



Strategies for optimizing pain management after ureteroscopy

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The prevalence of kidney stones in the United States has nearly doubled since the 1990s, affecting roughly one in 11 individuals (1). This surge in stone disease may be compounded by the effects of climate change, as elevated temperatures increase risk for kidney stones (2). Ureteroscopy (URS) is a common and effective procedure for stone removal; however postoperative pain, stent-related symptoms, and unplanned healthcare encounters can significantly affect patients' quality of life (3). Thus, considerable research has been dedicated to identifying optimal medications or regimens to mitigate patient pain and discomfort through peri-, intra-, and post-operative approaches. Several new, high-quality studies have expanded the knowledge base on this topic, looking at nonsteroidal anti-inflammatory drugs (NSAIDs), pregabalin, local anesthetics, drug combinations and alternative remedies.

NSAIDs have been shown to be highly effective for reducing pain after URS. The 2021 SKOPE trial, a randomized, double-blinded, placebo-controlled study, investigated the effectiveness of NSAIDs compared to opioids for post-URS pain control (4). This study compared ketorolac to oxycodone and showed that NSAIDs provided pain control that was non-inferior to opioids and, notably, led to a shorter recovery period. The outcomes of the SKOPE trial were corroborated by Demasi *et al.* in 2022, who conducted a randomized controlled trial comparing ketorolac to oxycodone-acetaminophen for pain control post-URS (5). Similarly, ketorolac was found to be non-inferior to opioids, furthering support for opioid-sparing medication protocols. In 2022, Beville *et al.* also studied

NSAIDs in a broader cohort including older patients, those on anticoagulation, and those experiencing chronic pain (3). In these patients, selective cyclooxygenase-2 (COX-2) inhibitor yielded comparable pain control without the potential risks associated with non-specific COX inhibitors which carry a risk of gastric and renal toxicity in longer courses.

Combinations of drugs have also been utilized to reduce symptoms after URS. In a 2023 meta-analysis assessing optimal post-URS pain control regimens, Hinojosa-Gonzalez *et al.* determined that the combination of an alpha-1 blocker, silodosin, and an anticholinergic, solifenacin, to be the most effective at for pain control post-URS. This was followed by silodosin alone, solifenacin alone, and the combination of solifenacin and pregabalin. This study included assessment of urinary symptoms, pain and sexual performance (6).

In a contrasting study published in 2023, Rosen *et al.* conducted a prospective, single-center, double-blinded, randomized controlled trial of the effect of a single, preoperative dose of pregabalin versus placebo on pain after URS (7). The primary outcome was patient-reported pain levels one hour after URS. Secondary outcomes included additional pain scores at various intervals, medication prescriptions in the month after surgery, post-operative communications with the urology team, emergency department visits, and re-admissions. Patients who received pregabalin actually showed increased pain scores compared to the placebo group. There were no measurable differences in recovery room time, patients receiving discharge opioids, or quantity discharge opioids between groups. Collectively,

these findings demonstrated that pregabalin did not offer a clinically significant benefit pain reduction. Even after controlling for age and preoperative pain scores through multivariable analysis, the results consistently indicated increased pain scores in patients who received pregabalin. This study stands out as a novel addition to the research on medication regimens for discharge planning, offering a distinctive perspective and contributing to the expansion of the limited literature on this subject.

Some alternative remedies have also been examined. A 2023 study showed that cannabinoid (CBD) oil lacked a significant impact on pain scores when compared to placebo (8). This finding was possibly limited by the utilization of the lowest dose of CBD in the study.

In contrast to the considerable research evaluating regimens for post-operative pain control, studies evaluating intra- and pre-operative medications remain relatively unexplored. In a randomized, single-blinded, placebo-controlled trial in 2022, Syed *et al.* investigated the impact of administering ketorolac during anesthesia induction on peri-operative pain and opioid requirements (9). Administration of ketorolac during URS was associated with a notable reduction in narcotic requirements. In 2020, Tawfeek *et al.* studied the administration of alpha blockers one week pre-operatively and two weeks post-operatively (10). Alpha blockers were associated with a decrease in post-operative pain, need for analgesia, and hospital stay in hours.

Topical anesthetics have also been shown to potentially reduce pain. In a 2017 randomized study of intra-ureteral lidocaine, Roberts *et al.* found that the direct instillation of lidocaine into the ureter did not significantly improve pain symptoms after URS (11). Overall, studies evaluating interventions to impact intra-operative analgesic requirements are limited and the impact on post-operative pain remains unclear. Studies of belladonna and opium (B&O) suppositories have yielded diverse results. Lee *et al.* showed that preoperative administration of B&O suppositories improved quality of life measures and reduced urinary-related pain, while Fetzer *et al.* observed a decrease in urinary urgency but no discernible impact on mean pain scores between cohort groups (12,13). The scarcity of studies investigating pre-operative medications to mitigate pain highlights a significant gap in research and stresses the need for additional research to enhance our understanding and improve these pain management strategies.

The rising prevalence of kidney stones and subsequent increase in endoscopic stone surgery has prompted intensified research into optimizing pain management

strategies during and after this procedure. The efficacy of NSAIDs in post-URS pain control regimens has been well-established through rigorous studies, offering an effective alternative to opioids. However, the nuanced outcomes of recent investigations, such as the contradictory findings regarding pregabalin's effects, highlight the complexity of improving pain management. The scarcity of research on intra- and pre-operative medications, as well as alternative remedies, underscores the need for further exploration to enhance patient outcomes and refine clinical protocols.

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