Evaluation of the Efficacy of Solifenacin for Preventing Catheter-Related Bladder Discomfort After Transurethral Resection of Bladder Tumors in Patients With Non-Muscle Invasive Bladder Cancer: A Prospective, Randomized, Multicenter Study

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Abstract

We evaluated the incidence of catheter-related bladder discomfort (CRBD) and the efficacy of solifenacin in preventing CRBD after transurethral resection of a bladder tumor (TUR-BT) in 134 patients with non-muscle invasive bladder cancer. The incidence rate of CRBD at 1 and 2 hours after TUR-BT was 72.2% and 68.1%, respectively. Solifenacin failed to decrease the incidence and severity of CRBD. Background: Catheter-related bladder discomfort (CRBD) secondary to an indwelling urinary catheter is worse after transurethral resection of a bladder tumor (TUR-BT). We evaluated the incidence of CRBD and the efficacy of solifenacin for preventing CRBD after TUR-BT in patients with non-muscle invasive bladder cancer. Patients and Methods: In the present prospective, randomized, multicenter trial, we enrolled 148 patients with non-muscle invasive bladder cancer who underwent elective TUR-BT under general anesthesia. The patients were randomized to group S (n = 72) or group C (n = 76). The primary outcome was evaluable for 134 patients, who were included in the final analysis. Group S received solifenacin (5 mg orally) on the day before, the day, and the day after TUR-BT. The control group (group C) received standard care. CRBD was assessed at 1 and 2 hours postoperatively. Pain was assessed for 3 days starting 6 hours after TUR-BT using the visual analog scale. Results: The incidence rates of CRBD in groups C and S were 72.2% and 64.5% at 1 hour and 68.1% and 53.2% at 2 hours, respectively. The incidence rates and severity of CRBD at 1 and 2 hours were not different between the 2 groups (P > .05 for both). The visual analog scale scores and the postoperative consumption of analgesics were not different between the 2 groups (P > .05 for both). None of the patients who received solifenacin experienced an adverse event. Conclusion: Pretreatment with solifenacin (5 mg) failed to decrease the incidence and severity of CRBD after TUR-BT.

Introduction

Approximately 429,800 new cases and 165,100 deaths from bladder cancer were reported worldwide in 2012.1 At the time that bladder cancer is diagnosed, approximately 70% of urothelial carcinoma cases will be classified as non-muscle invasive bladder cancer (NMIBC),2 for which the standard primary treatment is transurethral resection of a bladder tumor (TUR-BT). After TUR-BT, a urethral catheter is inserted temporarily to monitor...
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postoperative bleeding, prevent blood clots, and, potentially, remove floating cancer cells. However, irritative bladder symptoms are common and are burdensome to patients after transurethral resection (TUR). Moreover, the symptoms are often resistant to conventional opioid therapy.

An urge to void despite the good passage of urine and discomfort or pain in the suprapubic region are indications of catheter-related bladder discomfort (CRBD) secondary to an indwelling urinary catheter.\(^3\) This discomfort can reduce the quality of life postoperatively and increase the incidence of postoperative pain and agitation.\(^4,5\) Therefore, preventing or decreasing the severity of CRBD could be helpful for improving patients’ quality of life and reducing the occurrence of postoperative agitation.

The mechanism of CRBD is not well-defined; however, it is similar to that of the symptoms of overactive bladder caused by involuntary bladder contractions, which are mediated by muscarinic receptors located in the urothelium and efferent nerves.\(^6\) Antimuscarinic drugs such as tolterodine or oxybutynin have been reported to be effective treatment of CRBD. However, many studies have reported the results with only short-term indwelling urinary catheters.\(^3,4,7\)

Solifenacin, a selective muscarinic 3 receptor, was reported to have greater selectivity for the bladder over the salivary glands and less potent antimuscarinic action than tolterodine.\(^8-10\) Previous studies have confirmed the safety and efficacy of solifenacin compared with a placebo for overactive bladder.\(^11,12\)

The primary objectives of the present study were to evaluate the incidence of CRBD after TUR-BT and determine whether solifenacin can decrease the incidence of postoperative CRBD. The secondary objectives were to assess the efficacy of solifenacin for managing postoperative pain after TUR-BT using the visual analog scale (VAS) and to evaluate the side effects that can occur with the use of these drugs.

Materials and Methods

Study Setting

The present study was a prospective, randomized, single-blind, placebo-controlled, multicenter study (Clinical Research Information Service identifier, KCT0000498) conducted in Korea. The study was performed from April 2012 through May 2015 at 4 training hospitals in accordance with the ethical principles of the Declaration of Helsinki. The ethics committee at each study site (institutional review board approval no. NCCCTS-44-560) approved the protocol. All the patients provided written informed consent.

Eligible patients aged 19 to 84 years who presented with a bladder mass were screened. The exclusion criteria were any recent or current long-term use (> 3 months in < 1 year) of analgesic or antimuscarinic drugs; any history of cerebral or spinal disease, chronic kidney disease with a creatinine clearance < 30 mL/min, or hepatic failure with a Child-Pugh score of class B or more; any history of voiding problems either with residual urine > 200 mL or maximal flow rate ≤ 5 mL/sec; incomplete resection of the tumor after TUR; and any pathologic confirmation of muscle invasive bladder cancer.

Randomization

A previous study reported that approximately 55% of patients complained of CRBD after insertion of an indwelling urethral catheter.\(^3\) Assuming that this incidence would decrease to 30% after treatment, we calculated that a sample size of 60 patients would be needed in each group to achieve 80% power with a 2-sided type 1 error rate of 5%. Considering a 10% withdrawal rate, 74 patients were included in each group. We enrolled 148 patients with NMIBC who underwent elective TUR-BT under general anesthesia. Eligible patients were randomly assigned to either the solifenacin (group S; n = 72) or control (group C; n = 76) group, at a 1:1 ratio. Mixed, permuted, block randomization within the strata (sex and institution) was used. After confirming the eligibility criteria, randomization was performed using the sealed envelope method. Among the randomized patients, the primary endpoint was evaluable for 134 patients, and these patients were included in the final analysis (group S, n = 62; and group C, n = 72).

Treatment and Assessment

All operations were performed with the patient under general anesthesia. In group S, patients received solifenacin (5 mg orally) the day before, the day of, and the day after surgery. In group C, patients received standard care. All the patients were catheterized with a Foley catheter (usually 18Fr), and the balloon was inflated with 10 mL of distilled water after TUR-BT. CRBD was assessed at 1 and 2 hours postoperatively in the recovery room and general ward, respectively. Postoperative immediate mitomycin C instillation was not performed in the present study. Induction was performed with or without maintenance intravesical bacillus Calmette-Guérin or chemotherapy after pathologic confirmation instead of immediate intravesical chemotherapy. The severity of CRBD was graded using a simple 4-step severity scale: no pain, mild pain (determined only by interviewing the patient), moderate pain (a spontaneous complaint by the patient), and severe discomfort (determined by the patient’s agitation, loud complaints, and attempts to remove the Foley catheter). Pain was assessed for 3 days, starting 6 hours after TUR-BT using the VAS. Standardized postoperative analgesia was administered according to the policy of each institution. The dose of analgesics used at each institution was converted to the dose of tramadol/acetaminophen combination tablets (Ultracet; Ortho-McNeil Pharmaceutical, Inc) using the table for the drug dosage calculation of opioids.\(^13\) The Foley catheter was removed on the third postoperative day after confirming that no further active bleeding or risk of clot retention was present, and the uroflowmetry and postvoid residual volumes were assessed.

Statistical Analysis

The incidence of CRBD at 1 and 2 hours after TUR-BT was analyzed between the 2 groups using the \(\chi^2\) test, and the severity of discomfort (mild, moderate, and severe) was analyzed using Fisher’s exact test. An efficacy analysis was performed on the full analysis set, which included all randomized patients, except for those who had not met the study inclusion or exclusion criteria and were not evaluated for the primary outcome. The pain grade was evaluated using the VAS, and the VAS scores were compared between the 2 groups using the Mann-Whitney \(U\) test. The incidence of side effects was analyzed using Fisher’s exact test. Differences in the baseline characteristics between the 2 groups were analyzed using the \(\chi^2\) test, Fisher’s exact test, and the Mann-Whitney \(U\) test, as appropriate. Logistic regression analysis was performed to estimate the odds ratio and corresponding 95% confidence interval.
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