Effects of Analgesic and Anesthetic Medications on Lower Urinary Tract Function

Sammy E. Elsamra and Pamela Ellsworth

The lower urinary tract (LUT), which consists of the bladder, urethra, and urinary sphincter, serves to allow for the functional storage and elimination of urine. This complex process is orchestrated by reflexive neural pathways (which are under control from higher centers) that allow for the coordination of bladder and sphincter. The impact of anesthetics, general or regional, on this complex neural network may affect this delicate control and may result in urinary retention. Although the association between the use of certain medications and the occurrence of acute urinary retention is well established, the association is poorly defined (Thomas, Chow, & Kirby, 2004). Limited information is available regarding the effects of analgesic and anesthetic medications on the LUT. This article provides a summary of the current available literature on the effects of nonsteroidal, anti-inflammatory drugs (NSAIDs); opiates; and spinal anesthetics on LUT function.

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Note: *Objectives and CNE Evaluation Form appear on page 68.*

Analgesic and anesthetic medications may affect lower urinary tract function via a variety of mechanisms. This article reviews the more commonly used medications and their effects on lower urinary tract function.

Key Words: Anesthetic, opioid, ketamine, lower urinary tract function, urinary retention, analgesia.

Objectives:

1. Discuss the physiology of micturition.
2. Explain the effects of analgesics on the lower urinary tract.
3. Describe the effects of general anesthesia on the lower urinary tract.

Physiology of Micturition

Storage and voiding involves complex interactions between the bladder, urethra, urethral sphincter, and nervous system. The urinary bladder and urinary sphincter are the principle components of the LUT responsible for urinary storage and voiding. The urinary bladder, with a typical adult capacity of 400 to 500 ml, serves to store or expel urine by way of relaxation or contraction of the detrusor muscle, respectively. The urinary sphincter, composed of an internal component, a continuation of detrusor smooth muscle that converges to form a thickened bladder neck controlled by the autonomic nervous system, and a somatically controlled external component (striated muscle), must relax to allow for the contracting bladder to expel its load. Storage of urine is achieved by bladder relaxation and contraction of both the bladder neck (internal urinary sphincter) and the external urinary sphincter. Micturition occurs when the bladder neck and the external urinary sphincter relax and the bladder contracts, allowing for the unobstructed expulsion of urine.

Bladder storage and emptying, as well as coordinated contraction or relaxation of the urinary sphincter, are under the control of the sympathetic, parasympathetic, and somatic nervous systems (Ouslander, 2004). In general, urinary storage is a function of the sympathetic nervous system, whereas micturition is a function of the parasympathetic nervous system. While both are autonomic functions in nature, the somatic nervous system is responsible for the control of the external urinary sphincter, allowing for volitional continence. As seen in Figure 1, storage of urine (bladder relaxation and internal sphincter contraction) is under sympathetic control via impulses transmitted through the hypogastric nerve. The pelvic nerve is the principle conduit of the parasympathetic input for the LUT and allows for coordinated voiding by stimulating bladder contraction with sphincter relaxation. The somatic nervous system, through the pudendal nerve (and to a small degree the pelvic nerve), allows for the contraction or relaxation of the external urinary sphincter (striated pelvic diaphragm muscle under voluntary control). These nerves are lower motor neurons and are under the control of spinal reflexes and upper motor neuron input from the central nervous system (Ouslander, 2004).

Storage of urine is primarily a sympathetic and somatic function. Sympathetic input to the LUT is mediated through stimulation of adrenergic receptors. The stimulation of alpha-1 adrenergic receptors at the bladder neck by post-ganglionic norepinephrine results in bladder neck contraction. The sympathetic nervous system also inhibits parasympathetic input into the bladder, thus inhibiting stimulatory signals from reaching the detrusor. Further, stimulation of beta-3-adrenergic receptors with norepinephrine, as shown in animal models, allows for relaxation of the detrusor (Verhamme,

Figure 1.
Neurologic Pathways Involved in Lower Urinary Tract Function
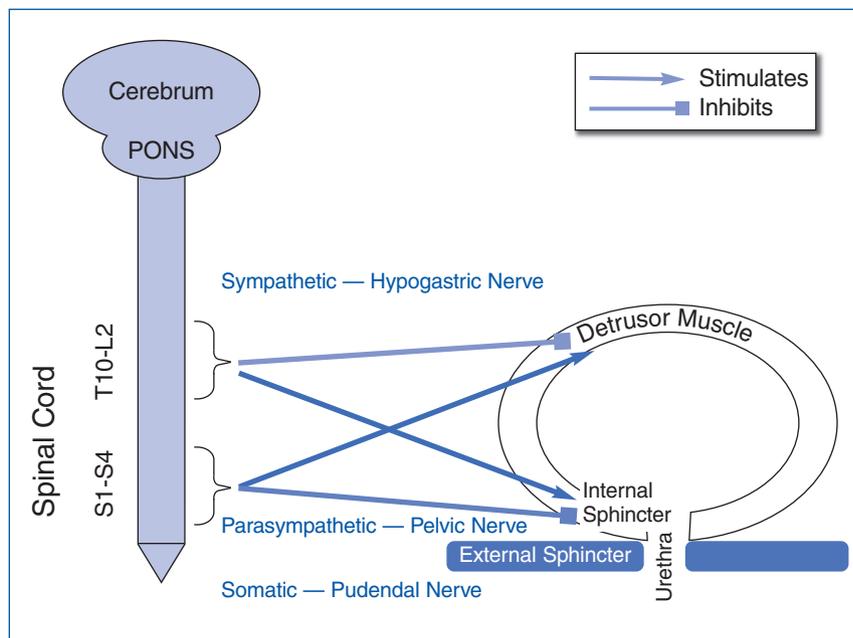
Description: The function of the lower urinary tract is under the control of several neurologic pathways. The sympathetic nervous system allows for bladder relaxation and internal sphincter contraction. This is mediated through the hypogastric nerve, and these signals originate from the spinal cord at levels T10-L2. The parasympathetic system allows for bladder contraction and internal sphincter relaxation. This is mediated through the pelvic nerve, and these signals originate from the spinal cord levels at S2-S4. The somatic (voluntary) system allows for the control of the external sphincter. All three of these systems are part of reflex pathways (not depicted in this illustration) and are under the influence of upper neurologic control (cerebrum and pons micturition center in the cerebellum).

Sturkenboom, Stricker, & Bosch, 2008).

External sphincter motor neurons originate from Onuf's nucleus, located on the anterior horns of the sacral spinal cord at levels S2-S4, and send their axons into the pudendal nerve (and to a lesser degree, the pelvic nerve) that stimulate the striated muscle to contract via the release of acetylcholine (Darrah, Griebling, & Silverstein, 2009; deGroat, 2006). This acetylcholine then binds to post-junctional nicotinic receptors, resulting in contraction of the external sphincter. Both alpha-receptors and serotonin 5-HT2 receptors are located in Onuf's nucleus and facilitate the storage reflex (Verhamme et al., 2008).

Bladder Filling/Storage

Bladder filling/storage is regulated by two separate storage reflexes – the sympathetic (autonomic) reflex and the somatic reflex (Thor & Donatucci, 2004). The sympathetic-mediated storage reflex is involved with bladder filling and is mediated by myelinated A-delta fibers. Afferent activity travels in the pelvic nerves to the spinal cord. At the L1-L3 level, sympathetic activity is initiated, which leads to a decrease in excitatory parasympathetic stimulation of the bladder. Postganglionic neurons release noradrenaline, which binds to beta-adrenoreceptors in the detrusor, leading to detrusor relaxation (Andersson, 2007).

The somatic storage reflex, often referred to as the "guarding reflex," occurs in response to sudden increases in intra-abdominal pressure. In this reflex, afferent activity travels along the myelinated A-delta fibers in the pelvic nerve to the sacral spinal cord, where efferent somatic urethral motor neurons in Onuf's nucleus are located. Afferent activity is also relayed to the periaqueductal gray (PAG) region and then on to the pontine micturition center (PMC). The PMC sends impulses to motor neurons in Onuf's nucleus, and axons from these neurons travel in the pudendal nerve and stimulate the rhabdosphincter to contract (Andersson, 2007).

Bladder Emptying

Studies in cats and rats indicate that the voiding reflex involves the PMC as well as other regions in the brain, including the hypothalamus and the cerebral cortex (Griffiths, 2004; Griffiths, Derbyshire, Stenger, & Resnick, 2005; Holstege, 2005). The PAG receives afferent activity from the bladder as well as from the cerebral cortex and hypothalamus. This activity is integrated in the PAG and PMC. The PMC controls the descending pathways involved in the micturition reflex, activating or inhibiting the parasympathetic pathways depending on the level of activity in the afferent fibers (Andersson, 2007).

Effects of Analgesics on the Lower Urinary Tract

LUT function is complex, and the addition of medications to this intricate physiologic balance may result in LUT dysfunction. Post-operative urinary retention (POUR) has been reported to occur in 6% to 50% of patients (Malinovsky et al., 1998). Many surgically related risk factors for POUR have been described (type of anesthesia used, duration and location of surgery,

post-operative use of opioid analgesia, and the administration of large volumes [greater than 500 ml] of perioperative intravenous fluids) (Koch, Grinberg, & Farley, 2006). Further, the use of orally ingested opioids in patients outside of the peri-operative setting has been shown to result in increased rates of urinary retention (Meyboom, Brodie-Meijer, Diemont, & van Puijenbroek, 1999). Other risk factors include underlying detrusor dysfunction or bladder outlet obstruction. The effect of analgesics, both narcotic and non-narcotic, and of anesthetics on the LUT will now be discussed.

Analgesics

Opioids

Opioids are products, both natural and synthetic, that bind to opioid receptors and result in analgesia. Morphine is commonly used in the post-operative period for analgesia and is a well-known risk factor for POUR. The treatment of pain with opiates or its analogues decreases the sensation of bladder fullness by partially inhibiting the parasympathetic nerves that innervate the bladder. In addition, opiates have been shown to increase the sphincter tone of the urinary bladder via sympathetic over-stimulation, resulting in increased bladder outlet resistance (Durant & Yaksh, 1988). The combination of decreased sensation of fullness and increased outlet resistance may increase the risk of urinary retention. Further, animal and human studies have shown that intravenous morphine directly binds to spinal opioid receptors and results in total bladder relaxation rather than having targeted effects on the detrusor alone (Chen, Shen, & Pan, 2005), and has been reported with epidural anesthesia (Malinovsky et al., 1998). Animal studies have demonstrated increased bladder

capacity and compliance following intravenous (IV) and intrathecal injections of tramadol. In humans, similar results on bladder capacity and compliance have been noted, with a reported increase in bladder capacity varying from 20% to 65% depending on the opioid, dose, patient group, and route of administration (Dray, 1988; Kuipers et al., 2004; Malinovsky et al., 1998).

Studies suggest that the half-life of the opioid used has an impact on urinary function and risk of retention. One study found that meperidine, an opioid with a relatively long half-life, use was an independent predictor of difficulty voiding after elective cholecystectomy (Kulacoglu, Dener, & Kama, 2001). In contrast, studies that evaluated orthopedic patients who received fentanyl (short half-life) for post-operative analgesia noted that these patients experienced significantly less risk for urinary retention than those who received morphine (intermediate half-life) (Gallo, Durand, & Pshon, 2008). Thus, the half-life of the narcotic may affect the risk for POUR; however, no prospective, comparative studies have been performed.

The mode of opioid delivery appears to also play a role in the risk of urinary retention (Chaney, 1995; Petros, Mallen, Howe, Rimm, & Robillard, 1993; Petros, Rimm, & Robillard, 1992). While, orally ingested opioids have been associated with an increased risk of urinary retention, the risk of POUR is higher with intravenous (IV) and epidural administration (Dolin & Cashman, 2005). A recent systematic review studied the occurrence of adverse effects (nausea, vomiting, sedation, pruritis, and urinary retention) related to post-operative pain management. Three analgesic techniques were compared: intramuscular (IM) analgesia, patient-controlled analgesia (PCA), and epidural analgesia. Overall, urinary retention occurred in 23%

of all patients, and the frequency was highest for the epidural group at 29% (Dolin & Cashman, 2005).

Several authors have demonstrated that the risk of retention is increased in patients using PCA compared to those receiving intermittent IV or IM opioids (Petros et al., 1992, 1993). The highest rates of opioid-mediated urinary retention have generally been associated with epidural administration (Darrah et al., 2009). A meta-analysis of 12,513 patients found that the use of epidural anesthesia for post-operative pain control was associated with urinary retention in nearly 25% of patients, a significant increase over the rate found in patients receiving IM or PCA (Darrah et al., 2009; Dolin & Cashman, 2005). A meta-analysis of patients undergoing colorectal surgery found that the incidence of urinary retention increased from 1% to 10% when patients received epidural anesthesia instead of parenteral opioids (Darrah et al., 2009; Marret, Remy, & Bonnet – Postoperative Pain Forum Group, 2007).

Animal studies have demonstrated that opioid mu-receptors are concentrated in the dorsal horn of the spinal cord, where the bladder afferents merge (Coggeshall & Carlton, 1997; Singh, Agarwal, Batra, Kishore, & Mandal, 2008). Delta and kappa receptors are also present, but in lower concentrations. Both mu and delta (but not kappa) receptors are involved in bladder realization and impaired sensations by inhibiting the sensory input at the level of the dorsal horn and PAG. This is supported by the absence of such action by non-mu-agonist opioids (such as nalbuphine [Nubain®] [kappa agonist and mu antagonist] or pentazocine [Talwin®] [kappa and delta agonist]) (Malinovsky et al., 1998; Singh et al., 2008). The inhibition of bladder afferents at the dorsal horn via mu-receptor activation diminishes bladder

sensations and may delay the micturition threshold, thus increasing compliance and bladder capacity. Furthermore, a direct effect of opioid receptor activation at the sacral parasympathetic innervations also improves compliance (Drenger, Magora, Evron, & Caine, 1986).

The role of opioid antidotes has been assessed in the management of opioid-related urinary retention. Opioid-mediated depression of bladder motility is largely secondary to action at the mu-opioid receptor, and can be reversed by intravenous naloxone (Narcan®), which results in the promotion of detrusor contraction and sphincter relaxation. Small doses of IV naloxone (0.1 mg) have been shown to decrease bladder distention without reversing analgesia (Gallo et al., 2008; Wren, 1996).

Naloxone, an antidote to morphine and its analogues, has been tested for the treatment of urinary retention after epidural and intrathecal anesthesia. Although naloxone was found to be very effective in reversing urinary retention, it also reversed the analgesic effect, and thus, was not recommended for the treatment of POUR (Rawal, Mollefors, Axelsson, Lingardh, & Widman, 1981; Verhamme et al., 2008). In fact, low dose naloxone in the treatment of urinary retention during extradural fentanyl (Actiq®, Fentora™, Duragesic®) use resulted in excessive reversal of analgesia (Wang, Pennefather, & Russel, 1993). However, nalbuphine, another opioid receptor inhibitor, appears to be effective in reversing urinary retention without compromising the analgesic effect (Verhamme et al., 2008), although further studies are warranted.

In an effort to decrease the effects of opioids on the LUT, studies have evaluated whether a decrease in the dose of opioid administered (by combining with NSAIDs) results in a decreased risk of POUR. In one meta-analy-

sis, Remy, Marret, and Bonnet (2005) showed that morphine use can be reduced significantly by the combination of acetaminophen and morphine; however, there was no effect in the incidence of morphine-related side effects, including urinary retention. Another recent meta-analysis demonstrated that while the addition of NSAIDs to PCA may decrease nausea and vomiting, the risk of urinary retention, pruritis, and respiratory depression was not significantly reduced (Marret, Kurdi, Zufferey, & Bonnett, 2005). Similarly, a third meta-analysis concluded that while the concurrent use of COX-2 inhibitors reduced opioid consumption by 35%, as well as decreased the risks of associated nausea, vomiting, pruritis, and constipation, there was no decrease in the risk of acute urinary retention (Romsing, Moiniche, Mathiesen, & Dahl, 2005).

NSAIDs

NSAIDs are commonly used in surgical and nonsurgical settings. Pharmacologically, NSAIDs inhibit the metabolism of arachidonic acid to prostaglandins and thromboxanes by cycloxegenase (COX)-1 and 2. Prostaglandins, especially prostaglandin E 2 (PGE2), play an important role in LUT function. PGE2 is up-regulated within the bladder as a result of bladder inflammation, trauma, or over distention. PGE2 stimulates the release of tachykinins, which stimulate neurokinin receptors on afferent nerves and the detrusor smooth muscle and as a result promote detrusor contraction (Andersson & Hedlund, 2002; Verhamme et al., 2008).

One recent study discovered that NSAID users have a two-fold increased risk of acute urinary retention (Verhamme et al., 2005). Similar outcomes were seen even with COX-2 specific inhibitors because there have been reports of acute urinary re-

tention that occurred within one week of starting such medications (Gruenenfelder, McGuire, & Faerber, 2002). By inhibiting the COX-2, PGE2, and tachykinin/neurokinin pathway, NSAIDs may decrease bladder contractility (Andersson & Hedlund, 2002; Darrah et al., 2009).

The effect of NSAIDs on urinary retention may be dose-specific. Verhamme et al. (2005) studied the association between NSAIDs and acute urinary retention and found the risk of acute urinary retention increased with higher doses of NSAIDs.

General Anesthetics

General anesthetics cause decreased bladder contractility by acting as smooth muscle relaxants. They also interfere with autonomic regulation of detrusor tone (Darrah et al., 2009). Some anesthetics substantially increase bladder capacity (Darrah et al., 2009; Doyle & Briscoe, 1976). In vitro work with isolated human bladder strips demonstrated that clinical doses of halothane (Fluothane®) and thiopentone (Trapanal®) decrease the response of the bladder to cholinergic stimulation (Doyle & Briscoe, 1976). Petros, Rimm, Robillard, and Argy (1991) noted that patients undergoing inguinal herniorrhaphy under general anesthesia with halothane, a potent smooth muscle relaxant, had a significantly higher rate of urinary retention compared with similar cases performed via a lidocaine (Lidoderm®) spinal anesthetic. Furthermore, sedative-hypnotics and volatile anesthetics inhibit the PMC and voluntary cortical control of the bladder, suppressing detrusor contraction and the micturition reflex (Combrisson, Robain, & Cotard, 1993; Darrah et al., 2009; Matsuura & Downie, 2000).

The urodynamic effect of volatile anesthetics and sedative-hypnotics, when combined with other agents commonly used for general anesthesia (pre-medication or reversal of neuromuscular blockade) on the LUT, has been evaluated. Glycopyrrolate (Robinul®) and atropine, two agents used for preventing bradycardia, do not appear to affect the incidence of urinary retention (Orko & Rosenberg, 1984). Sympathomimetic agents used to treat intraoperative hypotension can increase the risk of urinary retention as a result of their effects on beta-adrenergic receptors in the bladder and alpha-adrenergic receptors in the bladder neck and proximal urethra. In patients treated with ephedrine, a statistically significant increase in retention to 43.8% was noted (Darrah et al., 2009; Olsen & Nielsen, 2007).

Neuraxial Anesthesia

Intrathecal local anesthetics, spinal or epidural administered, are techniques in regional anesthesia that depend on the instillation of nerve-blocking agents with or without analgesics into the epidural space and interrupt afferent and efferent nerve impulses from and to that region's nerve supply. Two main bladder considerations are the inhibition of the afferent and efferent fibers as they enter and exit the spinal cord that are a part of the micturition reflex arc and the inhibition of the upward relaying of these signals to higher centers (PMC) within the spinal cord (Darrah et al., 2009; Kamphuis et al., 1998).

Blockade of afferent nerves results in bladder analgesia, while lack of transmission in efferent fibers causes a detrusor blockade that outlasts motor blockade by as much as several hours. Most patients will be incapable of spontaneous voiding until the sensory level has regressed to the S3 level (Darrah et al., 2009; Kamphuis et al., 1998). The use of longer-acting local anesthetics for spinal injection results in a duration of detrusor blockade sufficient for the bladder volume to significantly exceed preoperative bladder capacity. This over-distention can impair voiding function (Darrah et al., 2009; Kamphuis et al., 1998).

The effect of neuraxial opioids on voiding function may reflect peripheral, spinal, or supraspinal activity. Healthy volunteers given intrathecal morphine or sufentanil (Transdur®) demonstrate impaired bladder contraction within 15 to 60 minutes (Kuipers et al., 2004). The rapid onset suggests that intrathecal opioids affect micturition primarily by inhibiting the spinal reflex responsible for detrusor contraction. A primary lumbar-spinal site of action is also supported by the increased incidence of urinary retention associated with lumbar compared with thoracic epidurals (Basse, Werner, & Kehlet, 2000). Intrathecal opioids depress preganglionic neurons in the sacral parasympathetic nucleus, decreasing pelvic nerve activity. They also activate gamma, mu, and delta receptors in the dorsal horn of the spinal cord, inhibiting bladder afferents and decreasing bladder sensation. As a result, bladder capacity and compliance are increased, and the initiation of the micturition reflex is delayed (Dray, 1988).

The liphophilicity of intrathecal opioids affects POUR. Urodynamic studies have demonstrated that hydrophilic opioids, such as morphine, adversely affect bladder function to a greater degree than more lipophilic opioids (such as sufentanil). Enhanced systemic uptake of lipophilic agents limits local activity at the sacral level, which accounts for the difference (Baldini, Bagry, Aprikian, & Carli, 2009; Kuipers et al., 2004). In a prospective double-blinded, randomized, placebo-controlled trial, sufentanil was associated with a lower risk of POUR compared to morphine (Kim et al., 2006).

Many authors have identi-

Table 1.
Summary of Medications and the Effect on the Lower Urinary Ttract

Class of Medication	Risk of Urinary Retention	Mechanism of Effect on Lower Urinary Tract
Opiods	Increases	1. Decreases the sensation of bladder fullness by partially inhibiting the parasympathetic nerves that innervate the bladder. 2. Increase the tonus of the sphincter of the urinary bladder via sympathetic over-stimulation, resulting in increased resistance in the outflow tract from the bladder. 3. Intravenous morphine directly binds to spinal opioid receptors and causes total bladder relaxation rather than having targeted effects on the detrusor alone.
NSAIDs	Increases	Inhibit the production of PGE2. (PGE2 stimulates the release of tachykinins, which stimulate neurokinin receptors on afferent nerves and detrusor smooth muscle, and as a result, promote detrusor contraction.)
General Anesthetics	Increases	1. Smooth muscle relaxant. 2. Interfere with autonomic regulation of detrusor tone.
Neuraxial Anesthetics	Increases	1. Inhibition of the afferent and efferent fibers as they enter and exit the spinal cord (part of the micturition reflex arc). 2. Inhibition of the up-ward relaying of these signals to higher centers (PMC) within the spinal cord.
Ketamine	Decreases	Unclear mechanism; 80% with overactive bladder, causes irreversible irritative eosinophilic ulcerative cystitis.

fied an association between spinal anesthesia with long-acting local anesthetics and POUR. Ryan, Adye, Jolly, and Mulroy (1984) demonstrated a decrease in the need for catheterization among patients undergoing herniorrhaphy with lidocaine spinal anesthesia (6%) compared to bupivacaine (Marcaine®, Sensorcaine®) or tetracaine (Pontocaine®, Dicaine®) (30%). In another study, two of 201 ambulatory patients receiving short-acting epidural or spinal anesthesia developed urinary retention (Mulroy, Salinas, Larkin, & Polissar, 2002).

In male patients undergoing inguinal herniorrhaphy, the risk of POUR was greater after spinal anesthesia than epidural anesthesia (Faas et al., 2002). Other factors in addition to local anesthetic dose and duration of action may affect the likelihood of neuraxial anesthesia-related POUR (Darrah et al., 2009). A prospective, randomized trial demonstrated that the use of epidural anesthesia did not increase the incidence of retention after hemorrhoidectomy when intra-operative IV fluids

were limited to 200 ml +/- 2 ml/kg/hour of Lactated Ringers (Kau et al., 2003).

Patients undergoing lumbar spinal surgery experience increased rates of POUR when intrathecal local anesthetics are administered with opioids. The addition of fentanyl to spinal anesthesia and the choice of spinal over epidural anesthesia were found to significantly increase time to discharge of ambulatory surgical patents (Mulroy et al., 2002). Local anesthesia does not affect bladder function and is associated with a lower incidence of POUR than neuraxial or general anesthesia. A review of 72 studies found that urinary retention occurred in only 0.37% of patients undergoing hernia repair when local anesthesia was used, as opposed to an incidence of 2.42% with regional anesthesia and 3.0% with general anesthesia (Darrah et al., 2009; Jensen, Mikkelsen, & Kehlet, 2002).

The incidence of POUR after anorectal surgery ranges between 1% and 52% (Lau & Lam, 2004; Zaheer, Reilly, Pemberton, &

Ilstrup, 1998). Injury to the pelvic nerves and pain evoked reflex increase in the tone of the internal sphincter and are thought to account for the high incidence of POUR in patients undergoing anorectal surgery (Benoist et al., 1999; Cataldo & Senagore, 1991; Hojo, Vernava, Sugihara, & Katumata, 1991). The duration of spinal and epidural anesthesia can affect how long it takes to void postoperatively. Longer operations may increase the risk of urinary retention because more IV fluids may be administered or higher total doses of opioids and anesthetic agents may be used (Darrah et al., 2009; Wynd, Wallace, & Smith, 1996).

Ketamine

Ketamine is an anesthetic commonly used in pediatric and veterinary procedures, and has recently gained some attention within the urologic community. It is a non-competitive *N*-methyl-D-aspartic acid receptor antagonist that achieves short-lived general anesthesia and has become a drug of abuse. It is

metabolized by the liver to norketamine and ultimately excreted in the urine as hydroxynorketamine conjugated with gluconate. Several recent case series have demonstrated severe irritative LUT symptoms associated with eosinophilic ulcerative cystitis after ketamine use (Chu et al., 2008; Tsai et al., 2009). One review of 59 patients who abused ketamine revealed 71% had cystoscopic findings that were consistent with chronic interstitial cystitis, and 80% had detrusor overactivity or decreased bladder compliance on urodynamics. On radiologic imaging, 51% had either unilateral or bilateral hydronephrosis, and 7% had features suggestive of papillary necrosis. Renal insufficiency was identified in 14%. These changes may be irreversible (Chu et al., 2008).

Conclusion

Commonly used anesthetic and analgesic agents can have predictable effects on the LUT system. A condensed summary of the effect of anesthetics and analgesics on the LUT has been provided in Table 1. Opioids, NSAIDS, and anesthetics all tend to result in increased risk of urinary retention, with intrathecal delivery resulting in the highest rates of POUR. Ketamine, an anesthetic of abuse, is associated with severe and irreversible LUT damage. ◉

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