetic Agents on Non-Nerve Mediated Detrusor Contraction Elicited by Long-Pulse EFS

In the presence of TTX (0.3 μM) to block neurogenic responses, a train of long-pulse duration stimuli (70 V/cm², 5 Hz, 100 msec pulse duration, and 5 sec train duration) induced a small phasic contractile response. The effects of cumulative concentrations of local anesthetics were recorded on responses to trains of stimuli repeated every 2 min.

Effects of Local Anesthetic Agents on CCh-Induced Detrusor Contraction

In human bladder strips, CCh (5 μM) induced a large phasic contraction followed by a sustained tonic contraction (StTC) in the CO₂/bicarbonate-buffered Tyrode solution. Concentration-response relationships for different concentrations of the local anesthetic agents were obtained. Since the size of the tonic contraction recorded on repeated applications of CCh was very reproducible (preliminary study, data not shown), tonic contractile amplitude was used for the analysis of the response. Similar experiments were performed in Ca²⁺-free medium. Our previous study [Oh et al., 2001] and the study by Yoshimura and Yamaguchi [1997] revealed that a sustained tonic contraction can be elicited by CCh in the detrusor smooth muscle, and that this is independent of the mobilization of internal or external Ca²⁺ sources. In the present study, we performed the same type of experiments with human bladder strips. To remove external Ca²⁺, the medium was replaced with a Ca²⁺-free solution containing 2 mM ethyleneglycol bis-(aminoethyl ether)-N, N-tetraacetic acid (EGTA) and the baths were rinsed at least twice. Internal Ca²⁺ stores were subsequently depleted by applying thapsigargin (0.1 μM), an inhibitor of sarcoplasmic reticulum Ca²⁺-ATPase. After incubating a bladder strip in Ca²⁺-free medium for about an hour, contraction was induced by 5 μM CCh, and the effects of
cumulative application of local anesthetics on the tonic contraction were recorded.

**Data Analysis, Drugs, and Solutions**

Drugs used in this study were purchased from Sigma (St. Louis, MO). Ropivacaine was obtained from the AstraZeneca Pharmaceuticals (Wilmington, DE). All local anesthetic agents were dissolved in distilled water at 500 mM. In cumulative concentration-response studies, these solutions were diluted with distilled water when necessary, which was added directly to the baths, the volumes of water added were less than 2.1% of the bath fluid. In a preliminary study, the addition of 0.41 ml of distilled water to a 20 ml bath was found not to significantly change the tension of strips in the basal EFS or to CCh-induced contraction.

All experiments were performed in CO₂/bicarbonate-buffered Tyrode solution. The CO₂/bicarbonate-buffered Tyrode solution contained (in mM) NaCl 116, KCl 5.4, CaCl₂ 1.5, MgCl₂ 1, NaHCO₃ 24, and glucose 5 (36.5°C, pH 7.35–7.40, bubbled with 5% CO₂/95% O₂). The Ca²⁺-free solution was made by replacing CaCl₂ with 2 mM EGTA in bicarbonate-buffered Tyrode solution.

A preliminary pH study (Corning pH meter 220, Corning, Inc., Corning, NY) showed that high concentrations of local anesthetic agents changed the pH in CO₂/bicarbonate-buffered Tyrode solution; the pH was lowered from 7.35 to about 7.20 by adding 1 mM of the local anesthetic and to about 7.03 by adding 5 mM of local anesthetic agent. Since such acidification might have affected the amplitude of the bladder contraction, the pH of the bath solution was adjusted by adding an appropriate amount of NaOH solution with each local anesthetic application.

The data were analyzed using commercially available software (Graphpad Prism V4.0, Graphpad Software, San Diego, CA; SAS V6.12, SAS Institute, Inc., Cary, NC). Results are expressed as percentages of the maximal contractions induced by EFS, KCl, or CCh (mean ± SD). Small n denotes the number of individuals used for each set of experiments. Statistical analyses were performed using repeated measures ANOVA and a P-value of <0.05 was considered significant. Concentrations of local anesthetic agents causing half maximal inhibitory response (IC₅₀) were estimated from the nonlinear modeling of concentration-response relationships. This experimental protocol was reviewed by the Institutional Review Board of Seoul National University Hospital and informed consent was obtained from all patients.

**RESULTS**

**Effects of Local Anesthetic Agents on Spontaneous Bladder Contractions**

No spontaneous contraction was observed in 181 (96.8%) of 187 human bladder strips. The other six strips showed repetitive spontaneous phasic contractions. On these six strips, one of four local anesthetics increased the size of the spontaneous phasic contractions. The magnitude of contractile amplitudes increased up to 0.5 mM of local anesthetic agents in a concentration-dependent manner. However, at 1mM and above these local anesthetic agents abolished spontaneous phasic contractile activities and reduced the basal tone (Fig. 1). The application of forskolin (10 μM), which activates adenylate cyclase, produced maximal relaxation of the detrusor at the end of each experiment. The number of strips was insufficient for statistical analysis.

**Effects of Local Anesthetic Agents on Nerve-Mediated Bladder Contraction**

Local anesthetic agents inhibited the bladder contractions induced by short-pulse EFS concentration dependently, and this inhibitory response was completely reversed by washout. The order of inhibitory potency at maximal contraction was ropivacaine > tetracaine ≈ bupivacaine > lidocaine. No statistical difference was found between tetracaine and bupivacaine (P > 0.05) (n = 7 for each agent) (Fig. 2A). Actual mean and relative IC₅₀ values of the four local anesthetics on nerve-evoked responses are shown in the Table I.

**Effects of Local Anesthetic Agents on KCl-Induced Detrusor Contraction**

Bath application of 60 mM KCl induced an initial phasic contraction and a subsequent tonic contraction, which was reversed by washout with Tyrode solution. This KCl-induced contraction was completely abolished by pretreating with nicardipine (2 μM), a voltage-operated Ca²⁺ channel (VOCC) blocker (data not shown).

Local anesthetic agents inhibited this KCl-induced contraction in a concentration-dependent manner. The order of inhibitory potency on maximal contraction was ropivacaine > tetracaine > bupivacaine = lidocaine (n = 7 in each agent) (Fig. 2B). No statistical difference was found between lidocaine...
Effects of Local Anesthetic Agents on Non-Nerve Mediated Detrusor Contraction Elicited by Long-Pulse EFS

Nerve-mediated detrusor contraction by short-pulse EFS (0.8 msec, 50 Hz) was completely eliminated by the bath application of TTX (0.3 µM). Following nerve blockade, long-pulse EFS was applied (100 msec, 5 Hz) to activate VOCCs in bladder smooth muscle directly. Each train of long-pulse EFS induced a phasic contraction. Moreover, the application of local anesthetic agents except for tetracaine increased the amplitude of the phasic contraction at lower concentrations and inhibited it at higher concentrations (Fig. 3A). The order for inhibitory potency was ropivacaine = tetracaine > bupivacaine = lidocaine (n = 7 in each agent). No statistical difference was found between tetracaine and ropivacaine or bupivacaine and lidocaine (P > 0.05) (Fig. 3B). Actual mean and relative IC₅₀ values of the four local anesthetics on non-nerve mediated contraction are shown in the Table I.

Effects of Local Anesthetic Agents on CCh-Induced Detrusor Contraction

Ropivacaine, tetracaine, bupivacaine, and lidocaine concentration-dependently inhibited the CCh-induced tonic contraction of detrusor smooth muscle in the CO₂/bicarbonate-buffered Tyrode solution. The order for inhibitory potency was ropivacaine > tetracaine > bupivacaine = lidocaine (P < 0.05) (n = 7 for each agent) (Fig. 4A). No statistical difference was found between lidocaine and bupivacaine (P > 0.05). Actual mean and relative IC₅₀ values of the four local anesthetics on non-nerve mediated contraction are shown in the Table I.

![Fig. 2. A: Effects of local anesthetic agents on the nerve-mediated contractions of isolated rat detrusor strips elicited by electrical field stimulations (EFS) of 0.8 msec pulse duration. Response was completely reversed by washout. Concentration-response curves of local anesthetic agents are presented as mean ± SD (n = 7 for each agent). Responses were normalized versus the maximal amplitudes of the initial contractions. B: The effects of local anesthetic agents on KCl-induced contractions in human bladder smooth muscle. Local anesthetic agents were applied before KCl (60 mM) application. Concentration-response curves are presented as means ± SD (n = 7 for each agent). The responses were normalized versus the maximal amplitude of the initial contraction induced by KCl alone.](image)

<p>| TABLE I. Mean IC₅₀ Values of Four Local Anesthetics for the Detrusor Contraction to the Various Stimuli |
|-----------------------------------------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Ropivacaine (µM)</th>
<th>Tetracaine (µM)</th>
<th>Bupivacaine (µM)</th>
<th>Lidocaine (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerve-mediated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual</td>
<td>4.8</td>
<td>61.5</td>
<td>72.6</td>
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<tr>
<td>Relative</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>KCl-induced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual</td>
<td>71.0</td>
<td>199.3</td>
<td>1060.1</td>
</tr>
<tr>
<td>Relative</td>
<td>14.8</td>
<td>3.2</td>
<td>14.6</td>
</tr>
<tr>
<td>Non-nerve mediated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual</td>
<td>495.5</td>
<td>199.3</td>
<td>4012.2</td>
</tr>
<tr>
<td>Relative</td>
<td>103.2</td>
<td>3.2</td>
<td>55.3</td>
</tr>
<tr>
<td>CCh-induced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual</td>
<td>19.2</td>
<td>309.2</td>
<td>2350.7</td>
</tr>
<tr>
<td>Relative</td>
<td>4.0</td>
<td>5.0</td>
<td>32.4</td>
</tr>
<tr>
<td>CCh-induced SuTC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual</td>
<td>291.3</td>
<td>397.2</td>
<td>3085.7</td>
</tr>
<tr>
<td>Relative</td>
<td>60.7</td>
<td>6.5</td>
<td>42.5</td>
</tr>
</tbody>
</table>

Each relative IC₅₀ values are represented as relative values to the actual IC₅₀ of the nerve-mediated contractile amplitude of corresponding local anesthetic agents.

CCh, carbachol 5 µM; All experiments were performed in bicarbonate-buffered Tyrode solution.

CCh, 5 µM; SuTC, sustained tonic contraction of the detrusor; All experiments were performed in Ca²⁺-free bicarbonate-buffered solution.
SuTC was, concentration-dependently, suppressed by local anesthetic agents. The order of inhibitory potency on maximal contraction was ropivacaine = tetracaine > bupivacaine = lidocaine (n = 5 in each agent) (Fig. 4B). No statistical difference was found between ropivacaine and tetracaine or between lidocaine and bupivacaine (p > 0.05). Actual mean and relative IC_{50} values of the four local anesthetics on CCh (5 μM)-induced Ca^{2+}-independent SuTC are shown in the Table I.

**DISCUSSION**

The use of local anesthetics has extended slowly, as the intravesical application of local anesthetic agents is now used for analgesia and for diagnostic purposes. Moreover, the intravesical instillation of local anesthetic agent has been shown to offer safe, effective anesthesia for most invasive endoscopic procedures in the lower urinary tract [Fontanella et al., 1997]. The intravesical application of lidocaine before capsaicin was found to effectively reduce patient discomfort and the multiple bladder contractions seen after intravesical capsaicin administration, thus facilitating the use of capsaicin for the treatment of detrusor hyperreflexia [Dasgupta et al., 1998].

Response to the intravesical instillation of lignocaine has also been examined as a diagnostic or preoperative test to predict the outcome of certain procedures. This method was found to be useful in the differentiation of idiopathic detrusor instability and detrusor instability caused by infravesical obstruction [Reuther et al., 1983]. A local anesthetic effect was found to be a positive predictor for denervation procedures [Westney et al., 2002]. Similarly, the intravesical lidocaine test was found to be useful for differentiating an overactive bladder of spinal origin from other lesions [Yokoyama et al., 2000]. This was evidenced by their finding that the increase in bladder capacity and the disappearance of

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**Fig. 3.** Effects of local anesthetic agents on smooth muscle contraction induced by electric field stimulation (EFS) using a 100 msec pulse duration. **A:** A representative original trace showing the inhibitory effects of tetracaine. Note the complete inhibition of short-pulse EFS induced contraction by tetrodotoxin (TTX, 0.3 μM). **B:** Concentration-response curves are presented as means ± SD (n = 7 in each agent). Responses were normalized versus the maximal amplitude of the initial contraction induced by long-pulse EFS.

**Fig. 4.** **A:** Effects of local anesthetic agents on carbachol (CCh)-induced bladder contraction. Concentration-response curves of local anesthetic agents are presented as mean ± SD (n = 7 for each agent). Responses were normalized versus the maximal amplitudes of the initial contractions. **B:** Effects of local anesthetic agents on CCh-induced sustained tonic contraction (SuTC), which was observed after the elimination of known Ca^{2+} sources from both intracellular and extracellular spaces. Concentration-response curves of local anesthetic agents are presented as mean ± SD (n = 5 for each agent). Responses were normalized versus the maximal amplitudes of the initial contractions.
the detrusor contraction were significantly greater in the patients with spinal cord lesions than those with brain lesions or idiopathic bladder overactivity following the intravesical administration of 4% lidocaine.

The effects of the commonly used local anesthetics investigated in this study, that is, lidocaine, tetracaine, bupivacaine, and ropivacaine were similar, although their effective concentrations differed. The different inhibitory potencies of the local anesthetic agents examined in this study probably reflects differences in chemical structure, which dictates protein-binding properties, lipid solubilities, pKa values, etc. Sethia and Smith could not observe a consistent effect of lignocaine to increase bladder capacity in a group of patients with detrusor instability [1987]. They proposed that increased bladder capacity was mainly due to alkaline pH rather than to lignocaine based on the observation that filling the bladder with alkaline solution resulted in a significant increase in bladder capacity. However, our current in vitro study showed that the main effect of the local anesthetic agents on the intramural nerve and bladder smooth muscle is inhibitory. Under our experimental conditions of pH correction in CO2-bicarbonate buffered Tyrode solution, we observed a significant inhibition of detrusor contractility by local anesthetic agents. Therefore, we believe that the relaxation of detrusor muscle by local anesthetic agents reflects specific effects of these agents rather than nonspecific changes in the physicochemical environment of our study.

It is known that the effects of local anesthetics are caused primarily by a reversible blockade of voltage sensitive Na\(^+\) channels in the cell membrane, thereby, blocking the generation and conduction of the action potential in the nerve fiber [Catterall and Mackie, 1996]. It is likely that the main action mechanism of a local anesthetic agent in terms of changing urodynamic effects is effected through smaller unmyelinated sensory fibers, such as C afferents [Dasgupta et al., 1998; Henry et al., 2001]. Literature on this topic tends to focus and differentiate between effects on the sensory fiber, but may affect the efferent neuron and even the detrusor muscle. Moreover, the effect of intravesical local anesthetics may extend to the muscle layer of the bladder, especially under alkaline conditions, since they penetrate lipid bilayers of the cell membrane more easily with their nonionized form [Armel and Horowitz, 1994; Capogna et al., 1995]. This phenomenon might be more relevant under certain pathological conditions, because the microenvironment of the bladder with respect to the diffusion or the tissue penetration of certain chemicals into submucosal layers may differ from that of the normal urothelium [Tramontana et al., 1991].

In addition, many studies have demonstrated that the inhibitory effects of local anesthetics are not uniquely applicable to voltage activated Na\(^+\) channels, as they may also block other types of ion channels, including K\(^+\) channels in the canine trachea and Ca\(^{2+}\) channels in the guinea pig bladder [Kurihara and Sakai, 1976; Imaizumi and Watanabe, 1982]. In contrast with the inhibitory effect on contraction induced by external stimulation, our limited observation on the effects of the local anesthetics on the spontaneous contractions showed that the spontaneous contractions were augmented by local anesthetic agents. The inhibitory effects of LA agent, on the long-pulse EFS-induced contraction of detrusor muscle, were weaker in the lower range of concentrations tested. Consequently, the concentration-response curves of local anesthetic agents have a complex shape (Fig. 3B). We believe that these peculiar responses might be due to a parallel excitatory effect of the LA agent. Previously Kitamura et al. [1986] showed using the patch clamp technique that procaine induced depolarization of cell membrane and generation of spike potentials in vascular smooth muscle through the inhibition of K\(^+\) conductance [1987]. Kurihara reported that procaine increase the peak amplitude and duration of electrical spike potentials of detrusor smooth muscle, while higher concentrations of procaine had an inhibitory effect [1976]. He suggested that procaine inhibits the K\(^+\) conductance of smooth muscle cells and induces depolarization, which would increase the Ca\(^{2+}\) influx through the voltage operated Ca\(^{2+}\) channel. Therefore, local anesthetic agents have excitatory as well as inhibitory effects on smooth muscle contraction.

Previous studies have suggested that their action mechanisms involve multiple steps in the contractile process, including, the secondary messenger system [Minamoto et al., 1997], calmodulin [Tanaka and Hidaka, 1981; Nosaka et al., 1989], or even muscarinic receptor antagonism [Hisayama et al., 1989]. Such a wide spectrum of inhibition on detrusor contraction also suggests that the actions of local anesthetic agents on smooth muscle contraction are convergent, that is independent of involved steps in the contractile process. The elucidation of the mechanism involved in this inhibitory process is, however, beyond the scope of the present work. In the present study, we found that local anesthetics inhibit both nerve mediated contraction induced by EFS (0.8 msec) and non-nerve mediated detrusor contraction induced by KCl, carbachol (CCh), EFS (100 msec), or Ca\(^{2+}\)-independent SucC in the human detrusor muscle. These results suggest that local anesthetics may also block \(\alpha\) tipo Ca\(^{2+}\) channels [Ahn and Karaki, 1988; Sugiyama and Muteki, 1994], and that their action mechanisms may be more complex than previously believed.

However, the concentrations of local anesthetics required to inhibit non-nerve mediated detrusor contraction were 3.2–103.2-fold higher than those needed to inhibit nerve mediated contraction (see Table I). This finding suggests that at clinically applicable doses the major inhibitory property of local anesthetic agents would involve the blockade of nerve conduction rather than the direct inhibition of smooth muscle contraction. However, the effects of local anesthetics on the contractility and viscoelastic properties of normal and neurogenic bladder should be explored further.
The effects of local anesthetics on overall human bladder function are not straightforward since they are mediated by complex pathways involving various types of sensory receptors, such as, reflex centers in the brain and spinal cord, peripheral nervous connections, and the detrusor muscle. A deeper understanding of the action mechanisms of local anesthetics would widen our diagnostic and therapeutic options in the case of voiding disorders and provide us with useful additional indications.

CONCLUSIONS

Our study demonstrates that local anesthetics have a wide spectrum of inhibitory effects on the contraction of human bladder induced by various stimulants. Their effects and different potencies on both intrinsic nerves and the smooth muscle of the urinary bladder, suggest that they should be considered potentially useful diagnostic and therapeutic agents for bladder dysfunction.

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