



Botulinumtoxin Injection Versus Augmentation Cystoplasty for Neurogenic Bladder: Where Do We Stand?

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Abstract

Purpose of Review Patients with neurogenic bladder often present with overactive, low capacity, and poorly compliant bladders with discoordination of their internal and external urethral sphincters. As a result of poor compliance, high detrusor pressures can cause reflux into the upper tracts. This constellation of findings can also cause bothersome lower urinary tract symptoms. There are various modes of management for patients with neurogenic bladder ranging from conservative methods to major reconstructive surgery in efforts to prevent upper tract deterioration and to treat voiding dysfunction. This paper aims to review the current practices in treatment decision making when offering botulinumtoxin A versus augmentation cystoplasty for management of neurogenic detrusor overactivity.

Recent Findings A comprehensive review was performed using PubMed and Cochrane Library from January of 2018 to April of 2023. As treatment for refractory neurogenic detrusor overactivity advances, intravesical BTX-A and augmentation cystoplasty are effective options for management, both independently and when used in combination.

Summary From more recent literature, the approach in choosing which option is more clinically effective in terms of continence rates, improvement in urodynamic parameters, and patient satisfaction is progressing towards being more patient-centered rather than following an algorithm that progresses from least invasive to most invasive management.

Keywords Botulinumtoxin · Augmentation cystoplasty · Neurogenic bladder · Overactive bladder · Urology · Urological surgery

Introduction

Patients with neurogenic bladder often present with overactive, low capacity, and poorly compliant bladders with discoordination of their internal and external urethral sphincters. As a result of poor compliance, high detrusor pressures can cause reflux into the upper tracts. This constellation of findings can also cause bothersome lower urinary tract symptoms. The most common lower urinary tract symptoms experienced due to a poorly compliant bladder are incontinence, urinary urgency, recurrent infections, bladder stones, and upper tract deterioration [1]. Treatments for neurogenic detrusor overactivity aim to decrease overactivity with the goal of decreasing detrusor pressure and episodes of urinary

incontinence, thus, in return, improving quality of life [2•]. Treatments for low bladder compliance are aimed at renal preservation.

There are various modes of management for patients with neurogenic bladder ranging from conservative methods to major reconstructive surgery in efforts to prevent upper tract deterioration and to treat voiding dysfunction. Conservatively, these patients are managed with clean intermittent catheterization (CIC) and oral medications such as anticholinergics and/or beta-3 agonists. If conservative measurements fail to be effective, the patient can consider minimally invasive options which include sacral neuromodulation, peripheral tibial nerve stimulation, and botulinumtoxin A (BTX-A) injections [3]. Surgical management for neurogenic bladder was introduced in the 1950s as augmentation cystoplasty. Bladder augmentation remains a highly invasive option for patients with neurogenic bladder today and is advantageous for a specific subset of patients that cannot tolerate or fail conservative measures [2•].

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Intravesical Botulinumtoxin A

Long-term anticholinergic treatment with clean intermittent catheterization has been shown to be successful for some patients but can be inadequate in controlling bladder pressures and symptoms [4]. It is not considered a reliable long-term method of management due to the need for patient compliance to take oral medication daily and bothersome side effects associated with anticholinergics [5]. There is a growing concern that chronic exposure to antimuscarinics can also play a role in the development of dementia [6].

Intravesical BTX-A injections were first described in a study on pediatric patients with detrusor overactivity as a result of myelodysplasia. In this population, BTX-A was shown to decrease maximum detrusor pressure, increase bladder capacity, and increase detrusor compliance. With these findings, it was established that BTX-A is a suitable therapeutic option in patients that have failed anticholinergic treatment prior to considering reconstructive options such as augmentation cystoplasty [4].

Intravesical BTX-A was initially approved for neurogenic detrusor overactivity in 2011 after double-blind clinical trials completed by Cruz et al. (2011) and Ginsberg et al. (2012) found that continence and quality of life were improved with the use of 200 units and 300 units of botulinumtoxin A [7, 8]. Findings from Ginsberg et al. showed that continence rates improved by 67% in the 200 units group and 74% in the 300 units group compared to 30% improvement in the placebo group. It was also found that 36% of patients in the 200 units group achieved dry status and 41% of patients in the 300 units group achieved dry status. In reference to quality of life, patients who received BTX-A had significantly higher I-QOL scores compared to those in the placebo group. These quality of life scores were not affected by whether the patient required CIC after receiving BTX-A [7]. These findings further enforced what was found by the similar clinical trial completed by Cruz et al. [7]. When looking at video urodynamic parameters, maximum cystometric capacity and detrusor pressures were also improved when compared to the placebo group. Maximum cystometric capacity improved by 151 cc in the 200 units group and 168 cc in the 300 units group compared to only 16 cc in the placebo group. Maximum detrusor pressure decreased by 50 cmH₂O and 47.1 cmH₂O in the 200 and 300 units group compared to only a 2.4 cmH₂O change in the placebo group all of which are significant findings [8].

With BTX-A becoming a more well-known option for treatment of neurogenic detrusor overactivity, it was found that the number of patients treated with BTX-A has increased while the number of patients who underwent

augmentation cystoplasty for treatment of neurogenic detrusor overactivity decreased [3]. Although an accepted option for treatment of detrusor overactivity, BTX-A for detrusor overactivity is contraindicated in some patients. Patients with preexisting neuromuscular dysfunction are at risk for experiencing systemic effects of botulinumtoxin such as difficulty swallowing and muscle weakness. Although these effects are reversible, there is a boxed warning for patients with neuromuscular dysfunction that they are at higher risk for having an adverse event [9]. Patients who are unable to tolerate injections or do not desire temporary management that requires clinic visits at least twice a year should also not consider BTX-A for management of overactive bladder [3]. In general, patients with neurogenic overactive bladder undergo botulinum injections anywhere from 6- to 12-month intervals. However, patients can undergo injections more frequently as botulinum regimen in tailored to the individual rather than a standardized dose and schedule. There is still research needed on the long-term effects of botulinum injections and the ideal frequency and dosing for patients with neurogenic bladder. It is important to consider that BTX-A can cause urinary retention due to its mechanism of action and still requires patients to self-catheterize while undergoing repeated treatments. The injection procedure itself, the subsequent increased risk of urinary retention and infection of the bladder also places patients with neurogenic bladder secondary to spinal cord injury at higher risk for autonomic dysreflexia [9].

Augmentation Cystoplasty

Augmentation cystoplasty is the gold standard surgical option for neurogenic bladder management and is indicated in patients that suffer from overactive bladder and poor compliance who have failed conservative bladder therapies. The technique became popularized by Couvelair in the 1950s, initially intended for contracted tuberculosis bladders [10]. It has been shown to improve continence significantly; in a study looking at long-term outcomes of bladder augmentation, found that 61% of patients found that they were completely continent following bladder augmentation whereas 26% stated that they were socially continent with using 1–2 pads per day. Only 13% of patients in this study reported that they still suffered from incontinence following augmentation cystoplasty [11••].

There are different techniques for performing augmentation cystoplasty, in which different segments of the GI tract can be used to augment the bladder. With each segment of the GI tract comes a unique set of complications. The most used segment of bowel is terminal ileum because this has the lowest risk of metabolic abnormalities. Other options include gastric segment, cecum, and sigmoid [9].

Due to the need for a healthy bowel to prevent electrolyte imbalances, and as a result, prevent decreased bone density, growth retardation, and vitamin deficiency, augmentation cystoplasty should not be offered to patients with a history of inflammatory bowel disease, bowel anomalies, history of bowel injury from radiation, and bladder cancer [2, 12]. In reference to complications, the most serious complication is failure of augmentation cystoplasty which is typically defined as persistent symptoms despite reconstructive surgery often requiring revision. Other complications include continual mucus production due to secretory nature of the bowel, formation of bladder stones, and urinary tract infections [11••, 12].

Methods

A comprehensive review was performed using PubMed and Cochrane Library from January of 2018 to April of 2023. The search terms “neurogenic bladder,” “augmentation cystoplasty,” and “botulinumtoxin A” were used for this review.

Discussion

Both intravesical BTX-A and augmentation cystoplasty have had a significant impact in improving bladder function and quality of life in patients with refractory neurogenic detrusor overactivity. With each management having its own set of obstacles, several studies have compared the two modes of treatment since BTX-A and augmentation cystoplasty are becoming more accessible and more available to this patient population.

Urological Outcomes

In a prospective study looking at adult patients with neurogenic bladder secondary to a spinal cord injury, it was found that incontinence rates were better in patients that require CIC with an augmentation cystoplasty when compared to patients that require CIC with BTX-A [13]. When looking further into the urodynamic differences in patients who receive BTX-A for management versus augmentation cystoplasty for management, it was found that patients who underwent augmentation cystoplasty after failing BTX-A management had higher bladder capacity after augmentation cystoplasty. Cystometric bladder capacity after BTX-A was found to be $196 \text{ nml} \pm 123 \text{ ml}$ compared to $484 \text{ nml} \pm 126 \text{ ml}$ after augmentation cystoplasty ($p < 0.001$). Detrusor pressure at maximum flow (pdet) was lower after augmentation cystoplasty. Pdet after BTX-A was $27.5 \text{ ml} \pm 27.2 \text{ ml}$ compared to $9.6 \text{ ml} \pm 11.4 \text{ ml}$ after augmentation cystoplasty ($p = 0.005$). There was also a difference found

in filling volume at first sensation ($153 \text{ ml} \pm 95 \text{ ml}$ after BTX-A compared to $336 \text{ ml} \pm 136 \text{ ml}$ after augmentation cystoplasty, $p = 0.001$), filling volume at urgency sensation ($157 \text{ ml} \pm 99 \text{ ml}$ after BTX-A compared to $365 \text{ ml} \pm 130 \text{ ml}$ after augmentation cystoplasty, $p < 0.001$), PVR ($144 \text{ ml} \pm 188 \text{ ml}$ after BTX-A compared to $459 \text{ ml} \pm 147 \text{ ml}$ after augmentation cystoplasty, < 0.001) decreased detrusor pressure, and improvement in all cystometric measurements when compared to patients who continue to use BTX-A. It was also shown that patients who fail BTX-A can find significant improvement and “satisfaction” once undergoing augmentation cystoplasty [14••].

Augmentation cystoplasty is found to have a success rate of 77% (between 55–88%) with patients who fail this mode of treatment often being offered BTX-A injections after cystoplasty to improve urodynamic parameters and quality of life [15]. This is further supported by a retrospective multicenter study evaluating the clinical efficacy and urodynamic parameters in patients who receive BTX-A after augmentation cystoplasty in order to increase success rates. It was found that following BTX-A injections, 58% of patients found this to be a clinically effective option with an increase in 28% of maximum cystometric capacity and a decrease by 43% in maximum detrusor pressure [16].

Quality of Life

Quality of life scores were improved in patients that require CIC with an augmentation cystoplasty when compared to patients that require CIC with BTX-A. Patients that CIC with augmentation cystoplasty had a significantly improved total Neurogenic Bladder Symptom Score of -3.9 compared to patients that CIC with BTX-A. Patients that CIC with augmentation cystoplasty also had a significantly improved Spinal Cord Injury Quality of Life Measurement of -4.4 when compared to patients that CIC with BTX-A. In addition to qualitative findings, patients that CIC with augmentation have improved incontinence scores by -3.14 when compared to incontinence scores of patients that CIC with BTX-A based off the Neurogenic Bladder Symptom Score [13].

Using the two modes of treatment combined in the case of failed augmentation cystoplasty has also been shown to improve quality of life by preventing the need for more invasive surgery. In a study looking at improvements in urinary symptoms with BTX-A following failed augmentation cystoplasty, the most significant subjective improvement of urinary symptoms was in frequency and urgency. Despite the significant improvement of symptoms and quality of life, there were still patients in this study that failed BTX-A after augmentation cystoplasty and had to reconsider surgical correction [15].

Cost Comparison

The first cost analysis done comparing BTX-A injections to augmentation cystoplasty for adult patients with refractory neurogenic detrusor overactivity found that BTX-A injections that control symptoms for > 5 months are more cost effective in a 5-year period than augmentation cystoplasty in a patient with a complication rate of > 14% [17]. Looking at more recent studies, a projected 10-year cost model found that the mean 10-year cost of managing refractory neurogenic bladder with immediate augmentation cystoplasty in a pediatric patient was significantly higher than the mean 10 year-cost of bridging therapy with BTX-A prior to augmentation cystoplasty at \$123,573 compared to \$124,858. This model incorporated different complications that occur with each treatment modality [18]. It did not include significant electrolyte imbalances as a complication or the cost of malignancy screening in augmentation cystoplasty, although current guidelines have recommended decreased screening burden [18, 19•].

Current Practice

When looking at neurogenic lower urinary tract dysfunction provider's current practice patterns, it was found that there is significant variety in provider decision making and practice patterns. Sixty percent of providers felt that BTX-A injections have replaced the need for augmentation cystoplasty and 31% of providers believed that urinary tract malignancy risk occurrence is higher in patients who undergo augmentation cystoplasty compared to patients that are managed with more conservative options. There was also variety in surveillance for these patients, where 63% of providers felt that all patients with neurogenic bladder should undergo periodic urodynamics to make sure compliance and capacity is not worsening, compared to 25% who believed urodynamics should only be performed based on signs, symptoms, or changes of urinary symptoms which is more in agreement with the most recent AUA guidelines that recommend surveillance based on risk for upper tract deterioration [19•, 20••].

Conclusion

As treatment for refractory neurogenic detrusor overactivity advances, intravesical BTX-A and augmentation cystoplasty are effective options for management, both independently and when used in combination. From more recent literature, the approach in choosing which option is more clinically effective in terms of continence rates, improvement in urodynamic parameters, and patient satisfaction is progressing towards being more patient-centered rather than following

an algorithm that progresses from least invasive to most invasive management.

Patients that have obvious contraindications to botulinumtoxin or have low tolerance to injections and office procedures are less likely to benefit from BTX-A than from augmentation cystoplasty. However, augmentation cystoplasty remains highly invasive and is associated with more complications than minimally invasive procedures. Patients that are at high risk for electrolyte imbalances, developing sepsis from urinary tract infections, or may be noncompliant to bladder irrigations. These patients may not be appropriate candidates for augmentation cystoplasty as the morbidity from complications is higher than the morbidity from lifetime intravesical BTX-A injections. In addition, determining which option is more cost effective is also patient-centered and based on the predicted success of the treatment for the individual patient.

There are currently no patient-provider decision making aids to assist in having this discussion with patients and to support provider recommendations. Given high variability in practice, both patients and providers that are intimate with refractory neurogenic bladder would benefit from use of the current Neurogenic Lower Urinary Tract Dysfunction: AUA/SUFU Guidelines, as well as decision making aids to help make educated combined patient-provider decision making [19•, 20••, 21].

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