Review Article

Etiology, Management of Catheter-related Bladder Discomfort with Pharmacological Agents and Non-pharmacological Means

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Abstract

Self-retaining balloon catheters are essential for effective urine drainage following urological and other major surgeries. However, their use can sometimes lead to catheter-related bladder discomfort (CRBD), a condition that causes significant distress, reduces quality of life, and requires prompt management. A systematic review was conducted using Medline, PubMed, Google, and CINAHL to identify relevant articles aligned with the study's objectives. A total of 13 articles were included in the review, with some from CINAHL specifically focusing on non-pharmaceutical approaches for managing CRBD symptoms. In addition to pharmaceutical treatments, several non-pharmaceutical interventions, easily implemented by nurses, were found effective. These include reducing the catheter balloon size, securely fixing the catheter, properly positioning the urine bag, using a catheter valve, addressing constipation, encouraging increased fluid intake, and recommending a diet rich in fluids and fiber. These measures were demonstrated to alleviate CRBD symptoms significantly.

Key words: *Self-retaining Balloon Catheter, CRBD, Non-pharmaceutical Interventions, Quality of life.*

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Introduction

Self-retaining balloon catheters are generally used for easy urinary drainage from the bladder. Various purposes include suprapubic urinary diversion (SUD), per urethral urinary drainage, or after perineal urethrostomy for some clinical purposes. The catheter collects urine specimens for urinalysis, urine culture, and post-void urine measures for diagnostic purposes. For treatment purposes such as intravesical anticancer chemotherapy and immunotherapy for a short duration, an indwelling catheter is used. Long time per urethral catheter is used in case of neurogenic bladder or after any surgery that requires catheterization. About 15% to 25% of admitted patients in general hospitals and 50% of patients admitted to long-term care facilities require indwelling catheterization.[1-4] Many adverse effects are observed when a catheter is maintained for a short or long period, either for treatment or diagnostic purposes. In various urologic surgeries, especially after transurethral resection of a bladder tumor (TURBT) or prostate surgery (TURP), easy urine drainage and catheters have been used. Indwelling catheterization, which sometimes causes discomfort, varies from a burning sensation in the urethra, pain in the suprapubic and penile area, urinary urgency, etc., and all these symptoms together are called "Catheter-related bladder discomfort" (CRBD).[5] The incidence of CRBD ranges from 47% to 90%.[6] CRBD symptoms are usually accompanied by abnormal behavioral responses, such as attempting to pull out the urinary catheter, causing urethral injury and bleeding, and later on stricture urethra development.[7,8] These abnormal behavioral responses may result in decreased quality of life (QOL),

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increased incidence of post-operative complications, including bleeding, delayed wound healing, increased severity of coronary heart diseases, even exacerbation of post-operative pain, and delay in hospital stay. Although there are various treatment and prevention modalities for CRBD exist, effective treatment for CRBD without adverse effects is still lacking.

Materials and Methods

The management of post-operative catheter-related bladder discomfort (CRBD) is a critical aspect of patient care, as it significantly impacts comfort and recovery. Both pharmaceutical and non-pharmaceutical approaches have been advocated to address this issue. This review focuses on understanding the etiology of CRBD and explores various clinical management strategies. A comprehensive literature search was performed using multiple databases, including Medline, PubMed, Google, and CINAHL, to identify studies published between 2016 and June 2024. A total of 13 studies were selected based on their relevance to the study's objectives. These studies provided insights into both pharmaceutical interventions, such as the use of anticholinergics, analgesics, and sedatives, and non-pharmaceutical measures, including catheter size adjustments, fixation techniques, and dietary recommendations. This review highlights the importance of a multidisciplinary approach to CRBD management, emphasizing strategies that can be tailored to individual patient needs to optimize outcomes and improve post-operative quality of life. A total of 23 published articles were identified using various keywords. Of the total 23 articles, 10 were reviewed but were excluded from the study. The remaining articles were found to align closely with the objectives and suggested that both certain pharmacological agents and non-pharmaceutical interventions were effective in significantly improving symptoms and reducing the incidence of catheter-related bladder discomfort (CRBD) compared to the placebo group.

Literature review

Etiology of CRBD

The bladder has two types of innervations such as adrenergic innervation from the hypogastric nerve and cholinergic innervation from the pelvic nerve. An indwelling catheter stimulates the bladder cholinergic or afferent nerve to secrete acetylcholine, which causes the bladder involuntary contractions,[9] through muscarinic receptors. Detrusor muscles contain 2 types of receptors, such as M^2, and M^3, receptors, a subtype of cholinergic receptors, located in the bladder urothelium/suburothelium, which are the main pathway for CRBD.[10] For this reason, treatment of CRBD with antimuscarinic agents is effective.

Another susceptible cause of CRBD is the mechanical stimulation of the bladder mucosa by the catheter tip when the bladder is empty, causing the erosion of the bladder wall. When a suprapubic catheter meets the bladder trigon, patients feel severe pain due to the bladder and urethral spasm. Research on rats found that calcitonin gene-related peptide (CGRP) nerve fibers, which regulate the immune system, are associated with inflammation and venule relaxation located in the detrusor muscle and more in the bladder neck than in the dome of the bladder. So, we can say that CGRP may play a role in CRBD.[11]

Management of CRBD

Different treatment modalities have been described regarding the management of CRBD, no methods have been obtained up to the mark of desire. Pharmaceutical and non-pharmaceutical methods are two types of treatment modalities for CRBD control. Among the pharmaceutical agents used are solifenacin, Oxybutynin, darifenacin, tolterodine, gabapentin, pregabalin, tramadol, paracetamol, butyl scopolamine, ketamine, botulinum toxin (Botox), magnesium acetate, vitamin C, and vitamin D. Among the non-pharmaceutical methods are changing the size of Foley Catheter, fixing the catheter, etc. Above the mentioned treatment methods patient tolerated well but had a high incidence of treatment-related side effects.[12] Solifenacin is an antimuscarinic agent that relaxes the bladder muscle and is generally used for neurogenic detrusor overactivity. It blocks the M3 muscarinic receptor. As an indwelling catheter causes detrusor muscle contraction, solifenacin effectively controls CRBD. In a trial with 116 patients, solifenacin 5mg was given orally to 58 patients after TURBT, and compared with the placebo group (n=58) at all time intervals, CRBD improved significantly ($p<0.05$). Common side effects were constipation and dry mouth.[13] A study done with solifenacin found no result. Incidence rates of CRBD at 1 and 2 hours after TURBT were 72.2 and 68.1 % respectively. They used 5mg of Solifenacin, which causes no decrease in the incidence and severity of CRBD.[14] Another study was done with oral solifenacin and darifenacin and compared with the placebo group. CRBD was significantly less than that of the placebo group.[15]

Oxybutynin is a drug in the anticholinergic /antimuscarinic class. It relaxes bladder muscles blocking muscarinic receptors in bladder-afferent pathways. In a study with 46 patients who underwent radical prostatectomy, 5 mg oxybutynin was applied sublingually, (N=23) and compared with the placebo group (n=23). The CRBD-related pain was significantly less than that of placebo. ($p<0.05$). Patients in the oxybutynin group had no dry mouth.[16] So, sublingual oxybutynin reduces post-operative pain-related CRBD.

Tolterodine is a type of medicine called an antimuscarinic muscle relaxant, that works by relaxing bladder muscles.[17] It is as strong as oxybutynin and increases bladder storage function. Study with 165 patients who underwent urological surgery, 2 mg of oral tolterodine (n=50) was given 1 hour before surgery and compared with a placebo (n=165). The severity of bladder discomfort and behavioral responses were significantly less in tolterodine compared with the placebo group.[18] Dry mouth and incidence of other adverse events were less in the tolterodine group. Tolterodine was best in decreasing the severity of CRBD. They also compared 2 mg tolterodine, 5mg oxybutynin orally, and placebo groups. The placebo group had an increased incidence of CRBD symptoms ($p<0.05$).

Gabapentin is an antiepileptic and analgesic agent. In a study with 108 patients, Percutaneous nephrolithotomy underwent, 600mg of gabapentin administered orally before surgery for CRBD symptom control. CRBD symptoms were significantly

reduced compared to the placebo group ($p<0.05$). The research group observed and commented that the incidence and severity of CRBD could decrease by peripheral and central action of gabapentin.[19] In another clinical study with 100 patients, 33 patients received 600 mg, 34 patients received 1200 mg orally, and another 33 patients received placebo. CRBD incidence was 90% in the placebo group, 66% in patients who received 600 mg, and 26% in patients who received 1200 mg gabapentin. Here, the incidence of CRBD is significantly more than those who received 1200 mg of gabapentin. No significant side effects were observed.[20]

Pregabalin's effects are like gabapentin. A study was conducted on 60 patients who underwent spinal surgery. Pregabalin 50mg (N=30) was administered orally 1 hour before surgery. The incidence of CRBD was significantly lower in patients' group($p<0.05$.[21]

Botulinum Toxin injection (Botox) is a type of bacteria called Clostridium botulinum, a spore-bearing bacteria, produces the toxin, a neurotoxin protein. This toxin prevents the release of the neurotransmitter acetylcholine from axon endings, thus causing flaccid paralysis. Botox works by stopping the bladder muscle contraction too much in overactive bladder (OAB). A clinical study was done by injecting Botox into an intravesical route in 54 patients with bladder pain and catheter bypass leakage of urine who had an indwelling catheter for a long time, 100 units or 200 units of Botox were injected intravesical. Botox is an ideal treatment for CRBD symptoms. Before treatment, urine culture and sensitivity should be done, followed by antibiotics therapy if needed.[22]

Butylscopolamin is a peripherally acting antimuscarinic and anticholinergic agent. A prospective, randomized, placebo-controlled, double-blind study with 57 male patients following urologic surgery found that the butyl scopolamine group (20mg /i.v) significantly decreased CRBD symptoms than the placebo group ($p=0.001$).[23]

Tramadol is a centrally acting, synthetic opioid analgesic with a weak opioid agonist that inhibits the detrusor activity by inhibiting M1 and M3 receptors. A prospective, randomized, double-blind, placebo-controlled study was conducted with 50 patients who received I.V. tramadol (1.5mg/kg) intra-operatively, 30 minutes before extubation, and reduced the incidence and severity of CRBD significantly ($p<0.05$).[24]

Paracetamol is indicated for fever, common cold and influenza, headache, toothache, earache, body ache, myalgia, neuralgia, dysmenorrhea, sprains, colic pain, back pain, post-operative pain, postpartum pain, inflammatory pain and post vaccination pain in children. It is also indicated for rheumatic & osteoarthritic pain and stiffness of joints. Paracetamol (acetaminophen) can be used to treat a variety of urologic conditions, including catheter-related bladder discomfort (CRBD). A prospective, randomized, double-blind, control study on 32 patients who underwent percutaneous nephrolithotomy (PCNL) for renal calculus and compared with control (N= 32). Paracetamol 15mg /kg I.V. was administered in the patient group. They suggested that paracetamol is an effective drug in the management of CRBD.[25]

Duloxetine is a potent selective serotonin and norepinephrine reuptake inhibitor and is effective in the treatment of neuropathic pain, anxiety disorder, fibromyalgia, and depressive disorder. In a prospective, randomized, double-blind, placebo-controlled study conducted with 64 adult patients, 32 patients received (group D) 1 ranitidine tablet of 150mg and 1duloxetine tablet of 60 mg, while another group (group C) received 2 tablets of ranitidine of 75mg two hours before induction. A 16 F Foley catheter was inserted per urethra. Incidence and severity of CABD were significantly lower in group D but had no major side effects ($p=0.05$).[26]

Nefopam is a pain killer superior to tramadol. It is a benzoxazine compound used as a centrally acting analgesic and is neither an opioid nor an NSAID. A systemic review, meta-analysis, and randomized control trial evaluated the safety and efficacy of CRBD. A total of 405 patients were analyzed to assess the efficacy of nefopam on post-operative CRBD. Nefopam 20mg was mixed with 20 ml of normal saline and administered intravenously. Patients had a significantly lower incidence of CRBD in comparison with the placebo group. ($p<0.00001$).[27]

Vitamin C can be beneficial for urological health in several ways. Vitamin C can help reduce UTIs by making urine more acidic, which kills bacteria in the urinary tract. Vitamin C can also prevent biofilm formation on urethral catheters. Vitamin C can reduce the adhesion of uropathogens to silicone rubber and their colonization in urine Urinary storage or incontinence. It has role in CRBD also. A randomized, double-blind, placebo-controlled study was done with 118 patients. After vitamin C administration (n=59), the CRBD improved significantly, when compared with the control (n=59)($p<0.001$). The researcher's group commented that further research with oral intake of Vit. C with a larger sample size is warranted. Vitamin C deficiency causes muscle spasms and muscle cramps, so intake of vitamin C and I.V. vitamin C relieves CRBD symptoms.[28]

Magnesium is related to smooth muscle relaxation, decreasing CRBD. A prospective, randomized, placebo-controlled study showed that intravenous magnesium sulfate administration reduces the incidence and severity of CRBD after laparoscopic radical resection of gastrointestinal cancer.[29]

Lidocaine also known as lignocaine, is a local anesthetic of the amino amide type. It contains methyl salicylate, which is an NSAID. A randomized, double-blind, control study found that transurethral irrigation with 0.01% lidocaine (100mg) reduced the incidence of CRBD by 52% compared to irrigation with only normal saline. The study also found increased patient satisfaction, ($p<0.004$).[30] Another study done with intravenous lidocaine,1.5mg/kg bolus dose followed by a 2mg/kg/h continuous infusion, during the intraoperative, and continued 1-hour post-surgery, resulted in a lower incidence of moderate to severe CRBD symptoms with higher patient satisfaction after TURBT without evidence of significant side effects.[31]

Numerous studies with non-pharmaceutical means have been done for the management of CRBD symptoms. The following

interventions are easily applied by nurses, health assistance, such as reduction of the balloon size, fixing the catheter in the upper thigh, securing the urine bag or use of a catheter valve, advice for constipation relief, increasing fluid intake, and advice for a balanced and fiber-rich diet. A prospective study evaluated pain and CRBD, relating to balloon sizes of indwelling catheters. After the reduction of balloon sizes ($P<0.05$), they found a significant reduction in pain.[32] Another study found the effects of various catheter fix sites on catheter-associated LUTs, if a catheter fixes on the top one-third of the thigh, the incidence of urgency, and urethral pain improved significantly ($p=0.002$). That's why some articles suggest catheter fixation in the top one-third of the thigh decreases bladder spasms.[33] Gently pulling the catheter to ensure the tip is not touching the bladder wall but not pushing against the bladder neck, decreases CRBD symptoms to some extent. In some articles, authors described that blockage of the catheter can cause bladder spasms and suggested saline irrigation could be used to solve problems. Some reports suggested that constipation may cause pressure on the bladder and catheter, causing bladder symptoms and relief of constipation to decrease CRBD. They also suggested dietary advice, plenty of water intake, and avoiding bladder irritants, such as alcohol, Caffeine may help symptoms decrease CRBD.[34] Zugail et al. did a non-randomized, prospective study with 49 patients admitted to the hospital with an indwelling catheter. Two hours after the reduction of the balloon volume by half, and assessed by visual analog scale for pain, and CRBD symptoms questionnaire, found pain score and grade of CRBD before and after balloon size reduction was significant($P<0.05$).[35] Further study is recommended. If this simple, non-invasive method proves to be effective, its association with pharmaceutical treatment will help decrease CRBD symptoms. In a clinical study conducted, using a catheter valve (CV) and a leg bag (LB) for urine drainage, the mean score of satisfaction for the CV was significantly higher than that of LB ($p=0.05$).[36] Transcutaneous electrical acupoint stimulation (TEAS) was given to patients who underwent transurethral radical prostatectomy (TURP). The CRBD incidence of the TEAS group decreased significantly than that of the control group ($p<0.001$).[37]

It was found that constipation causes bladder spasms, increasing CRBD symptoms.[38-40] Hard stools apply pressure on the bladder walls and the catheter inside, which causes CRBD.[41] Dietary modification with increased fluid intake, a balanced diet, and a fiber-rich diet as well as avoiding bladder stimulants improve CRBD.[42]

Discussion

CRBD is characterized by discomfort in the suprapubic region with urinary urgency, frequency with or without urge incontinence which is like(Over active bladder) OAB.[43] The incidence of CRBD is 47 to 90 % among patients who underwent general surgery.[44] The symptoms of CRBD sometimes become intolerable, even decrease quality of life, and require urgent appropriate management, even causes poor patient satisfaction, increases postoperative agitation, and prolongs hospital stay. A literature review was conducted and found that management can be done in two ways. One is pharmaceutical drug use, and another is non-pharmaceutical methods. Both help in the correction of CRBD symptoms. A better understanding of the pathophysiology of CRBD will help achieve better management of CRBD when patients are undergoing urologic surgery or other types of surgery. Over and above, inflammatory mediators such as arachidonic acid derivatives (leukotrienes and prostaglandins) vasoactive peptides (kinins) phospholipid mediators and cytokines (interleukin), and catheter-mediated detrusor contraction, initiate prostaglandin (PG) synthesis, which may play a role for CRBD symptoms. That's why pharmaceutical agents and PG synthesis factors may play a role in the occurrence of CRBD symptoms.[45] There have been various studies on drugs and interventions to manage CRBD, but their comparative efficacy and safety are still a topic of debate. Many drugs are used to manage CRBD symptoms. Not all, but a few studies, did not assess the dose-response titration and impact of drugs in the postoperative period. Few studies did not use any additional tests for the evaluation of patient's pre- and post-operative mental status, as few drugs may affect the mental health of senior citizens patients. The quantification of CRBD depends upon the patient's ability to understand and the evaluator`s assessment. For this reason, various study results showed different incidences of CRBD.[44, 46] Data regarding incidences and severity of CRBD may give more accurate data if strictly adherence to study protocol. The percentage of CRBD incidence is unknown, but after urologic surgery, it is 50%.[8]
Literatures were also reviewed to identify non-pharmaceutical interventions for the control of CRBD. Through the survey, seven non-pharmaceutical interventions were found to alleviate CRBD symptoms. It is hypothesized that the application of both interventions would be highly effective in managing CRBD symptoms.

Conclusion

The reviewed data indicated that muscarinic antagonists, anesthetics, antiepileptics, acupuncture, and non-pharmaceutical methods achieved significant improvement and reduction in CRBD symptoms compared to placebo. Although a high incidence of side effects was observed with the use of these drugs, they were generally well-tolerated by patients. The combination of pharmaceutical drugs with non-pharmaceutical interventions was found to enhance the quality of life. Non-pharmaceutical interventions, which can be implemented by nurses and medical assistants, are expected to further contribute to treatment success. However, additional studies are required to validate these findings.

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