Approach to female urinary incontinence: Part 1: Medical Management

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Introduction
Urinary incontinence is defined as the involuntary loss of urine.1 It is a ubiquitous disorder, thought to occur more commonly than more familiar health issues such as hypertension, diabetes, and depression. It is a condition whose profile of affected patients includes women of all age groups and which transcends socio-economic and cultural circumstance.2 Given the above, the social, emotional, and economic impact of the disease on individuals and communities is self-evident.

The true prevalence of urinary incontinence worldwide, and in South Africa is essentially unknown. Community based studies have reported the prevalence as ranging between 14% and 67%, showing a large discrepancy from the estimates of physician-based studies, which show an estimated prevalence of between 0.5-5%.2,3,4 This disparity is thought to arise from a combination of under-reporting, under-diagnosis, and under-treatment of the disease.

Types of urinary incontinence
For clinical purposes, incontinence can be divided into three subtypes as defined by the International Urogynaecological Association / International Continence Society (IUGA/ICS) joint report.5

SUI makes up approximately half of all reported urinary incontinence, with the next prevalent subtype being MUI making up around a third, and UUI accounting for just over 10% of all urinary incontinence.6

Pathophysiology
SUI: To maintain continence under stress (i.e. during periods of raised abdominal pressure, the urethra and bladder neck must maintain satisfactory intra-urethral pressures at rest. Inadequate intra-urethral pressures will allow for incomplete transmission of abdominal pressure to the urethra, and therefore compromised continence.2

Proximal urethra hypermobility (as result of disruption of the musculofascial architecture) and descent have also been postulated as contributing to SUI.

Nerve dysfunction, particularly secondary to pudendal nerve damage during childbirth may also contribute to SUI by causing atrophy of portions of the levator ani and/or other voluntary muscles forming the pelvic floor and perineum.2 Gyhagen et al. showed that 20 years later, vaginal delivery correlated with a 67% increased risk of SUI. They found that when compared to caesarean section, the risk of UI following vaginal delivery after 10 years was 275%, illustrating that to prevent one case of UI it is necessary to perform 9 caesarean sections.6

Other factors which may contribute to the development or severity of SUI include disease which cause chronically raised abdominal pressures such as obesity, chronic cough of diverse aetiology, and pelvic tumours.2,6

UUI:
The pathophysiology of UUI, otherwise known as Overactive Bladder (wet) is complex and multifactorial. It is thought that the symptoms of UUI can be brought about by dysfunction in smooth muscle contractility and/or changes in bladder innervation. Specific conditions such as outlet obstruction, inflammation, and spinal cord injury, and even some mood disorders (such as depression, anxiety, and attention deficit disorder) have all been linked to UUI.7

Assessment and investigations
According to the American College of Obstetricians and Gynaecologists, there are six aspects of clinical evaluation to be covered for all patients with UI. Although typically described for the evaluation of uncomplicated stress incontinence, the principles outlined apply to all patients who present with the complaint of involuntary loss of urine.8

These are:
1. History
2. Urinalysis
3. Physical examination
4. Clinical demonstration of SUI
5. Urethral mobility assessment
6. Postvoid residual volume assessment

History:
Important aspects of the history include elucidating the type and nature of the incontinence, the frequency and severity of the disease, as well as its impact on daily living. Validated questionnaires are available to assist the clinician in the assessment of disease severity and determine the proportionate contributions of urge and stress symptoms to the overall clinical picture (see table 2). Short form questionnaires are quick, simple and relatively easy to complete, and their value in the characterisation of incontinence in the clinical setting should not be underestimated.

Urinalysis:
The main purpose of urinalysis is to exclude underlying infections, which can mimic and/or exacerbate incontinence symptoms, and should be treated prior to further investigations or management.

Physical examination:
The aim of the physical examination is to eliminate any factors which may potentially confound or aggravate the assessment or management of the incontinence, such as vaginal discharge, urethral diverticulae, and extra-urethral causes of incontinence such as vaginal fistulae or ectopic ureters. Pelvic organ prolapse is also known to complicate the assessment of incontinence, and in these cases an effort should be made to reduce the prolapse to unmask potential stress incontinence during the physical examination.

Clinical demonstration of SUI:
It is important to clinically demonstrate leakage of urine prior to incontinence procedures. The patient should have a comfortably full bladder (approximately 300ml), and if no leakage is demonstrated on cough in the supine position, the test should be repeated with the patient standing before the test can be deemed negative. Leakage of fluid from the urethra coinciding with cough or Valsalva is pathognomonic of SUI. Delayed urine leakage may be suggestive of cough induced detrusor overactivity. In the case of delayed emptying, or in cases where SUI cannot be demonstrated despite clear symptomatology described by the patient, urodynamic studies may be appropriate.

Urethral mobility assessment:
Tests of urethral mobility include the visualisation of movement of an ear bud placed in the urethra, palpation, and the use of ultrasound. When the urethra is displaced more than thirty degrees from the horizontal plane (with the patient straining in the supine or lithotomy position) and decent of the bladder neck equal to or over 25 mm, it is regarded as hypermobile (see fig 1). Recently, the ear bud test has been replaced by trans-perineal ultrasound (TPUS) as the standard method of urethral mobility assessment, due to increased patient discomfort with the former. Urethral mobility is indicative of SUI, and its presence is a marker for successful anti-incontinence surgery. In the absence of urethral mobility, it may behove physicians to consider alternatives to traditional anti-incontinence surgery such as urethral bulking agents.

Post void residual volumes:
Post void residual (PVR) volumes are an important measure of voiding function, and only when volumes are less than 150ml should a patient be considered as having uncomplicated SUI. Large post-void residual volumes should alert the physician to the possibility of a dysfunction in the mechanism of bladder emptying, or to chronic urinary retention, and should prompt further evaluation of the above.

Further investigations are directed by your findings and have been detailed in the table below.

| Table 2. Validated Questionnaires to evaluate the impact of urinary incontinence as suggested by the ACOG. |
|-----------------|---------------------------------------------------------------|
| UDI             | Urogenital Distress Inventory                                 |
| IIQ             | Incontinence Impact Questionnaire                             |
| QUIID           | Questionnaire for Urinary Incontinence Diagnosis             |
| ISI             | Incontinence Severity Index                                   |
| ICIQ            | International Consultation in Incontinence Questionnaire      |

**Table 3. Special investigations in the assessment of urinary incontinence.**

**SIMPLE INVESTIGATIONS**
- Screening for diabetes
- Screening for urinary tract infections
- Measurement of PVR
- Bladder diary

**SPECIAL INVESTIGATIONS**
- Urodynamic Studies (UDS) with/without EMG
- Urethral pressure profilometry (UPP)
- TPUS

Treatment options
Conservative management:
General measures such as limiting overall fluid intake, decreasing intake of caffeine, alcohol, and carbonated drinks are standard practice in the initial management of UI. Other strategies such as weight loss and smoking cessation are also recommended.

SUI: Pelvic floor muscle therapy forms the foundation of conservative management for SUI. Although limited by small study
sizes and a number of confounding factors a 2011 meta-analysis of the available research of 21 studies including 1490 women demonstrated that women who undertook regular and continual PFMT with a practitioner directing their exercise and supervising their progress showed superior subjective improvement. This in conjunction with manual or biofeedback strategies can improve exercise technique and outcomes. Devices, including catheters, incontinence tampons, incontinence pessaries are available for those patients who are unfit for, or do not desire surgery including pregnant women, and those in whom previous surgical interventions have failed. Benefits of such conservative therapy includes a low risk profile and cost, and they achieve rapid results.

UUI: In the absence of cognitive impairment, lifestyle modification is the first line in the management of UUI. This includes but is not limited to bladder drill/retraining, pelvic floor muscle therapy (PFMT) including the use of biofeedback strategies. Patients with some element of cognitive impairment present more of a challenge in this regard, but some improvement has been reported with methods such as scheduled voiding, prompted voiding and habit training.

Table 4. Main anticholinergics available in South Africa.21

<table>
<thead>
<tr>
<th>Antimuscarinics</th>
<th>Drug name</th>
<th>Brand name South Africa</th>
<th>Dosage guidance</th>
<th>Special features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolterodine Tartrate</td>
<td>Detrusitol XL</td>
<td>Uricon</td>
<td>4mg daily</td>
<td>Quaternary amine. Theroretically less CNS effects as does not cross blood brain barrier</td>
</tr>
<tr>
<td>Trospium Chloride</td>
<td>Vescicare</td>
<td></td>
<td>5mg - 10 mg daily</td>
<td></td>
</tr>
<tr>
<td>Solifenacin Succinate</td>
<td>Enablex</td>
<td></td>
<td>7.5mg – 15mg three times daily</td>
<td>Tertiary amine derivative. Selective M3 receptor antagonist</td>
</tr>
<tr>
<td>Darifenacin</td>
<td>Detranorm</td>
<td></td>
<td>15mg daily to three times daily</td>
<td>Tertiary amine with antimuscarinic and musculotrophic effects. Also available as ER (Detranorm XL, dose 30mg daily). Long term clinical data limited.</td>
</tr>
</tbody>
</table>

that the long term effects of the drug were yet to be established, the authors concluded that further good quality trials on the topic are needed before consensus on the topic could be reached.13,15 As of last publication, the UK National Institute for Health and Care Excellence (NICE) guideline states that practitioners should not consider the use of Duloxetine as first line treatment in women with stress predominant SUI. It goes on to state that while it does not generally consider Duloxetine to be a viable second-line treatment, it may be offered to patients who show a preference for medical management or who are not surgical candidates for whatever reason.24

Oestrogen: The use of Oestrogen for the treatment of SUI is contentious. Multiple studies have been undertaken to elucidate the relationship between SUI and circulating endogenous sex hormones, with conflicting results. This conflict can partially be explained by the fact that many of the available studies have looked at the effect of oestrogen and urinary incontinence (as an umbrella term), or focused specifically on UUI, and the role of oestrogen and SUI has not been fully explored.12,13 Compounding the conflict is the fact that the effect of the hormone appears to differ according to the route of administration. A Cochrane review in 2012 demonstrated that local oestrogen creams had a small favourable effect on urinary incontinence. In contrast to this, oral oestrogens appeared to worsen urinary tract symptoms. The authors of the 2012 review concluded that additional large robust trials were needed before a thorough recommendation could be provided.17 The European Association of Urology and NICE Guidelines currently endorse the use of topical vaginal creams in postmenopausal women with UI in the presence of vaginal atrophy.14,15 Recently, a prospective multinational pilot study looking at the effect of topical vaginal oestrogen creams on vaginal atrophy and SUI symptoms was undertaken, with South Africa as one of the participating centres. The authors found that subjective SUI symptoms in postmenopausal women were lessened by topical oestrogen creams. Although further long term follow-up is needed, in view of the fact that oestrogen cream is safe, relatively inexpensive, and readily available- it may be of use in patients requesting conservative management, or for those awaiting definitive surgical treatment.16

Desmopressin: There is some evidence that the use of Desmopressin, a synthetic vasopressin, may decrease urinary incontinence episodes within
four hours, but that no long-term improvement is shown with chronic use. Based on the current evidence, the EAU therefore recommends that Desmopressin should not be used as a long-term measure for the control of incontinence, but may be used on occasion as interim measure. Patients treated in this fashion must be warned that the drug is not currently approved by the FDA for the purpose. The NICE guidelines state that Desmopressin should be offered only to that subset of patients that suffer from nocturia in addition to daytime UI, and caution against its use in patients with cystic fibrosis, and those over 65 years of age with pre-existing cardiovascular dysfunction.

UII

Anticholinergics:

Although they vary somewhat in structure and functional profile, all anticholinergics affect the detrusor muscle and its afferent innervation. Anticholinergics are widely used in the treatment of UIU, the merits being that they are relatively safe, can be quite inexpensive, and have shown significant efficacy over placebo. The major disadvantage of anticholinergic medications is the side effect profile, particularly the effect on cognitive function. Given that the prevalence of urinary incontinence increases with age, which is in itself a risk factor for altered cognitive states, the addition of anticholinergics may increase the probability of mental health decline. In an attempt to circumvent the adverse side effects, various iterations of anticholinergics are available on the market today. Head to head comparison data is lacking, but in 2012 a systematic review by the Cochrane Library found that the continuation rate for Tolterodine when compared to Oxybutynin was higher due to an improved side effect profile. In terms of quality of life, cure or improvement, and adverse effects, Solifenacin was found to perform better than Tolterodine. Fesoterodine was also found to perform better than Tolterodine in the above categories, but had a higher drug withdrawal rate due to adverse effects. Extended release (ER) formulations (of Oxybutinin and Tolerodine had equivalent efficacy, but with mild improvement of dry mouth at up to three month that was more marked in the ER Tolerodine group.

Mirabegron:

Stimulation of the sympathetic nervous system via β3-receptor agonists causes relaxation of the detrusor muscle, facilitating storage of urine by the bladder. Mirebeogron is a selective β3-agonist which has been the focus of large, phase III randomised controlled trials, which concluded that use of Mirebeogron effected a reduction in incontinence episodes, and an improvement of quality of life when compared to placebo. A 2014 mixed treatment comparison analysis of 44 studies found that compared to most of the drugs currently approved for UIU in Europe, Mirebeogron showed a effectiveness against UIUI. The only exception to this was Solifenacin at a dose of 10mg which proved superior in improving frequency of UIU episodes when compared to 50mg Mirebeogron. It should be noted, however that patients administered Solifenacin at that dose, or Fesoteradine 8mg reported the highest incidence of detrusor overactivity, specifically dry mouth. In contrast, the incidence of dry mouth associated with Mirebeogron was equitable with placebo. Given the reduction in antimuscarinic side effects, Mirebeogron may prove to be a viable option for those patients who require an alternative to anticholinergics, whether due to adverse effects or non responders. Combinations of newer generation anticholinergics and Mirebeogron have also been investigated, with the aim of minimising adverse effects while obtaining maximal drug efficacy. The combinations of Solifenacin and Mirebeogron for the treatment of UIU has shown significant gains in terms of frequency and urgency, without the adverse effects associated with higher dose anticholinergic monotherapy. The most common adverse events associated with Mirabegron include hypertension, nasopharyngitis, headache, and urinary tract infections. Due to its effect on the blood pressure, it should be used with caution on patients with uncontrolled hypertension.

Oestrogen:

The bulk of the evidence pertaining to Oestrogen therapy and incontinence has focused on the treatment of UIU. Although the exact pathophysiology of oestrogen in the treatment remains unclear, current evidence supports the use of oestrogen in postmenopausal women. The pathophysiology behind this may be merely the correcting that atrophic changes in the vagina, or may be due to an effect on the bladder itself.

Conclusion:

Female urinary incontinence is a condition which, due to many factors including cultural and societal norms and taboos, is still under-reported and under-diagnosed. Global and local statistics on the subject are scanty, and even where we have been able to institute medical therapies large gaps still exist in our knowledge due to limited good quality data. As practitioners who has sustained relationships with their patient it behooves us to screen for, assess, and manage such conditions as they arise in our patient who we see as a matter of course yearly for annual review. Complicated cases should be referred to subspecialists for further assessment an opinion.

References:

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