Prevention of urinary tract infections in patients with spinal cord injury

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Urinary tract infections remain the most frequent infection in patients with either traumatic or nontraumatic spinal cord injury and occur at a rate of 2.5 events per patient per year. Most cases of septicemia in these patients can be attributed to the urinary tract, with a death rate of about 15%.[1] Most, if not all, patients with spinal cord injury have urinary stasis due to neurogenic bladder, which promotes bacterial colonization and impairs the phagocytic ability of epithelial cells that line the urinary bladder. Bladder catheterization can introduce microorganisms into the urinary tract and is always considered a risk factor for urinary tract infections.[1] The limitations of the usual measures (e.g., use of regular latex indwelling catheters) in prevention of urinary tract infections in this population have led the way to explore more innovative modalities and approaches. Here, we review the evidence for novel and well-established approaches to the prevention of urinary tract infections in patients with spinal cord injury (Box 1).

How can urinary tract infection be prevented in patients with spinal cord injury?

Catheter insertion

Neurogenic bladder leads to urinary stasis that often requires catheterization. Avoiding the insertion of indwelling catheters is considered the best strategy to prevent urinary tract infections. Different strategies for catheter insertion, such as inserting a catheter only when appropriate, early removal of the catheter and use of aseptic techniques, are vital in lowering the rates of catheter-related urinary tract infections.[1] Almost 50% of urinary catheters are placed inappropriately and retained longer than needed.[1,2]

According to the Infectious Diseases Society of America, acceptable indications for urinary catheter use are substantial urinary retention (if medical therapy is not effective), urinary incontinence in terminally ill patients, accurate monitoring of urine output in critically ill patients, and use during prolonged surgical procedures.[3] In a prospective study involving 202 patients admitted to the medical intensive care unit or medical floors of a tertiary hospital, researchers determined that the initial indication for indwelling urinary catheters was inappropriate in 21% of patients, whereas continued catheterization was inappropriate in 47% of patients.[4]

Early removal of indwelling catheters is associated with less bacteriuria.[5] When indwelling catheters are used for long-term bladder drainage in patients with spinal cord injury, it is recommended to routinely change the catheters every two to four weeks to reduce the risk of asymptomatic bacteriuria and urinary tract infections. The catheter should also be changed if urinary tract infection is suspected.[5]

Bacteriuria is less common with intermittent catheterization (70%) than with indwelling catheters (98%).[2] However, a longer duration between intermittent catheterizations has an increased risk of bacteriuria.[6,7] The usual schedule for intermittent

Box 1: Evidence used in this review

We searched MEDLINE from 1970 to 2014, using a combination of medical subject headings and words in text as follows: "urinary tract infections," "prevention" and "spinal cord injury." We limited this review to literature published in English. We included clinical trials with the highest level of evidence for each topic we discussed and observational studies when no controlled trials were available. In this review, we appraise different methods for prevention of urinary tract infections in patients with spinal cord injury.

KEY POINTS

- Most patients with spinal cord injury have urinary stasis due to neurogenic bladder, which promotes bacterial colonization and impairs the phagocytic ability of epithelial cells that line the bladder, making them prone to urinary tract infections.
- Approaches to the prevention of urinary tract infection in patients with spinal cord injury include optimal technique for bladder drainage (e.g., use of hydrophilic-coated catheters and closed catheter drainage systems, placement of indwelling catheters only when indicated and avoidance of permanent catheters) and use of antibiotics only when needed for symptomatic bacteriuria.
- Further research is needed to assess the efficacy, effectiveness and safety of several promising techniques, including bacterial interference, injection of botulinum toxin A into the detrusor, and sacral neuromodulation.

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catheterization is at least every six hours and at bedtime. This frequency can be modified depending on the urine output, but, in general, not allowing the bladder to hold more than 400 mL of urine can prevent stasis and infection.[6]

Hand hygiene is a simple and yet very important method to prevent transmission of health care–associated infections; its implementation is fundamental in the care of patients with spinal cord injury. Sterile technique (i.e., use of sterile gloves and drapes) and clean technique (i.e., gloves and drapes are not sterile) are used for catheter placement.[2,8] There is no difference between sterile and clean techniques in the occurrence of bacteriuria and urinary tract infections.[2] No data exist to suggest that catheterization by a care provider is associated with lower rates of bacteriuria or urinary tract infections than self-catheterization.

Studies of interventions, such as paper-based reminders, face-to-face reminders, preinsertion checklists and nurse-driven protocols, to encourage clinicians to insert catheters only when necessary and remove them quickly showed a decline in catheter retention, but no concomitant reduction in bacteriuria has been shown.[9,10] One randomized controlled trial (RCT) assessed 692 admitted patients with indwelling urinary catheters inserted for less than 48 hours.[9] Patients were randomly assigned into a group with a stop order for urinary catheters and a group with usual care. The stop-order group had 1.69 fewer days of inappropriate catheter use (95% confidence interval [CI] −1.23 to −2.15) and 1.34 fewer days of total catheter use (95% CI −0.64 to −2.05 days).[9]

Closed catheter drainage system

A closed catheter drainage system is recommended for all patients with indwelling catheters.[7,11] An RCT showed that patients with preconnected sealed junctions were less likely to have urinary tract infections than those with catheters without similar junctions (relative risk [RR] 2.7, 95% CI 1.3 to 5.4).[12] Positioning of the catheter below the level of the bag or above the level of the bladder, and breach of the closed drainage system are both associated with a significantly higher risk of catheter-associated bacteriuria.[7,13]

What is the initial approach to treatment of suspected urinary tract infection?

Evaluation of urinary tract infection in patients with spinal cord injury is challenging because the typical manifestations of urinary tract infection (e.g., dysuria, urgency, frequency, suprapubic discomfort, and, in patients with pyelonephritis, costovertebral angle pain and tenderness) are rarely encountered in this population. Instead, nonspecific symptoms, including change in voiding habits, increase in the residual volume of urine in the bladder, foul-smelling urine, worsening of muscular spasticity and/or aggravation of autonomic dysreflexia, can be indicative of urinary tract infection. Pyuria is a nonspecific finding, but the absence of pyuria reasonably predicts the absence of urinary tract infection in patients with spinal cord injury.

The development of nontypical symptoms in the context of coexisting conditions is a major challenge that can lead to delayed diagnosis. A prospective case review involving 147 patients with spinal cord injury who thought they had a urinary tract infection showed that 39% (57/147) were not accurate in attributing their symptoms to this infection.[14] Of this group, 12 had other medical problems accounting for their symptoms, such as bowel obstruction, dehydration, fecal impaction or other processes, and the remaining 45 had bacteriuria with no pyuria.[14] Therefore, urinary tract infections should be suspected based on the presence of symptoms that are often nontypical, as discussed above, in addition to demonstration of substantial pyuria on urinalysis.

Asymptomatic bacteriuria in catheter-dependent patients should not be treated with systemic antibiotics.[15] Prophylactic antibiotics in this patient population may result in emergence of resistant bacteria.[15]

Prophylactic weekly oral cyclic antibiotic programs (i.e., alternate administration of antibiotics) show some promise in the prevention of urinary tract infections in these patients, but data are limited to small observational studies.[15] These studies showed significant reductions in the frequency of urinary tract infections per year by using weekly oral cyclic antibiotics, without demonstration of severe adverse effects or development of multidrug-resistant organisms.[16,17] However, there is insufficient evidence to support routine use of weekly oral cyclic antibiotics in patients with spinal cord injury who have frequent urinary tract infection.

Antimicrobial stewardship

Antimicrobial stewardship is essential in the prevention of multidrug-resistant microorganisms. It refers to the practice of choosing an appropriate antimicrobial regimen and selecting an optimal dose and duration while minimizing toxicity, drug reactions and antimicrobial resistance.[18] This is particularly important in the care of patients who are susceptible to recurrent infection, such as those with spinal cord injury. It has been estimated that antibiotic use was unnecessary or inappropriate in

about half of cases in the United States, leading to the selection of resistant species.[18]

Several methods have been applied to improve antibiotic use. These methods include auditing and feedback, restriction and/or preauthorization, prescriber education, guideline implementation, computer-assisted programs, intravenous-to-oral switch, de-escalation or streamlining, antibiotic cycling or dosage optimization.[18] Further research is needed to evaluate which method is most effective.[19]

What kind of catheters should be used for patients with spinal cord injury?

Urinary catheters can be manufactured from latex, plastic, silicone or polytetrafluoroethylene (Teflon). None of these materials is entirely biocompatible or complication-free. The surface of latex catheters is much more uneven than silicone counterparts, which predisposes to bacterial adherence.[20] Moreover, toxic effects in vitro and proinflammatory responses in vivo are more common with latex catheters, and long-term exposure can lead to polypoid cystitis.[21–23] Silicone catheters have a larger lumen and are less associated with infection than latex catheters. However, they are less comfortable due to increased rigidity.[24,25] Several advances have been made in the manufacturing of urinary catheters to increase comfort and reduce the likelihood of infection. These include hydrophilic or silver-hydrogel coatings, and catheters impregnated with antibiotics.

Hydrophilic-coated catheters

The use of hydrophilic-coated catheters is an innovative technique that leads to better patient comfort and satisfaction, decreased microbial adherence and reduced encrustation.[26,27] Hydrophilic-coated catheters have been associated with lower rates of symptomatic urinary tract infection in patients with acute spinal cord injury; fewer complications related to urinary tract infection; fewer inflammatory episodes at the scrotal level; fewer episodes of post-, intra- and intercatheterization bleeding; lower treatment costs; fewer days of rehabilitation; and a reduction in the emergence of antibiotic-resistant organisms.[26,27]

In a randomized parallel comparative trial assessing urinary tract infection in 57 patients with spinal cord injury, 64% of patients with hydrophilic-coated catheters had one or more urinary tract infections compared with 82% of patients with uncoated polyvinyl chloride catheters.[28] There was no significant difference in the incidence of hematuria, pyuria and bacteriuria.[28]

A larger randomized multicentre trial recruited 224 patients with traumatic spinal cord injury of less than three months' duration who used intermittent catheterization.[26] There was a substantial delay in the first symptomatic urinary tract infection in the group who received hydrophilic-coated catheters compared with the group who received uncoated polyvinyl chloride catheters. This led to a one-third reduction in the daily risk of symptomatic urinary tract infection in the group receiving hydrophilic-coated catheters (hazard ratio 0.666, 95% CI 0.453 to 0.978).[26] One recent systematic review of eight studies involving patients with spinal cord injury showed that urinary tract infections were less common in those who used gel-reservoir (i.e., catheters with integrated lubrication) and hydrophilic-coated catheters than in those who used sterile noncoated catheters.[29]

Silver-hydrogel catheters

Silver coating is another promising but not well-established modality of preventing urinary tract infection in patients with acute spinal cord injury with indwelling catheters. Silver ions contain many antimicrobial properties through the inactivation of enzymes in vivo and the formation of electron-dense granules leading to cell-wall death.[30] Silver alloy–coated catheters have been found to decrease the risk of nosocomial urinary tract infections only in the short term;[31] there are no data available thus far on its use to prevent urinary tract infection in patients with spinal cord injury who need long-term indwelling catheters. Additionally, sufficient data are not available to suggest that long-term use of silver hydrogel catheters is not associated with silver toxicity.[32]

Antibiotic-impregnated catheters

The use of antibiotic-impregnated catheters is associated with delayed and decreased incidence of asymptomatic bacteriuria over the short term. However, no evidence is available to suggest that they decrease symptomatic urinary tract infections, and they cannot be recommended for either short- or long-term indwelling urethral catheterization.[3]

Do cranberry products have a role?

Because conflicting data are available on the efficacy of cranberry products in reducing bacteriuria and urinary tract infection in patients with spinal cord injury, use of cranberry products is not routinely recommended in this setting.[3] One crossover study showed no significant difference in urinary pH levels, bacterial counts, white blood cell counts or urinary tract infections in patients with neurogenic bladders after four weeks of administration of cranberry tablets.[33]

An RCT involving 305 patients with neuropathic bladder following spinal cord injury showed no benefit of cranberry tablets in the prevention of urinary tract infection.[34] However, another crossover study involving 47 patients with spinal cord injury found that the frequency of urinary tract infection was reduced to 0.3 infections per year in the group taking cranberry tablets compared with 1.0 infections per year in the placebo group (odds ratio 0.3, 95% CI 0.1 to 0.7).[35] The response was more significant in patients with a higher glomerular filtration rate.[35]

What other modalities are being developed?

Bacterial interference

Bacterial interference refers to colonization of surfaces with nonpathogenic microorganisms, thus preventing the adherence of pathogens and ultimately infection. This can be achieved using catheters that have been preinoculated with nonpathogenic bacteria.[6,36] Small observational trials have shown that patients whose bladders were successfully colonized with the nonpathogenic strains of *Escherichia coli* had a lower incidence of urinary tract infections than patients with noncolonized bladders.[36–38] An RCT compared inoculation of the bladder with a nonpathogenic *E. coli* 83972 strain to saline in 27 male patients with spinal cord injury.[37] All six participants in the placebo group had at least one urinary tract infection during the one-year follow-up period, compared with 13 of 21 participants (62%) in the experimental group ($p = 0.07$). During the follow-up period, episodes of urinary tract infection were less frequent in the experimental group (mean 1.6 episodes) than in the control group (mean 3.5 episodes) ($p = 0.036$).[37] However, data on effectiveness and safety are currently insufficient to recommend bacterial interference in routine clinical care.

Effective bladder drainage and low detrusor pressure

Patients with spinal cord injury often have hyperactivity of the detrusor muscle and lack detrusor–sphincter relaxation, leading to increased intrabladder pressure. The increase in pressure may result in vesicoureteral reflux and promotes ischemic injury of bladder walls. Reflux and stasis will eventually result in urinary tract infections. Anticholinergic drugs lower detrusor pressure and may be offered, combined with intermittent catheterization, to patients with evidence of substantial postvoiding residual urine. However, one-third of patients may not tolerate these medications owing to adverse effects or may not respond to treatment (i.e., found to have persistently high postvoiding urine despite therapy).[39]

Injections of botulinum toxin A into the detrusor, although not yet approved by the US Food and Drug Administration or Health Canada, can lower the frequency of symptomatic urinary tract infections by ameliorating detrusor overactivity and inducing chemical denervation of the detrusor muscle. This leads to improvement in urodynamic parameters and increased reservoir capacity of the urinary bladder while maintaining low intrabladder pressure.[40,41] The evidence for the role of botulinum toxin in the prevention of urinary tract infection in patients with spinal cord injury comes from small observational studies. In one study, the mean number of urinary tract infections over six months was 1.75 ± 1.87 in 30 patients with spinal cord injury and detrusor hyperactivity.[40] This number was reduced to 0.2 ± 0.41 after botulinum injections ($p = 0.003$). Three patients showed less improvement in their urodynamic parameters and had urinary tract infections.[40]

Sacral neuromodulation

Early surgical implantation of a sacral nerve stimulator can help reduce the frequency of urinary tract infections by preventing detrusor overactivity and improving bladder urodynamics. The exact mechanism of action for sacral neuromodulation is poorly understood and requires more research.[41]

Sacral neuromodulation can help to achieve normal bladder capacity, avoid incontinence and increase self-catheterization time intervals, which in turn helps to avoid urinary tract infections. It is also anticipated to improve bowel and erectile functions. A small observational study demonstrated these findings in 10 patients who underwent implantation of these devices.[41] The control group (6 patients), who took antimuscarinic agents and relied on more frequent self-catheterizations or used urinary condoms, had a mean of 3.8 urinary tract infections per year, compared with 0.5 infections in the study group.[41]

Box 2: Unanswered questions

- Should weekly oral cyclic antibiotic be systematically used in patients with spinal cord injury who have frequent urinary tract infections?
- Is bacterial interference safe and effective?
- What is the role of botulinum toxin A injections and sacral neuromodulation in the prevention of urinary tract infection in patients with spinal cord injury?

Conclusion

Urinary tract infections constitute a substantial health burden for patients with spinal cord injury. Although unanswered questions remain (Box 2), innovative and well-established approaches to

prevent urinary tract infection in this population exist. Optimal bladder drainage technique, use of hydrophilic-coated catheters, placement of indwelling catheters only when indicated, avoidance of permanent catheters and use of antibiotics only when needed for symptomatic bacteriuria are among the most important measures in prevention of urinary tract infection in patients with spinal cord injury.

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