Intravesical Antineoplastic Therapy Following Transurethral Resection of Bladder Tumors: Nursing Implications From the Operating Room to Discharge

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An aging population and latent effects from exposure to carcinogens will likely augment the current trend of increased incidence of urinary bladder cancer. Intravesical antineoplastic therapy is a common treatment for urinary bladder cancer. Transurethral resection of bladder tumors often is followed immediately by the instillation of an antineoplastic agent in the operating room or postanesthesia care unit. Oncology nurses, who have a unique knowledge of safe handling and patient care, can improve staff safety and patient outcomes in several areas of healthcare organizations, as well as reduce the mortality and morbidity of urinary bladder cancer by learning more about the disease and intravesical antineoplastic therapy.
Presenting symptoms of urinary bladder cancer primarily result from the effects of destructive tumors on the bladder wall. About 85% of patients diagnosed with urinary bladder cancer present with painless hematuria; other common symptoms resemble those of a urinary tract infection (Montie, Smith, & Sandler, 2004; Tanagho & McArinch, 2004). Unfortunately, hematuria is not always noticeable and no recommended screening for urinary bladder cancer currently exists (Agency for Healthcare Research and Quality, 2005); however, new screening recommendations may be offered soon. In May 2006, the National Library of Medicine posted a report of a study comparing several men who discovered bladder cancer while performing urine dipstick tests for hematuria in their homes to men who were diagnosed traditionally, without urine dipstick. The men who found the cancer with the urine dipstick test had lower stages and grades of cancer when diagnosed and, as a result, had a lower rate of recurrence after treatment and no deaths from bladder cancer after 14 years; the unscreened group had a 20% mortality rate after only 1.8 years.

Urinary bladder cancer usually is diagnosed and treated by urologists because of the presenting symptoms and specific body system involved. Treatment by urologists often includes instilling antineoplastic agents directly into the bladder through a catheter and may be the primary treatment or an adjuvant to transurethral resection of a bladder tumor (TURBT). Patients receiving intravesical antineoplastic treatments are cared for in a variety of settings, such as urology practice offices, outpatient surgery suites, and inpatient general medical and surgical units in a hospital. The variety of treatment locations creates unique challenges. Patients with urinary bladder cancer and nononcology medical professionals caring for them may not be able to benefit from the experience and expertise provided by oncology professionals. In addition, the diversity of patient care areas results in an increased need for oncology nurses who are knowledgeable about urinary bladder cancer and the nursing implications of intravesical antineoplastic therapy. Oncology nurses can offer consultation and teaching for safe handling and patient care.

More than 90% of cases of urinary bladder cancer originate in the urothelium, which forms the inner lining of the bladder and is most vulnerable to carcinogen exposure (Johns Hopkins University, 2006). Urinary bladder cancer can be a high-grade invasive cancer that penetrates the muscle lining of the bladder and quickly metastasizes to other sites. More often, urinary bladder cancer is low grade and noninvasive, with a higher rate of recurrence (Montie et al., 2004). Noninvasive, stage Ta (i.e., noninvasive papillary carcinoma), Tis (i.e., carcinoma in situ), and T1 tumors have not invaded the muscle wall (AUA, 1999; Campbell, 2006). Noninvasive tumors also are known as superficial bladder tumors.

Viewed through a cystoscope, some bladder tumors appear as velvety, red, slightly raised patches on the bladder wall and others appear as warty growths resembling cauliflower, which bend and move with the flow of fluid in the bladder. The tumors may be localized in one small area or scattered extensively on the bladder wall. Fulguration of a tumor during TURBT may not always eliminate all of the diseased tissue. For example, the flattened red patches of carcinoma in situ may blend into the bladder wall and be in an area that is difficult or impossible for the cystoscope to reach. Intravesical antineoplastic therapy helps eliminate remaining cancerous tissue and reduce recurrence (AUA, 1999). Invasive bladder cancer may require partial or total removal of the bladder, as well as radiation and chemotherapy; however, intravesical instillation of antineoplastic drugs immediately after removal (fulguration) of visible tumors during TURBT is a preferred treatment for noninvasive urinary bladder cancer (AUA, 2003). After TURBT and initial instillation, intravesical antineoplastic therapy may continue on a regularly scheduled basis in an outpatient setting for at least a cycle or used alone without surgical intervention (AUA, 1999).

Agents for Intravesical Treatment of Bladder Tumors

The advantage of intravesical treatment rather than IV administration is twofold. Intravesical instillation places the tumor(s) in direct contact with an antineoplastic agent as the bladder wall reduces the systemic absorption of the drug, lowering the incidence of systemic effects (O’Rourke, 2001; Polovich, White, & Kelleher, 2005). In addition, intravesical treatment shortens antineoplastic exposure for patients and caregivers. Excretion of the drug is much faster when administered into the bladder and released compared to systemic treatment and requires special handling precautions for urine when emptying the bladder for approximately eight hours (Polovich, Blecher, Glynn-Tucker, McDiamid, & Newton, 2003; Sanofi Pasteur Limited, 2006; U.S. Food and Drug Administration & Center for Drug Evaluation and Research, 2001). Patients also benefit from the effectiveness of the treatment. Instillation of antineoplastic chemotherapy agents into the bladder immediately following fulguration of the tumors reduces recurrence (AUA, 1999, 2003). Antineoplastic agents used most commonly for intravesical treatment include bacillus calmette-guerin (BCG), mitomycin, and thiotepa (see Table 1) (AUA, 1999; Switters, Soares, & White, 1992). The National Comprehensive Cancer Network (2007) recommended mitomycin and BCG for intravesical treatment because of their proven effectiveness.

BCG, primarily administered in an outpatient setting, such as a physician’s office, is a live, attenuated strain of bovine tuberculosis that causes an acute inflammatory reaction inside the bladder (AUA, 1999, 2003). The reaction encourages the body’s immune system to attack and destroy cancer cells. Immediately after treatment, many patients experience flu-like symptoms, as well as painful and frequent urination. Those side effects occur more often with BCG than with other agents, but BCG also has the lowest incidence of bone marrow suppression (AUA, 2003). AUA (1999) warned that sepsis is a possibility if the drug is given too soon after TURBT or a traumatic catheterization. BCG should not be used in patients who are immunocompromised, have liver disease, or have a history of tuberculosis (Boyd, 2003; Sanofi Pasteur Limited, 2006). Some intravesical agents administered immediately after TURBT result in decreased tumor recurrence; however, delayed BCG treatments given up to two weeks after TURBT are not associated with increased tumor recurrence (Lamm, McGee, & Hale, 2005). ACS (2006) called BCG one of the most effective drugs at treating noninvasive urinary bladder
Table 1. Comparison of Frequently Used Drugs in Intravesical Treatment

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DESCRIPTION</th>
<th>INTRAVESICAL DOSAGE AND ADMINISTRATION</th>
<th>SPECIAL CONCERNS AND SIDE EFFECTS</th>
<th>NURSING MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus calmette-guerin</td>
<td>Live, attenuated bovine tuberculous</td>
<td>Dosage varies and is administered two weeks after TURBT or at least seven days after a traumatic catheterization to minimize the risk of sepsis.</td>
<td>Incidence of painful, frequent urination and flu-like symptoms, including fever, is increased. Bone marrow suppression is extremely rare.</td>
<td>Report signs and symptoms to a doctor. Report cough immediately, as it may be a sign of systemic infection. Use biohazard precautions. Immunosuppressed patients must not be treated or come into contact with the drug. Do not reconstitute more than two hours before use. Use bleach in toilets equal to the amount voided and let stand for 15 minutes before flushing. Disinfect any contaminated nondisposable items with bleach.</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>Antineoplastic, antitumor, antibiotic vesicant</td>
<td>20–40 mg in 1 ml of sterile water per mg immediately after TURBT, then once a week for six weeks</td>
<td>Extravasation into or through the bladder wall can result in serious tissue injury. It may cause a burning sensation and frequent urination.</td>
<td>Monitor patients for signs and symptoms of extravasation after instillation and during the treatment period. Release bladder contents immediately if extravasation is suspected. Wash any exposed skin with soap and warm water.</td>
</tr>
<tr>
<td>Thiotepa</td>
<td>Antineoplastic, alkylating agent; not a vesicant</td>
<td>60 mg in 30–60 ml of sterile water immediately after TURBT, then once a week for four weeks</td>
<td>Absorption through the bladder mucosa is more common than with other agents because of a lower than average molecular weight. Risk of neutropenia and thrombocytopenia is increased.</td>
<td>Monitor complete blood count, especially platelet and white blood cell counts. Teach patients to report signs and symptoms of infection, bruising, or bleeding. Be aware that repeated regimens increase the risk of bone marrow suppression.</td>
</tr>
</tbody>
</table>

TURBT—transurethral resection of a bladder tumor

Note. Eliminating fluid intake for six hours before outpatient follow-up therapy will minimize urine production during treatment and help ensure therapeutic retention of the agent. Patients should retain treatment in the bladder for two hours while lying down and turning approximately every 15 minutes if possible. Safe handling must be used for all antineoplastic drugs. Encourage patients to consume fluids for six to eight hours after treatment to help flush the bladder. Tell patients to void while sitting and avoid splashing when emptying Foley drainage bags.

Note. Based on information from Spratto & Woods, 2005.

cancer. In addition to safe handling techniques recommended by Polovich et al. (2003) for antineoplastic agents, precautions for handling BCG include wearing a mask and using bleach to clean exposed objects, such as toilets and examination tables. Organizational policies should include procedures for safe handling of biologic agents. Healthcare professionals with weakened immune systems are especially vulnerable to BCG and should avoid working with or near the drug.

Mitomycin is an antineoplastic antibiotic and a very potent vesicant. Mitomycin is given immediately after TURBT and may be one treatment or part of a regimen with repeated instillations administered in a physician’s office on an outpatient basis. Despite mitomycin's vesicant property and administration into a fresh surgical bladder, extravasation rarely occurs. In a study of intravesical mitomycin after TURBT, 177 treatments resulted in “only two minor patient-related complications and no staff-related adverse events” (Mostafid, Rajkumar, Stewart, & Singh, 2006, p. 509). Nieuwenhuijzen, Bex, & Horenblas (2003) described extravasation as an unusual postoperative complication, with a main symptom of “severe, continuous pain in the pelvic region” (p. 711). Nursing assessment of pain after the procedure for possible extravasation is imperative. Careful hand washing and cleansing of the perineal area on the day of treatment, recommended in 1981 by Nissenkorn, Herrod, and Soloway still apply today.

Thiotepa is an alkylating agent chemically related to nitrogen mustard and is one of the oldest drugs used. Thiotepa rarely is given in IV form and is not a vesicant; however, it carries the highest risk of absorption because of a low molecular weight (AUA, 1999). Molecular weight of a drug has an effect on how easily the drug permeates cell membranes. The average molecular weight of a drug is 300–500 daltons (Lehne, 2004). Thiotepa has a molecular weight of 189 daltons and absorbs easily into the bloodstream. Bone marrow suppression, specifically neutropenia and thrombocytopenia, has resulted in death (U.S. Food and Drug Administration & Center for Drug Evaluation and Research, 2001). Monitoring blood work for thrombocytopenia and neutropenia before subsequent thiotepa treatments is an important nursing intervention. Patients also must learn how to avoid infection, prevent bleeding, and report symptoms of thrombocytopenia or neutropenia to a doctor immediately. New drugs and treatments are being evaluated continuously for the treatment of urinary bladder cancer. The National Institutes of Health (2007) listed 70 clinical trials for urinary bladder cancer, with 65 still open and 9 specifically for intravesical administration of antineoplastic agents.

Safety Precautions

Healthcare professionals can suffer several ill effects from the unsafe handling of antineoplastic agents, including a higher incidence of leukemia and lymphomas, DNA damage, menstrual dysfunction, and a higher rate of miscarriage (Polovich et al., 2003). However, pharmacists, who are more likely to use appropriate personal protective equipment (PPE), are less likely to suffer the same ill effects. Oncology nurses are becoming more aware of the need for and importance of proper safety precautions when handling antineoplastic agents. However, other
nursing departments may not be aware of required precautions and need assistance from oncology nursing professionals in the form of in-services and consultations. Nurses working in nononcology settings need information about safe handling, storage, disposal, and special patient care needs before, during, and after treatment with antineoplastic agents. Common questions include the following.

- How should antineoplastic agents be handled?
- Are special gloves or other PPE required?
- Should antineoplastic agents be secured or locked up like narcotics?
- How are antineoplastic agents handled during and after procedures?
- What are the precautions for patients, urine, and the Foley bag?
- What is the proper way to discard waste?
- What are the restrictions for pregnant staff?
- What information is available for patient teaching?
- Who is available to educate healthcare professionals about antineoplastic agents?

Pharmaceutical references used by nurses typically do not answer all of those questions, only providing general warnings about the need to use safe handling and appropriate discard techniques. Available material safety data sheets also can be very confusing. If antineoplastic policy references are in an area specific to oncology or do not address nursing organization-wide, nurses in nononcology settings may not have easy access to them or may be confused about which policies apply.

Administration

In a typical inpatient or same-day-surgery facility, administration of intravesical antineoplastic therapy occurs in the operating room suite or postanesthesia care unit. Before the procedure, a nurse must obtain the agent ordered. A few days of notice for the pharmacy helps ensure the availability of the agent on the day of the procedure. Agents used for intravesical treatment may not be in stock at the pharmacy if they are used infrequently. After receiving the agent, keep it in a sealed bag with an attached chemotherapy drug-warning label until ready for use. A urologist or chemotherapy nurse trained in intravesical administration should wear PPE, including chemotherapy gloves, a face shield, a gauze, and a disposable gown, when instilling the agent. The bladder is allowed to drain all urine and fluids used for irrigation during TURBT to minimize dilution of the drug. Eliminating fluid intake for six hours before outpatient follow-up therapy will minimize urine production during treatment and help ensure therapeutic retention of the agent. Absorbent, plastic-backed disposable pads protect the area under and around the perineum. An assistant facilitates the administration and disposal of the drug without touching the syringe or the inside of the bag. The bag is held open by the assistant until the procedure is complete and the empty syringe is returned to the bag for disposal. See Figure 1 for illustrated safety precautions when instilling intravesical antineoplastic therapy.

After the procedure and a short recovery period, most patients leave the facility on the same day, with a small percentage requiring overnight evaluation on a medical and surgical nursing unit. Urologists often have patients keep the Foley catheter in place until the follow-up visit in the office one or two days after the procedure. Regardless of nurses’ experiences with antineoplastic agents, they must be aware of the special nursing care required during the recovery of patients who have received intravesical treatment.

Patient Recovery and Management After Discontinuation of Intravesical Treatment

Knowledge of the treatment procedure and safe handling guidelines, as well as the signs and symptoms of extravasation, help ensure safe and effective recovery of patients after intravesical antineoplastic therapy. Post-TURBT patients require different consideration than outpatients treated in physicians’ offices. Patients who receive intravesical treatments in an office setting may have the Foley catheter removed immediately and be asked to hold the agent in their bladders until they are instructed to void. Ideally, patients should remain lying down for two hours. To maximize contact with all surfaces of the bladder wall, patients should turn every 15 minutes onto their stomach, sides, and back. Patients who are recovering from anesthesia, however, are unable to communicate and cannot move on the recovery bed. Patients also have a period of confusion when awakening. Nurses must take measures to prevent patients from pulling on the plugged catheter. Dislodgment of the balloon into the urethra or complete removal can cause additional trauma to tissues and exposure of patients and staff to the antineoplastic agent. In addition, removal of diseased tissue from the bladder compromises the integrity of the protective epithelial wall, which places patients at risk for extravasation when a vesicant is used. Subsequently, nurses must be attentive to patients so they can assess for extravasation when patients awaken (see Figure 2).

Patients may become aware of a feeling of fullness in their bladders when they awaken. Give reassurance and explain that the feeling is normal. If patients who have received a vesicant, such as mitomycin or doxorubicin, complain of discomfort, nurses should consider the possibility of extravasation into or through the wall of the bladder and take appropriate action. Most patients experience some pain, aside from feeling that their bladders are full, that generally responds to the routine analgesic regimen. Encourage patients with discomfort to hold the fluid for the ordered time, which is no more than two hours. As patients become more oriented and awake, explain the procedure and purpose of holding the agent in the bladder. However, if patients complain of acute pain in the pelvic region or lower back that is continuous and unrelied by the normally administered pain regimen, nurses must drain the bladder immediately and notify a doctor of possible extravasation of the drug. Extravasation is rare but can result in peritoneal tissue necrosis, fistula formation, the need for surgical interventions, and chronic pain (Nieuwenhuijzen et al., 2005). Releasing the agent and accumulated urine as soon as symptoms become apparent helps limit extravasation.

Regardless of whether the release of the agent is at the ordered time or a result of extravasation symptoms, proper precautions should be taken. Use all appropriate PPE, including chemotherapy gloves, a disposable gown, a face shield, a gauze
The Phaseal™ (Carmel Pharma) device is connected to a urinary catheter adaptor to administer the medication; these safety devices, along with personal protective equipment (e.g., face mask or goggles, chemotherapy gloves and gowns) minimize the risk of exposure.

Using the wrong equipment may result in unnecessary exposure to the antineoplastic agent. Water and red food coloring are used to demonstrate spilling that might go unnoticed when using an irrigation syringe to administer chemotherapy into the bladder through a urinary catheter. This in-service demonstration is effective and inexpensive.

The physician or nurse administering the antineoplastic agent should retrieve the nonsterile syringe from the bag; verify the correct patient, route, drug, and dose; and note the time of instillation with a licensed staff member.

After instillation of the antineoplastic agent, the Foley adaptor and tip of the Phaseal luer lock are detached from the syringe and kept in place to plug the catheter.

The empty syringe should be disposed in a hazardous materials bag held by an assistant.

For most patients, the catheter is removed after the procedure and voiding takes place in the bathroom. If the patient is connected to a urinary drainage bag, labeling the bag will alert caregivers to special handling precautions.

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Figure 1. Safety Precautions When Instilling Intravesical Antineoplastic Therapy

Pad, and absorbent pads. Place an absorbent, plastic-backed disposable pad(s) under the patient’s perineum and have a washcloth and soap ready to cleanse the perineum and any skin on the patient exposed to the agent. In addition, be sure to have a labeled drainage bag ready to attach to the catheter, placing the collection bag below the level of the bladder. Using all PPE, clamp the Foley catheter and hold a sterile gauze pad around the end of the Foley catheter while quickly and carefully removing the adaptor or plug, maintaining sterile connections and inserting the drainage bag tubing. Release the clamp. The gauze will help absorb any drops that could become airborne or drip during the switch of the plug for the drainage bag. Cleanse the patient as needed and dispose of all PPE and other waste in appropriate containers. If a physician ordered complete removal of the catheter, ensure that the patient is able to sit and use the toilet immediately without
splashing bladder contents. Be sure to wash any areas exposed to bladder contents.

Patients and their caregivers require detailed instructions on how to use the drainage bag and safe handling precautions. Because the initial drainage from the bladder contains the greatest amount of antineoplastic agent, changing the drainage bag before discharge or transfer is the best way to reduce the chance of exposure for patients and caregivers after they leave nurses' care. Remind patients and caregivers that children and pregnant and nursing women should not come into contact with urine or items contaminated with urine. Teach them to use the special precautions for at least eight hours after the agent is released from the bladder. Hand washing is an important intervention in the prevention of contamination with hazardous and infectious waste. Patients and caregivers should wash their hands for 10–15 seconds with warm water and soap any time they come in contact with the drainage bag or urine, even if gloves are used. After catheter removal, the same hand-washing vigilance is required each time patients use the bathroom. In addition to hand washing, patients should avoid splashing when urinating and wash any exposed skin with soap and water. Remind patients and caregivers to discard disposable waste immediately into a closed, lined container and to wash contaminated sheets or clothing twice in warm soapy water. Contaminated items should be separate from other laundry for the first wash.

Teach patients about signs and symptoms to report immediately to a doctor. Patients and caregivers must understand that although infection and bleeding are rare, they may occur. Instruct them to call a doctor about any signs and symptoms, such as bleeding, a fever of more than 100.4°F, or any other concerns that arise before the follow-up office visit. A teaching sheet could include postoperation instructions for TURBT and special instructions for intravesical treatment. Patients admitted for observation may receive care on a nononcology unit. Remember to continue the use of all appropriate PPE for eight hours. Providing excellent and safe care requires that all nurses who care for patients with urinary bladder cancer demonstrate competency according to the institution’s evidence-based policies and procedures. Nursing management of patients with urinary bladder cancer also includes encouraging patients to view the disease as a chronic process, requiring a lifetime of follow-up visits to screen for tumor recurrence and treatment if needed (O’Rourke, 2001).

**Conclusion**

Prevention and detection of urinary bladder cancer, as with all other cancers, are important. Prevention of urinary bladder cancer begins with education about the effects of exposure to chemicals, especially tobacco. Education about early detection can focus on reporting of symptoms, such as painless hematuria. Oncology nurses have a wealth of knowledge and experience to share that are unique to the profession and have the opportunity to play major roles in developing policies, procedures, and competencies for the safe and effective care of patients with urinary bladder cancer. Implementing safe handling precautions for all those potentially exposed to hazardous drugs is imperative. In addition, educating the community about urinary bladder cancer and increasing awareness of risk factors, signs, and symptoms can help to reduce the morbidity and mortality rates associated with the disease. Nurses should be alert for new screening guidelines and proactive in the implementation of screenings in their institutions and communities. Intravesical antineoplastic therapy for urinary bladder cancer presents a great opportunity for nurses to communicate with other departments to improve patient care.

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**References**


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