Research Journal of Medical Sciences 11 (4): 186-190, 2017
ISSN: 1815-9346


# The Impact of using Botulinum Toxin-A on Urinary Tract Infection in Patients with Overactive Bladder

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**Abstract:** Botulinum toxin-A has been used in the treatment of overactive bladder effectively. The objective of this study was to investigate the effects of using Botulinum Toxin-A (BoNT-A) in reducing the frequency of urinary tract infections. The 119 patients were included in this study. A retrospective design was conducted to collect data from patients who visited urology clinics at King Abdulla University Hospital. Results showed that the mean age of study participants was 25.80+22.63 years, among them were 35(29.4%) males, 68.1% of participants had at least one positive urine culture in the 6 months preceding the treatment. Among positive cultures, *E. coli* was the most prevalent organism (42.6%) and the rate of mixed growth was about 30%. Post-treatment urine cultures showed that about 44.5% were positive of which *E. coli* was the most prevalent (37%). The rate of mixed growth had increased to about 39.22%. Taken together, our study showed that using botulinum toxin-A is helpful in reducing urinary tract infection. Furthermore, botulinum toxin-A increased the frequency of mixed growth and we might speculate that using a prophylactic antibiotic course accompanied with its use is recommended.

**Key words:** Overactive bladder, botulinum toxin-A, urinary tract infection, *E. coli*, prophylactic, antibiotic

## INTRODUCTION

Botulinum Toxin type A (BoNT-A**)** was introduced for the treatment purposes of voiding dysfunction due to various causes (Lie *et al*., 2010). Its first use was to treat spine-injured patients who had detrusor-sphincter dyssynergia (Dykstra *et al*., 1988). Other studies reported its use as chemical sphincterotomy for voiding dysfunction (Phelan *et al*., 2001; Kuo, 2002). Further studies have confirmed the use of BoNT-A to treat urinary urgency and incontinence resulting from detrusor overactivity (Schurch *et al*., 2000a, b; Reitz *et al*., 2002).

It has become well established to use Botulinum Neurotoxin Type A (BoNT-A) to treat patients who have Idiopathic Detrusor Overactivity (IDO) and Neuro pathic Detrusor Overactivity (NDO) (Seth *et al*., 2013). This treatment is widely used worldwide when conventional treatments failed (Anonymous, 2006). In addition, according to Mangera *et al*. (2011), the efficacy of the toxin has been confirmed in treating several types of lower urinary tract dysfunction such as Detrusor Overactivity (DO).

BoNT/A blocks the release of acetylcholine into the synaptic gap of the neuromuscular junction causing muscle relaxation (Chancellor *et al*., 2008). Local injections result in a temporary chemodenervation and the loss or reduction of neuronal activity at the target organ (Leippold *et al*., 2003). It has been reported in the treatment of Detrusor Sphincter Dyssynergia (DSD) (Dykstra *et al*., 1988), dysfunctional voiding (Kuo, 2002), NDO (Schurch *et al*., 2000a, b; Chancellor *et al*., 2008), chronic prostatic (Zermann *et al*., 2000) and pelvic pain (Jarvis *et al*., 2004).

In most studies reporting the success of anticholinergic therapy for overactive bladder, urodynamic results were present mainly when detrusor overactivity had been detectable before drug administration (Thuroff *et al*., 1998; Jonas *et al*., 1997). Other studies presented changes in bladder diaries and Quality-of-Life (QOL) outcomes (Appell *et al*., 2001; Chapple *et al*., 2004).

D'Ancona *et al*. (2012) showed the efficacy of using BoNT-A in treating urinary tract infection. Other studies have also reported that the use of botulinum toxin was associated with both effective treatment of urinary tract infection and lowering the economic cost of treating these infections (West *et al*., 1999; Feifer and Corcos, 2008; Pannek and Kullik, 2009; Wefer *et al*., 2010). The present study aimed to

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support the previous studies in the efficacy of using botulinum toxin-A in reducing urinary tract infections.

**Study objectives:** The aim of the study was to assess whether BoTN-A injected into the detrusor muscle produces a significant change in symptoms and quality of life as shown by changes in the frequency of UTI.

## MATERIALS AND METHODS

**Study design:** A retrospective study design was conducted to collect data from files of renal patients who visited urology clinics at King Abdulla University Hospital and received intravesical BoNT-A.

**Study sample:** A total of 119 patients were included in the study. Some of those patients received more than one intravesical BoTN-A injection, only the procedures that were more than 1 year apart were included in the analysis; a total of 119 encounters were included in our analysis.

**Study procedure:** Electronic medical charts of participants were reviewed, summarized and the data extracted was entered into excel sheet. Data included the following variables:

- Demographics including age and gender
- Clinical variables including the use of BoNT-A, presenting conditions and kidney function
- Frequency of positive urine cultures 6 months before BoNT-A and 1 and 6 months after the injection
- The type of organism grown in urine cultures before and after intravesical BoNT-A injection
- Statistical analysis: the data was analyzed using SPSS Version 21. The data was presented as means and standard deviations for non-categorical variables, frequency and percentages for categorical variables

## RESULTS AND DISCUSSION

Demographic variables of participants are discussed in Table 1.

**Clinical variables associated with study participants:** As seen in Table 2, all study participants received BoNT-A. Overactive bladder was diagnosed in 80 cases out of 89; of the total 119 encounters, 92.44% received the BoNT-A as treatment for overactive bladder, the indication in the remaining cases included interstitial cystitis and small bladder capacity. Kidney Function Test (KFT) was reported as normal in the majority of cases (98.4%), 21 subjects (17.6%) had chronic kidney disease (Fig. 1).

The results of pre BoNT-A urine cultures showed that 31.9% of cases had a negative urine culture, whereas about 68.1% of cultures were positive (Table 2 and Fig. 2). About 254 positive cultures were

Table 1: Demographics variables of participants

| Variables | Description |
|---|---|
| **Gender (N, %)** | |
| Males | 35 (29.4%) |
| Females | 84 (70.6) |
| Age (M±SD) years | 25.80±22.63 |

Table 2: Clinical variables associated with study participants

| Variables | Description |
|---|---|
| The use of botulinum toxin-A (N, %) | 119 (100%) |
| **Presenting cases (N, %)** | |
| Hyperactive bladder | 110 (92.44%) |
| Others | 9 (7.56%) |
| **KFT (N, %)** | |
| Normal | 98 (82.4%) |
| Chronic kidney disease | 21 (17.6%) |
| **Urine culture before BoNT-A (N, %)** | |
| Negative culture | 38 (31.9%) |
| Positive culture | 81 (68.1%) |
| Total number of positive cultures | 254 |
| **Types of microbes (%)** | |
| *E. coli* | 42.63% |
| Mixed infection | 29.50% |
| Other organisms | 27.87% |
| **Urine culture 0-6 months after BoNT-A (N, %)** | |
| Negative culture | 66 (55.5%) |
| Positive culture | 53 (44.5%) |
| Total number of positive cultures | 109 |
| **Types of microbes (%)** | |
| *E. coli* | 37.26 |
| Mixed infection | 39.22 |
| Other organisms | 23.52 |
| **Urine culture 0-1 months after BoNT-A (N, %)** | |
| Negative culture | 98 (82.4%) |
| Positive culture | 21 (17.6%) |
| Total number of positive cultures | 22 |
| **Urine culture 1-6 months after BoNT-A (N, %)** | |
| Negative culture | 71 (59.7%) |
| Positive culture | 48 (40.3%) |
| Total number of positive cultures | 87 |

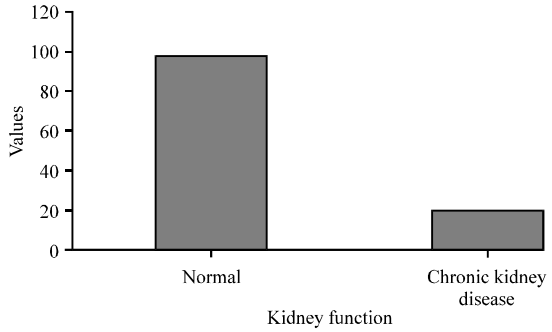


Fig. 1: The frequency of KFT in study participants

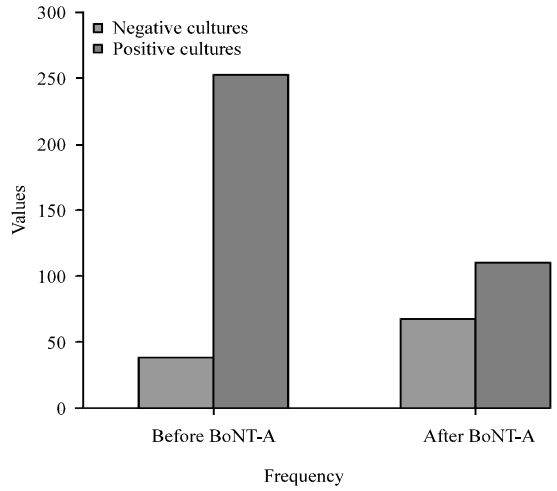


Fig. 2: The frequency of positive and negative cultures in before and after BoNT-A

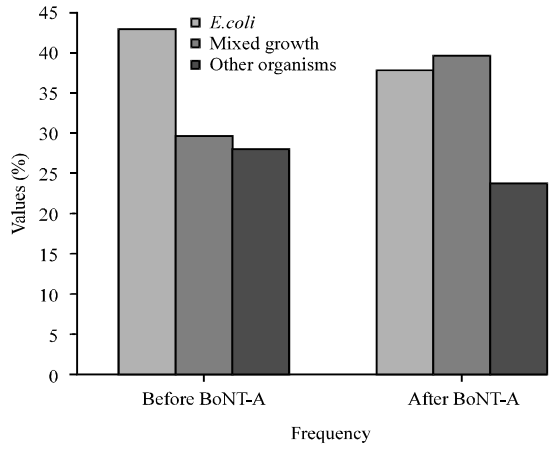


Fig. 3: The frequency of different organisms grown before and after BoNT-A injection

obtained, the majority of cases (42.63%) were positive for *E. coli*, followed by *Pseudomonas aeruginosa* (9.84%), similar culture rates were reported for *Enterococcus fecalis* and *Morganella morganii*, Klebsiella was noted in (3.28%) and Candida in (1.64%). Mixed growth was reported in about 30% of culture results whereas insignificant growth was reported in 6.55% of cases where the organism were not specified (Fig. 3).

In the 6 months following BoNT-A injection, 109 positive cultures were obtained in 44.5% of the study participants while 55.5% had negative results (Table 2 and Fig. 2). The organisms isolated include *E.coli* (37.26%), *Enterococcus fecalis* (11.76%), pseudomonas (7.84%), *K. pneumonia* (1.96%), mixed infection (39.22%) and insignificant growth (1.96%) (Fig. 3).

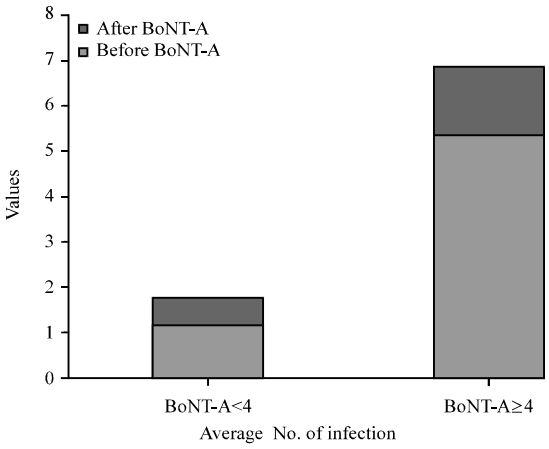


Fig. 4: A comparison of the average number of infections before and after BoNT-A in patients who had <4 or ≥4 infections in the 6 months preceding the procedure

Following the injection, 21 patients had a positive culture (17.6%) in the first month compared with 40.3% in the next 5 months. Finally, despite the significant reduction in the number of positive cultures after BoNT-A, we noticed that the patients who benefited more were hose who had more than 4 positive cultures in the 6 months preceding the injection of BoNT-A with a reduction in the average number of positive cultures from 5.36-1.46; compared to 1.18-0.6 in those with <4 in preceding 6 months. The average reduction rate of 72.8% compared to 49.1% in both groups, respectively (Fig. 4).

The main objective of this study was to investigate the efficacy of using botulinum toxin-A in the occurrence of urinary tract infections. The study revealed that the incidence of urinary tract infection was 68.1% before administration of intravesical BoNT-A which dropped to 44.5% after the procedure. These findings are consistent with several previous studies which reported the use of BoNT-A to be effective in reducing both the frequency and treatment cost of urinary tract infections (West *et al*., 1999; Feifer and Corcos, 2008; Pannek and Kullik, 2009; Wefer *et al*., 2010; D'Ancona *et al*., 2012).

For the patients who still had infections after the procedure (44.5%), the number of infections decreased significantly by almost half (254-109 positive cultures). Almost one fifth of the infections (20.2%) occurred in the first month after the procedure which raises the question whether prophylactic antibiotics should be used preoperatively. There has been no consensus on the use of antibiotics as prophylaxis before or after the procedure; even when used there is no agreement on the

type, the duration or even timing of antibiotics administration (Jimenez-Cidre and Arlandis-Guzman, 2016). Upon literature review, the Spanish group set their own guidelines, where antibiotic prophylaxis is recommended to reduce the risk of urinary tract infections. Jimenez-Cidre and Arlandis-Guzman (2016). Harris *et al.* (2011) recorded the rate of symptomatic UTIs in patients receiving BoNT-A injections, their data showed that patients who received prophylactic antibiotics preoperatively were 4.8-times less likely to develop symptomatic UTI.

Although, the most prevalent pathogen was *E. coli* in pre and post-therapy cultures but the use of botulinum toxin-A reduced the frequency of positive cultures for this pathogen. These findings are consistent with other studies including the study by Mouttalib *et al.* (2010) where the urinary colonization rate was around 30% at 6 days and 6 weeks after the injection. Despite the reduction in the rate of *E. coli*, our findings showed a concomitant increase in the rate of mixed bacterial growth after using botulinum toxin-A, a phenomenon indicating a potential impact on immune system.

The risk of developing a urinary tract infection has improved after the administration of BoTN-A. The patients who benefited most were those who had a higher frequency of infections (≥4/6 months) before the procedure with a risk reduction rate of 72.8% compared to 49.1% in those with fewer infections.

## CONCLUSION

The present study showed efficacy of using botulinum toxin-A in reducing urinary tract infection; especially in those with higher frequency of infections. Furthermore, botulinum toxin-A increased the frequency of mixed bacterial growth in urine cultures; indicating a potential impact on immune response. We suggest using prophylactic antibiotics in patients receiving BoNT-A injections either perioperatively or during the first month after the procedure.

## ACKNOWLEDGEMENTS

The researchers would like to thank both 5th year medical students Mutaz A. Alrawashdeh and Aya N. Al Tawalbeh from medical school at Jordan University of Science and Technology for their efforts in collecting the data for this study.

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