Abstract #45 - Intravesical OnabotulinumtoxinA. What patients are most at risk of the most common adverse events?

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Introduction

- The negative impacts of idiopathic overactive baldder (iOAB) on health-related quality of life, as well as a significant economic burden, are well documented.[1,2]
- This study's purpose is to review the rates of urinary retention requiring intermittent catheterization (IC) post intravesical OnabotulinumtoxinA (BTN/A) injection for iOAB from a single practicing specialist urological surgeon.
- OAB treatment
  - First line → lifestyle modifications
  - Second Line → pharmaceutical anticholinergic agents.
  - Third line → intravesical OnabotulinumtoxinA (BTN/A)
- OnabotulinumtoxinA is becoming a well-used tool for management of overactive detrusor refractory to medical management, with its efficacy and safety profile well documented in the literature.[3-5]
- A commonly reported side effect post this procedure is urinary retention requiring intermittent catheterization (IC). Allergan®, the primary botox preparation used for this procedure, conducted a clinical trial that reports urinary retention requiring IC at approximately 6% for patients post treatment of idiopathic detrusor overactivity.[4]
- Despite this, internationally, multiple studies report rates of IC notably higher, up to 43% in some populations.[5-7]
- This study aims to review the experience of a specialist urological surgeon to assess if current quoted rates of urinary retention are in line with prior experiences; as well as to identify preoperative predictors for retention to help guide future informed consent and patient management.

Methods and Materials

- Study methodology utilised a retrospective review of a single Australian urologist. The two primary outcomes were post-void residual (PVR) post 100units of intravesical OnabotulinumtoxinA and the other was identifying rate of intermittent catheterization within this cohort. Electronic medical records were collected for all female patients who underwent intravesical OnabotulinumtoxinA for management of idiopathic detrusor overactivity. Patient data was retrospectively collected from February 2016 to March 2021. Neurogenic OAB patients were excluded. Further exclusion for patients if they did not have a complete preoperative urodynamic assessment available for analysis, previous history of IC, prior retention or if lost to follow up
- Logistical regression was employed to establish statistical significance.
- All patients had a preoperative urine microculture completed one week pre-operatively. If a positive result was identified, they received a minimum of 3 days of appropriate sensitive antibiotics prior to the procedure. Each patient had 100units of OnabotulinumtoxinA diluted in 30mls of normal saline, delivered to the bladder in 1ml aliquots sparing the trigone. Patients were seen 2-3 weeks postoperatively and a post-void bladder scan was completed. Depending on patients voiding volumes and PVR a clinical decision was made by the urologist, who has a special interest in functional urology, whether to commence IC
- The associations between requirement of postoperative IC and age, preoperative PVR, prior sling, preoperative urinary tract infection (UTI), maximum detrusor pressure at peak flow during urodynamics (pDet@Qmax), detrusor overactivity and bladder capacity were assessed with multiple logistic regression.

	Total (n=94)	No IC (n=60)	IC (n=34)	p-value
Patients	94	61 (64%)	34 (36%)	
Age (years)^	69.7 (17.2)	67.5 (19.3)	73.6 (11.8)	0.10
Past medical history risk factor:				
Stroke or TIA *	25 (27%)	17 (28%)	8 (24%)	0.61
Diabetes **	12 (13%)	9 (15%)	3 (9%)	0.39
Pelvic radiotherapy **	2 (2%)	2 (3%)	0 (0%)	0.28
Prior sling *	16 (17%)	5 (8%)	11 (32%)	0.003
Prior vaginal prolapse surgery *	18 (19%)	6 (10%)	12 (35%)	0.003
Prior SNS **	5 (5%)	4 (7%)	1 (3%)	0.44
Prior urethral stenosis **	2 (2%)	1 (2%)	1 (3%)	0.68
Interstitial cystitis **	6 (6%)	5 (8%)	1 (3%)	0.30
Preoperative urinary tract infection *	15 (17%)	5 (9%)	10 (29%)	0.01
Preoperative PVR (mL)* (n=91)				
0-50	81 (86%)	52 (87%)	29 (85%)	0.68
51-100	6 (6%)	3 (5%)	3 (9%)	
>101	4 (4%)	2 (3%)	2 (6%)	
Preoperative urodynamics assessment:				
pDet@Qmax (cmH2O)^ (n=79)	23.5 (12.6)	23.4 (12.9)	23.5 (12.3)	0.97
Detrusor overactivity seen during urodynamics *	51 (54%)	32 (53%)	19 (56%)	0.81
Bladder capacity (mL)^	349.0 (136.5)	336.6 (148.1)	370.9 (112.0)	0.24
Qmax (mL/s) (maximum urinary flow)^ (n=79)	21.0 (11.7)	23.3 (13.2)	16.7 (6.4)	0.017
Normal compliance * (n=91)	75 (82%)	48 (84%)	27 (79%)	0.56

Table 1. Patient demographics
(n=94)^ reported as mean (standard deviation) with p-value from student t test. *reported as number and percentage with p-value from *chi-squared test, or **Fisher exact test if cell n<5. ~defined as presence of any of the risk factors (listed in the table below the total). TIA (transient Ischaemic attack), SNS (sacral nerve stimulation), PVR (post void residual), pDet@Qmax (maximum detrusor pressure at peak flow on urodynamics)

Results

•Demographics and preoperative characteristics of patients (total and grouped by required IC) are presented in table 1.

•In total 34 (36%) of patients in the sample required IC. The average age was 69.8 years (SD 17.1). Of patients requiring IC, 32% had a prior sling, 35% had prior vaginal prolapse surgery, and 29% had a preoperative UTI, with evidence of a bivariate association between IC and prior sling, prior vaginal prolapse surgery, preoperative UTI, maximum flow (Qmax) and preoperative PVR. Table 2 shows the results of a multiple logistic regression analysis. It assesses the relationship between clinical factors thought to predict urinary retention and the need for IC.

•Only 76 patients with complete data can be included in this model. The odds of requiring IC for patients with a prior sling is 7 times greater than for those without a prior sling, holding all other variables constant. Similarly, the odds of requiring IC for patients with preoperative UTI is 3 times greater than those without a UTI. It is also worth noting that all patients were treated with appropriate antibiotic therapy prior to their procedure

•There is strong evidence of an association between prior sling and IC (OR 6.96, 95%CI: 1.57, 30.91, p-value 0.011), and mild evidence of association between preoperative UTI and IC (OR 3.97, 95%CI: 0.93,16.94, p-value 0.062), however, there is no evidence of relationship between IC and any other risk factor in our sample that may have been thought to be predictive of IC.

Table 2. Association between intermittent catheterisation and patient risk factors for urinary retention. ^ n = 76 available for full regression model.

Exposure	OR	95% CI	p-value
Age	1.01	(0.98, 1.05)	0.553
Preoperative PVR (categorical^)	1.09	(0.32, 3.74)	0.888
Preoperative UTI	2.89	(0.61, 13.55)	0.179
Prior sling	6.85	(1.52, 30.92)	0.012
Prior vaginal prolapse surgery	3.05	(0.73, 12.75)	0.127
pDet@Qmax	1.00	(0.96, 1.04)	0.929
Proven detrusor activity	1.13	(0.35, 3.72)	0.834
Bladder capacity	1.00	(1.00, 1.01)	0.283

Table 3. Post operative PVR and initiation of intermittent catheterization. Number and percentage of patients within each category (n=94)

Postoperative PVR (mL)	Total (n=94)	No IC (n=60)	IC (n=34)	Proportion started on IC
Units of 100ml				
<100	41 (44%)	41 (68%)	0 (0%)	0 (0%)
100-199	10 (11%)	9 (15%)	1 (3%)	1/10 (10%)
200-299	15 (16%)	8 (13%)	7 (21%)	7/15 (47%)
300-399	11 (12%)	1 (2%)	10 (29%)	10/11 (91%)
>=400	17 (18%)	1 (2%)	16 (47%)	16/17 (94%)

Discussion

- Despite being limited by retrospective methodology, these results are in line with internationally recognized studies with similar rates of IC post 100units OnabotulinumtoxinA,[6] which are up to six times those reported from Chappel et al.[3]
- It is difficult to determine if the Chappel et al trial excluded patients with positive preoperative urine microculture results, but they did exclude key patients who had prior sling, prior vaginal prolapse surgery.
- If all patients with these clinical characteristics were excluded from our dataset, the overall rate of IC would be 22% (n=13).
- Multivariable analysis within this subset (n=45 with complete data of the n=60 subset) can assess only relationships between ISC and age, preoperative PVR, detrusor overactivity, bladder capacity, and maximum flow. There was no evidence of association between IC and any of these possible risk factors in bivariate or multivariate analyses of this subset of 60 patients.
- Patients who undergo intravesical botox injections for iOAB would benefit from a greater understanding of the risk of urinary retention and IC when consenting to intravesical BTN/A for iOAB. Further studies should look to larger cohorts, preferably with multisite participation and analysis to evaluate if this trend is more prevalent within urological practice, with the inclusion of patients representative of complex urological history.
- Limitations. We acknowledge that the retrospective nature of data collection may result in a selection bias and that our review was limited by a single surgeon.

Conclusion

Prior urethral sling surgery and positive preoperative UTI, despite treatment, were found to be associated with a higher rate of initiation of intermittent self-catheterization. The rate of IC initiation of 36% was higher than reported in prior clinical trials.

References

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