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Review Article

Female urinary incontinence: a systematic overview and non-surgical treatment

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ABSTRACT

Urinary Incontinence was acknowledged in 1998 by World Health Organization as a disease, to raise the awareness of the condition**.** Literature suggests that 50% of the incontinent women would be less than 50 years of age. Despite the great evolution in the area of gynecology, incontinence remains a real problem for number of women around the world. In some area the embarrassing nature of urinary incontinence has lead women to hide the existence of syndromes. Most of the women will seek health care at a late stage, when there is little or nothing to do. Alternative opportunity of surgery reveal to be a costly choice as popular believes that urinary incontinence is a fatality to all women. Little is known or rather little is provided to women in order to understand the process which causes urinary incontinence, whereas to the shame inflicted to them. This review paper aims to give a systematic overview of female urinary incontinence, and to a certain extent to present its non-surgical approach.

Keywords: Urinary incontinence, Obstetric fistula, Non-surgical treatment, Pharmacotherapy

INTRODUCTION

Urinary incontinence is common in women, but is under-reported and under treated. Despite the great work of awareness of Urinary Incontinence (UI) by the World Health Organization (WHO), popular belief is still an essential problem to providing care to the numerous women suffering of urinary incontinence. UI is more prevalent than most chronic diseases yet largely under-reported. In a study conducted in sub-Sahara region, 77% of patients with UI would not seek medical care,[1] same results were found in another study in Taiwan where only an average of 29% of women seeking medical advice on UI.[2] In Majorca (Spain), 1 woman out of 4 suffers from UI and would seek medical care when quality of life has decreased, highlighting the severity of the condition.[3] Kinchen et al. had come to the same conclusion earlier in their study, which is the sad reflection of UI reality.[4] Many women suffer in silence,[5] believing that it is a normal aging process, however research reported countless situation related to leak of urine.

METHODOLOGY

A computerized literature search was performed to identify all published articles on the subject. The following databases: PubMed (Medline), Highwire, Google Scholar, Scopus, Cochrane Database of Systematic Reviews and Cochrane Library were used. The search strategy involved entry of the word "urinary incontinence" with a combination of other words such as, "classification", "assessment", "obstretic fistula", "physiotherapy", "pharmacotherapy", "complementary alternative treatment", "non-surgical treatment", and "female" or "women". English-language full publications and English published abstracts (case reports, prospective study, clinical trials and scientific guidelines) were

reviewed. The data were extracted and presented here in an optic to review this subject.

DEFINITION

According to International Continence Society (ICS), urinary incontinence is a storage symptom and defined as the complaint of any involuntary loss of urine even if the leak does not cause a social or hygienic problem.[6] UI is a common symptom that can affect women of all ages, with a wide range of severity and nature. While rarely life-threatening, incontinence may seriously influence the physical, psychological and social wellbeing of affected individuals. The impact on the families and carers of women with UI may be profound, and the resource implications for the health service considerable.[7]

PREVALENCE AND CLASSIFICATION

Female urinary incontinence differs greatly between less developed and more developed countries. Even after taking into account differences in definitions, epidemiology methodology and demographic characteristics, there exists a large variation in the estimated prevalence of UI.[8-12] The involuntary loss of urine has a prevalence of approximately 25% in young women (aged 14 to 21 years),[13] 44% to 57% in middle-aged and postmenopausal women (aged 40 to 60 years),[14] and 75% in elderly women (aged ≥75 years).[15] However, these statistics may be underestimated due to the fact that at least half of incontinent women do not report the issue to their physicians as revealed some studies.[16,17]

With the complexity and difficulties to identify with accuracy urinary incontinence; terms such as Lower Urinary Tract Symptoms (LUTS) try to designate both urinary urgency and overactive bladder. In the past years, 3 important definitions have served to identify urinary Incontinence: Stress Urinary Incontinence (SUI), Urge Urinary Incontinence (UUI) and Mixed Urinary Incontinence (MUI). The ICS has published several new symptoms categories - nocturnal enuresis (the complaint of loss of urine during sleep); continuous urinary incontinence (the complaint of continuous leakage, classically associated with a fistula or urethral diverticulum); situational incontinence may be reported, e.g. giggle incontinence.[18] Moreover, incontinence in the elderly has been categorised individually as acute or chronic.[19] Known as "transient" incontinence, it is relatively common in the elderly, affecting up to one-third of community-dwelling elderly population and up to 50% of inpatients.[20,21] Another type of incontinence known as "functional incontinence" includes cases of urinary incontinence where no organic cause can be found by which implying that urinary tract function is normal whereas research shows that normal urinary tract function is the exception, even in continent subjects, and is rare in incontinent.[18,21] There is also an uncharacterized phenomenon of UI diagnosed in children. This type of UI is called "Phantom" Urinary Incontinence (PUI). In this condition, children with lower urinary tract symptoms and constipation feel the sensation of wetness because of presumed urinary incontinence despite being completely dry.[22] Most children presenting with this condition had a prior diagnosis of Obsessive-Compulsive Disorder (OCD) or OCD traits as reported by parents.

The prevalence of UI by type in female incontinence is represented approximately as follows: SUI (50%), MUI (32%), UUI (14%) and the remaining 4% represent other types of incontinence.[23] However, what we know about UI are conclusions obtained from studies and observations on late stage of the condition.[24] ICS has set a crucial distinction on the UI condition, symptoms, signs and urodynamic diagnosis which are shown in Table 1.[24]

Table 1: Terminology for urinary incontinence.

	Symptom	Sign	Urodynamic diagnosis
Stress urinary Incontinence	Involuntary loss of urine, with effort or exertion, or on sneezing or coughing.	Involuntary leakage from the urethra, with exertion or effort, or on sneezing or coughing.	Involuntary leakage of urine shown during raised abdominal pressure, in the absence of a detrusor contraction is referred to as urodynamic stress incontinence.
Bladder neck hypermobility	Involuntary loss of urine, with effort or exertion, or on sneezing or coughing.	Hypermobile bladder neck on Q-tip* or other objective measure.	High valsalva leak point pressure or high maximum urethral closure pressures.
Intrinsic sphincter deficiency	Involuntary loss of urine, with effort or exertion, or on sneezing or coughing.	Bladder neck could be raised or hypermobile.	Low valsalva leak point pressure or low maximum urethral closure pressure.
Urge Urinary Incontinence	Involuntary leakage accompanied by or immediately preceded by urgency	Urine leakage seen during examination from the urethra associated with urgency.	Incontinence due to an involuntary detrusor contraction, usually with a sensation of urge, is known as detrusor over-activity Incontinence.
*Q-tip: Insertion of a small lubricated cotton swab into the urethra to the level of the bladder neck. With valsalva, rotation greater than 30° often indicates evidence of bladder neck hypermobility			

MECHANISM AND PATHOPHYSIOLOGY

The complex anatomy of the urinary tract is such in a way that it regulates and harmonizes the moves of the urinary tract maintaining the continence. Coming to understand the anatomy and physiology of the urinary track and pelvic floor is the enigma of UI, which allows a better understanding of each type of urinary incontinence.[25] The bladder is a hollow muscular that is sited on the pelvic floor. The detrusor is the main muscle of the bladder made of smooth muscles, which maintain the bladder for any unnecessary movements. There are also urinary sphincters (urethral sphincter) a group of muscles that contract around the urethra in order to maintain bladder control. These muscles can be categorized in two. The first one known as internal sphincter seems to be less developed in female, it is a muscle that is contracted at every moment except during voiding (urination), but it relaxes during voiding. The second one known as external sphincter is contracted the whole time, when bladder is full to avoid involuntary leak of urine.

These 2 kinds of muscles work like water tap, they are most of time contracted (closed), and they relax and open when voiding, to allow the urine to be evacuate. When there is a feeling of bladder fullness and need for voiding, a sensorial message is sent from the brain to the sphincter, giving them signal to relax, which will resolve to urination. In the other hand detrusor which is the most important muscle of bladder, remains relaxed to allow the bladder to store urine. When signal from the brain is given, detrusor contracts in a squeezing movement to allow the urine to descend from bladder to urethra.[25]

CAUSES AND RISK FACTORS

According to De Lancet 2006, UI is simply caused by dysfunction in the storage of Urine, especially in the emptying process of the lower urinary tract.[26] The etiology of UI is still poorly understood, but various scientific papers present UI as inevitable result of aging, causing changes in urine flow due to the aging of tissues and neurologic connections. For women, the aging process induces imbalance or deficiency of hormones that cause the mucosal tissues to become weak.[27]

Mode of delivery and parity is considered as factors contributing towards worsening of urinary incontinence.[28-31] It is well known that the vaginal delivery generates neurologic changes that affect the Urethra; these changes seem to be less pronounced in cases of caesarian section (C/section),[32,33] giving c/section a protective role against UI. A Chinese study[34] on primipara who delivered either vaginal way or by c/section concluded a high occurrence of UI in the vaginal birth group than in the Caesarian section group; it also suggested that vaginal delivery, lateral episiotomy and new born weight (over 4000 g) were risk factor of postpartum UI and pelvic Organ prolapse. Questions remain about the protective role of C/section as a selective option or after experiencing contractions.

Mallett and colleagues refuted that multiparity was a risk factor for UI, showing that neurologic changes that lead to UI would be occurring at the first vaginal delivery.[35] Would then UTI be a risk for UI? The drop of estrogen in peri-menopause and menopause would be able to cause weaken of the urethra, assertion that the European Association of urology disagrees with, in its 2009 guidelines for UI: "menopause per se does not appear to be a risk factor for UI and there is conflicting evidence regarding hysterectomy".[12] The 2013 UI guidelines for UI suggested that there were no evidence Urinary Tract Infections (UTI) causes UI or that treating UTI would improve UI.[7] Women weight is considerable as a potential risk factor of urinary incontinence.[36,37] A Spanish review reported similar findings of weight loss after pregnancy or retained BMI during pregnancy, by which have had important impacts on prevalence of UI. Women who undergo weight loss were found to improve the condition of their UI.[38]

Alcohol and medication use are also causes and risk factors of UI. In the elderly, they are major causes of acute incontinence. Polypharmacy and the use of psychotropic medication compound problems with incontinence, and are most prevalent in women aged 85 years or over and appear to be increasing.[18] Medications including diuretics (e.g.: Frusemide), anticholinergics (e.g.: Antihistamine), narcotic analgesia (e.g.: Opioids), α-blockers (e.g.: Prazosin), Ca^{2+}-channels blockers (e.g.: Nifedipine), prostaglandins (e.g.: Misoprostol) may aggravate or predispose to UI.[18]

FISTULAE IN THE DEVELOPING WORLD

Obstetrical fistulae is defined as defect in the genital tract connecting the vaginal or uterine cavity to the bladder (vesicovaginal fistula), urethra, erecters, rectum or colon (rectovaginal fistula) caused by obstructed birth canal or a too long labor.[39] The most direct consequence/complication of fistulae is the constant leaking of Urine, which leads major of time to kidney disorders, skin infections, and death for unattended cases.

In Western society, urogenital/rectal fistulas are mostly caused by radiotherapy and/or surgery.[40,41] However, in the developing countries, obstetric fistulae are common.[42] Estimates indicate that 2-3 millions women live with obstetric fistulae worldwide, the majority of whom are in Africa and Asia.[43-45] Fistulas are preventable and treatable, however, many women are still unaware of the availability of treatment and 80% of them never seek treatment due to lack of knowledge.[43] Moreover, women suffering from this condition are initially kept hidden; subsequently, they find it difficult to maintain decent standards of personal hygiene because water for washing is generally scarce; divorce becomes inevitable and

destitution follows, these women being forced to beg for their livelihood.[46]

Despite much debate, there is no universally accepted system for classifying fistulae, and a wide variety of different systems have been proposed [including Marion Sims (1852), McConnachie (1958), Lawson (1968), Goh (2004), WHO (2006) and Arrowsmith (2007)].[47] Classification of fistulas is important only to the extent that the classification has a meaningful relationship to the prognosis of the injury. However, most surgeons base their classification on simple descriptive terms involving three factors: site, size and scarring.[48] Based on the WHO, Fistulae can be categorized as simple fistula (good prognosis/simple) and complex fistula (larger than 3 cm, complicated/uncertain prognosis).[47]

ASSESSMENT OF INCONTINENCE

Not all kinds of UI necessitate special treatment; initial assessment will be able to reveal which case is complicate and needs to be referring to a specialist. The obstetric and gynecological history is the first steps in assessing any patients suspected with UI, throughout the history the patient will be asked questions that will lead the care provider to categorize the kind of UI, timing, severity or association with other conditions. Patients with pain, recurrent Urinary tract Infections, hematuria, Pelvic Organ Prolapse, fistula, previous pelvic surgery and radiotherapy are called "complicated incontinence group".[12]

Questionnaire such as ICIQ-UI (International Consultation on Incontinence Questionnaire - Urinary Incontinence), ISI (Incontinence Stress Index), RUIS (Revised Urinary Incontinence scale), LSA (Life space assessment), UDI-6 (Urogenital Distress Inventory), EPI (Estimated Percent Improvement) and PSQ (Patient Satisfaction Question) are tools often used to understand the patient's symptoms and to assess her quality of life (QoL).[49]

URODYNAMIC ASSESSMENT AND PHYSICAL EXAM

The term 'urodynamics' encompasses a number of varied physiological tests, of bladder and urethral function, which aim to demonstrate an underlying abnormality of storage or voiding.[7] An urodynamic assessment must interpret urodynamic findings in relation to the clinical picture and symptoms taking into consideration Frequency-volume chart, Pad testing, Flow rate, ultrasound, conventional cystometry and videocystometry as key tests.[50] The Figure 1 shows a convential cystometrogram of an incontinent patient. In this test, the detrusor overactivity is apparent on filling and after coughing (the pressure spikens on P_{abd} and P_{ves}). Increasing overactivity occurs on filling until the patient voids off an overactive contaction. The rate if filling is 90 ml/minute.[50] Moreover, other than urodynamics studies, tests such as the Q-tip, POP-Q, Bonney, Marshall and Fluid-Bridge can assess urethral competence, in terms of hypermobility of the urethrovesical junction.[7]

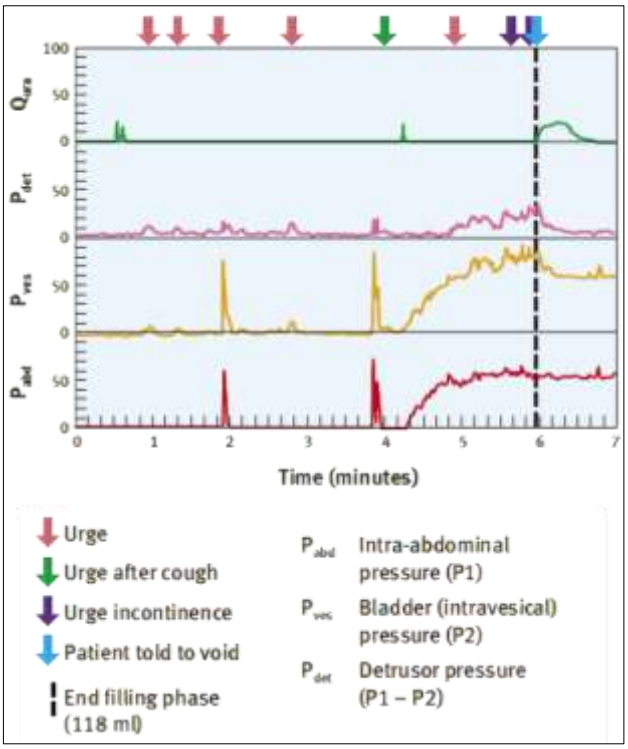

Figure 1: Cystometrogram trace from an incontinent patient.[50]

THE MANAGEMENT AND TREATMENT OF URINARY INCONTINENCE

After a throughout evaluation of the condition, treatment will depend on the type of UI and the severity of the symptoms. Management should be taken into 2 phases: an initial management which consists basically on change of lifestyle, reeducation also called conservative treatment and use of drugs; specialized management is the next step for UI which failed Initial treatment, or for very complicated case of UI.

Healthy elderly persons should be offered a similar range of treatment options as younger persons. However, frail/elderly persons, require a different approach. Their evaluation must address the potential role of co-morbidity, current medications (prescribed, over-the-counter, and/or naturopathic), and functional and/or cognitive impairment for the management of UI. The management should take into consideration the degree of bother to the patient and/or carer, their goals for care, level of co-operation, and the overall prognosis and life expectancy.[12]

The Figures 2-5 present the various algorithms in assessment of incontinence in terms of management recommendations.

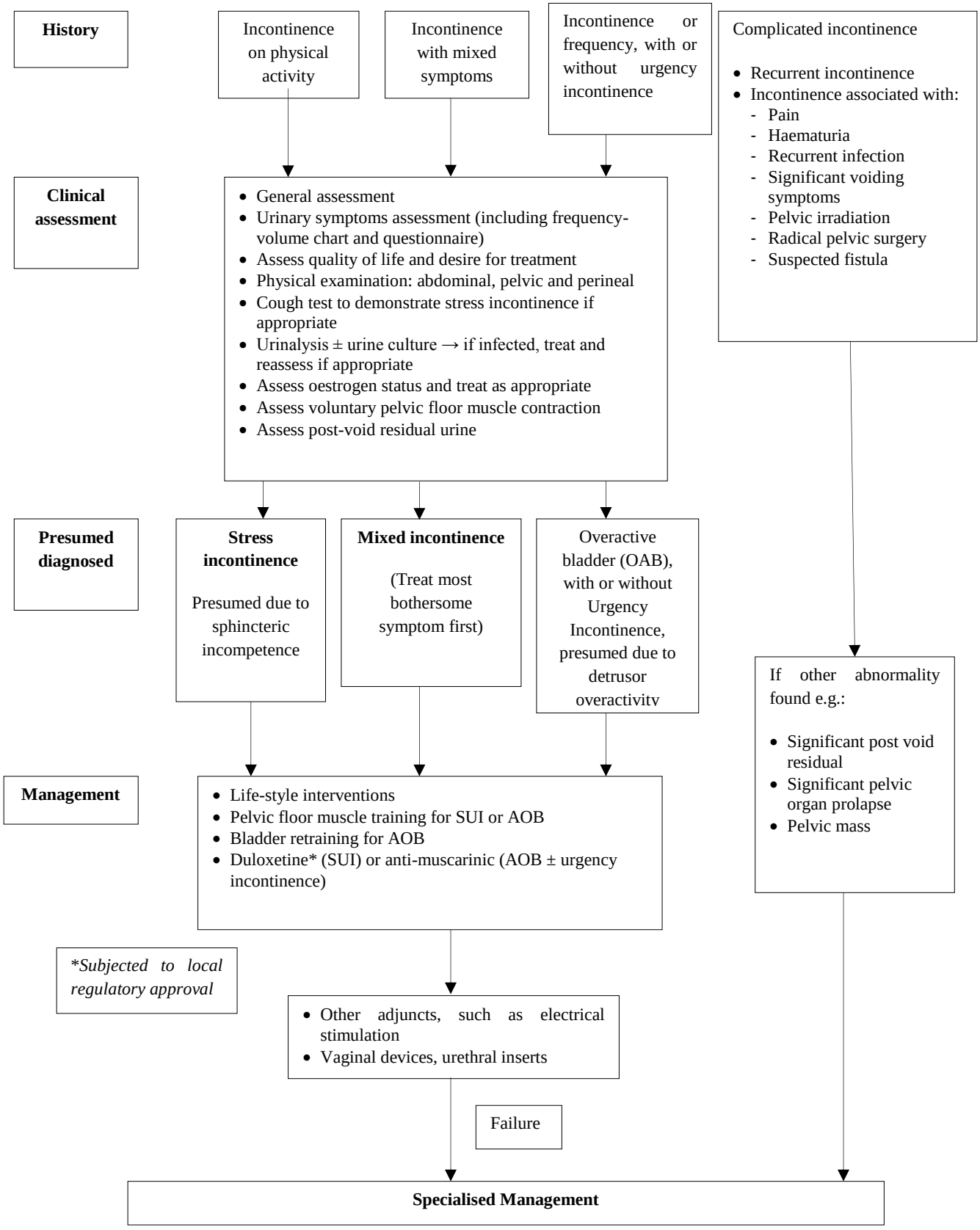

Figure 2: Algorithm of initial management of UI.[12]

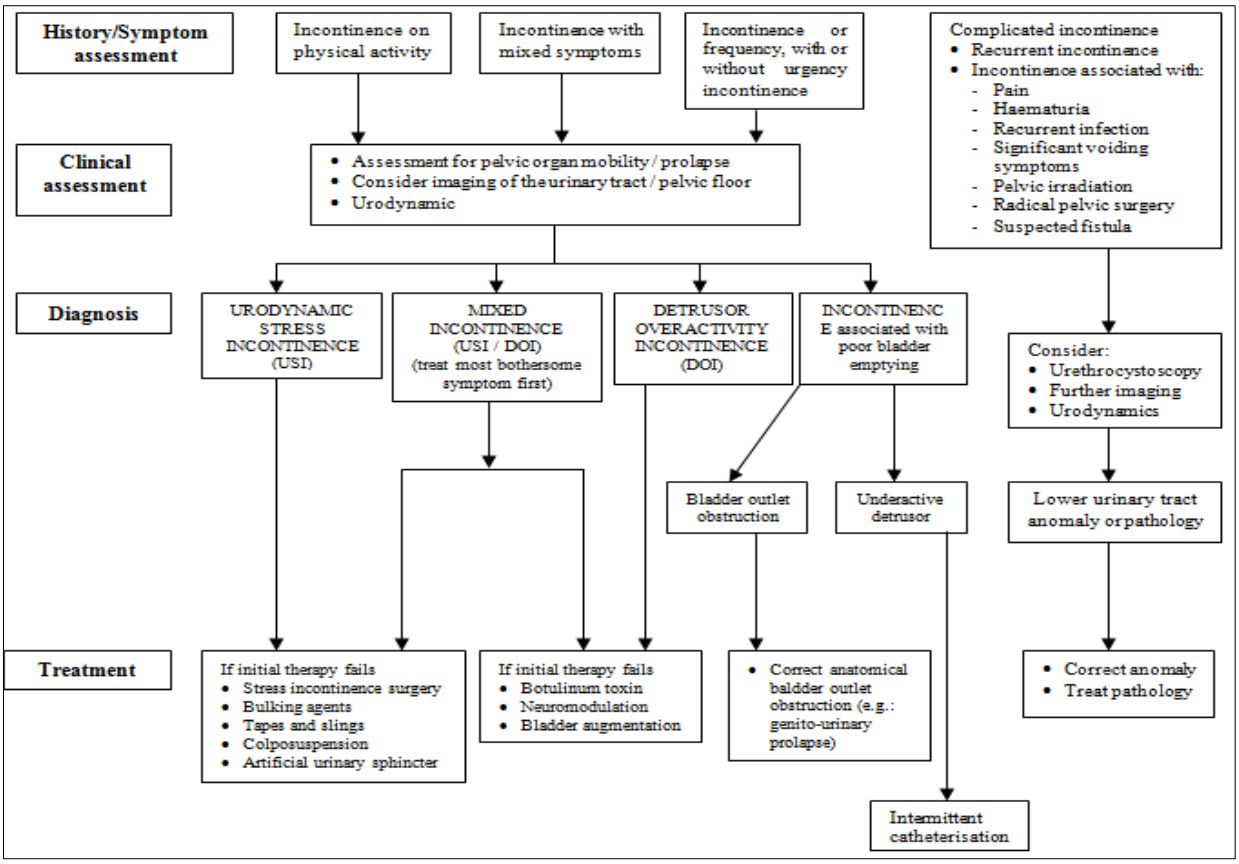

Figure 3: Algorithm of specialised management of UI.[12]

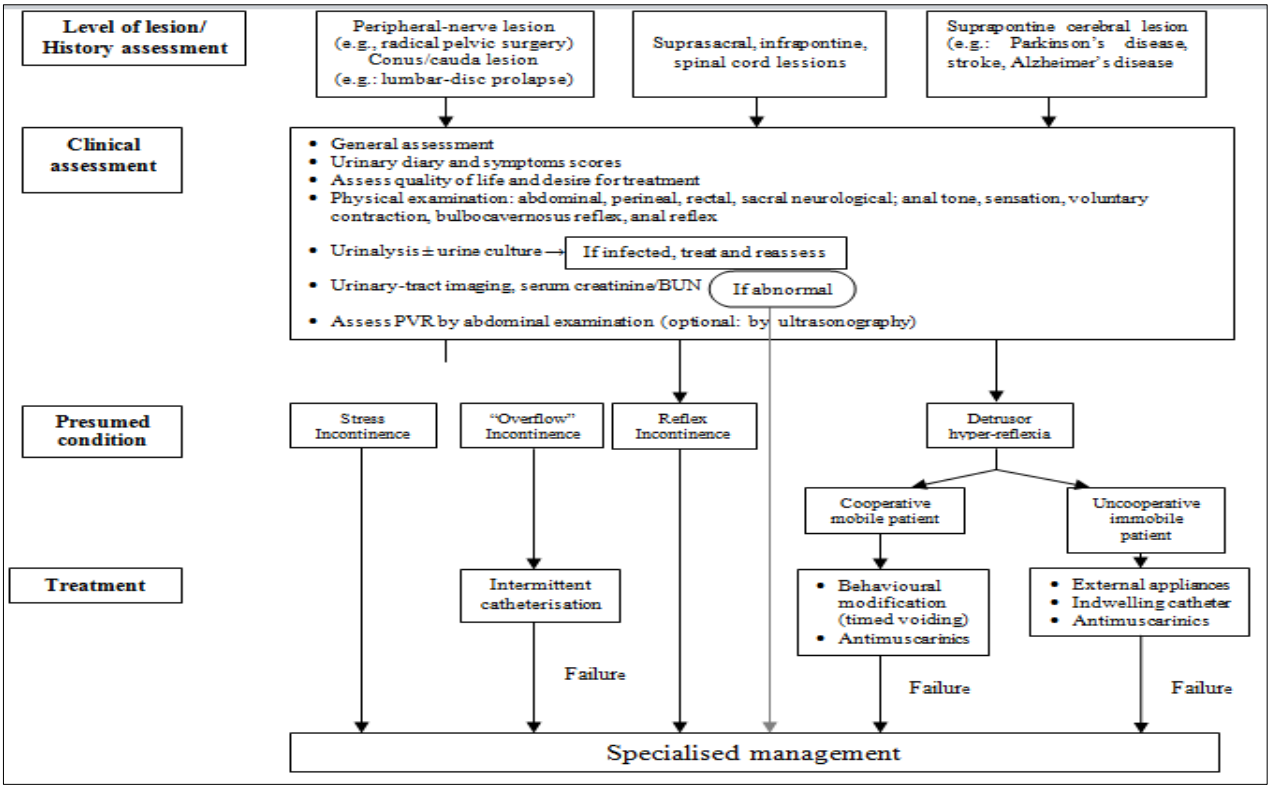

Figure 4: Algorithm of initial management of neurogenic urinary incontinence.[51]

Note: BUN = Blood urea nitrogen, PVR = Post-void residual

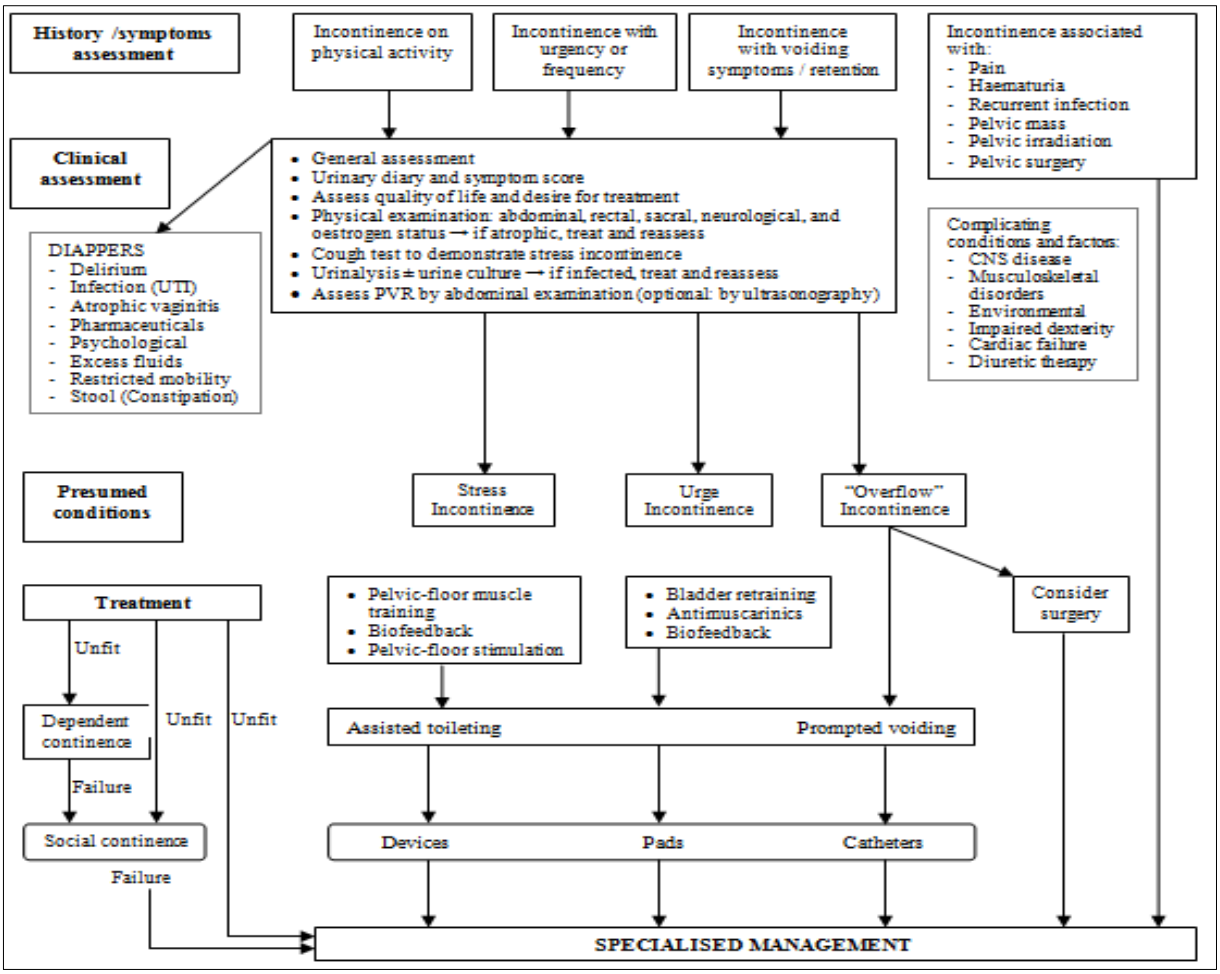

Figure 5: Algorithm of initial management of UI in frail disabled elderly people.[51]

UTI = Urinary tract infection; CNS = Central nervous system; ADL = Activities of daily living; PVR = Post-void residual

CONSERVATIVE TREATMENT

Defined by the ICS, 'Conservative treatment' is a group of therapies that are usually low cost, and managed principally by the person with UI with instruction/supervision from a healthcare professional. These include lifestyle interventions, physical, behavioural, drug and complementary therapies, and non-therapeutic interventions (such as products that collect or contain leakage).[7]

Lifestyle interventions

Various observational studies have considered the possible association between lifestyle factors and UI, many of which include both men and women, investigating how lifestyle factors may affect the prevalence, or incidence, of UI or OAB were considered. These factors include bowel habit, dietary factors, caffeine, fluid intake, smoking, weight and physical exercise.[7] Mounting data of observational studies and few clinical trials have addressed the evidence impact for lifestyle interventions.[52-55]

Physiotherapy

Physiotherapists have become involved in the clinical management of UI in women, as the presumptive underlying impairments (i.e., decreased pelvic floor muscle strength and/or endurance, decreased awareness of bladder irritants) fall within the scope of physiotherapy practice according to the Guide to Physical Therapist Practice.[56] Pelvic floor muscle training (PFMT, also known as Kegel Exercises), vaginal cones, neurostimulation, biofeedback, magnetic therapy and electrical stimulation are varieties of physical therapies used in the management of female UI.[57-61]

Behavioural therapies

Behavioural therapy involves individual learning new patterns of response or re-establishing previously learnt

behaviour to fit in with what is considered usual. Women with OAB (wet or dry) usually void more frequently than usual due to urgency. Women with stress UI also often void more frequently in the belief that they will pre-empt an involuntary urine loss associated with any increase in intra-abdominal pressure.[7] Bladder training and toileting programmes (prompted voiding and timed voiding) are various behavioural therapies usually used. All these therapies appear to show improvements in leakage episodes.[62]

Evidence-based complementary therapies

Incontinent women who do not find conventional treatments acceptable often explore the use of complementary therapies for UI, and as adjuncts to conventional treatments. Acupuncture and moxibustion,[63,64] hypnosis,[65,66] yoga[67] and herbal medicines such as ginsenoside Rh2[68] are most of the complementary therapies used for UI. These therapies have shown satisfaction in UI treatment. Symptomatic improvement has been reported, women with UI were even "successfully" treated.[66]

Alternative conservative management options

Alternatively, there are few options used in UI management in order to collect or contain leakage (absorbent products, urinals and toileting aids, catheters) and to prevent leakage (e.g. Contrelle® continence tampon, contiform® and urethral plug).[69-71] Scientific evidence showed that the majority of users reported improvement or cure after 3-5 weeks of treatment (up to 1 year study).[69]

PHARMACOTHERAPY

More than 50 million people are affected by UI worldwide and many drugs have been clinically used for the treatment of different types of UI. Although drugs may be efficacious in some patients, side-effects mean they are often discontinued after short periods of time and they are best used as an adjuvant to conservative and surgical therapy.[8]

Antimuscarinic drugs

Most anticholinergic drugs are antimuscarinics. They are often used to treat overactive bladder (OAB). They block muscarinic receptors in the bladder, which reduces the ability of the bladder muscle to contract and affects bladder sensation, reducing urinary urgency and the related symptoms of urgency incontinence, frequency and nocturia. The drugs differ in their selectivity for various muscarinic receptors, and some drugs have additional actions, such as direct smooth muscle effects. Anti-muscarinic drugs are available in Immediate-release (I.R); Extended-Release (E.R), Long acting and transdermal formulations. Recent large meta-analyses of the most widely used antimuscarinic drugs have clearly shown these drugs provide a significant clinical benefit.[10,11]

More research is needed to decide the best drugs for first-, second-, or third-line treatment as none of the commonly used antimuscarinic drugs (darifenacin, fesoterodine, oxybutynin, propiverine, solifenacin, tolterodine and trospium) is an ideal first-line treatment for all OAB/DO patients. Therefore, optimal treatment should be individualised, considering the patient's co-morbidities, concomitant medications and the pharmacological profiles of the different drugs.[11,72]

Drugs with mixed actions

Various drugs with mixed actions have been clinically used for the treatment of different types of UI. Oxybutynin, propiverine, diclyclomine, flavoxate are the more common drugs of this category. With its mixed action antimuscarinic activity, antispasmodic, anesthetic and antihistamine effects, Oxybutynin is available in IR and ER formulations. Its clinical evidence suggested increased continence rate and improved UI.[73] The use of oxybutynin topical gel has been investigated in a large North American multicentre randomised, placebo-controlled study of 789 patients with OAB.[74] Overall oxybutynin gel was associated with a significant decrease in urge incontinence episodes and urinary frequency when compared to placebo with a corresponding increase in voided volume. Propiverine hydrochloride is an antimuscarinic with Ca^{2+} channel antagonism activity. It is also recommended in pediatric patients with idiopathic or neurogenic detrusor overactivity at doses of 0.8 mg/kg body weight/day.[75] Duloxetine (Yentreve®) is a potent serotonin/noradrenaline reuptake inhibitor (SNRI), approved by the European Medicines Agency (EMA) in 2004, and represents a major therapeutic advance for the treatment of SUI.[76] Clinical trials showed that duloxetine; at the recommended dose of 40 mg b.i.d. for 4 weeks, further increased to 60 mg b.i.d. for 8 weeks, improves voiding episodes and quality of life.[77]

α-Adrenergic antagonists

α-Adrenergic antagonists (or a-blockers), increase urethral sphincter tone. Alfuzosin, doxazosin, prazosin, terazosin and tamsulosin represent the common drugs with Tamsulosin as the best studied compounds for the treatment of OAB/UUI. However, terazosin has successfully treated voiding symptoms in women with functional outflow obstruction, or Lower Urinary Tract Symptoms (LUTS).[78,79]

β-Adroneceptors agonists

Various studies have been investigating β-Adroneceptors agonists (especially β3-AR agonists) as valid alternative to treat OAB by increasing bladder capacity with no change in micturition pressure and residual volume. Mirabegron, a β3-adrenoceptor agonist approved by the

EMA in 2012 for OAB, can relax detrusor smooth muscle during filling by activating β3-ARs with a consequent increase of bladder capacity.[80] With its good safety/efficacy profile, mirabegron might be a convenient therapy for OAB in elderly people with cognitive deficit because it is well tolerated and reduces at the same time the number of incontinence episodes and mean micturition frequency.[80] It was even suggested as second-line treatment for OAB in patients who are poor responders or intolerant to anticholinergics.[81]

Neurotoxin

The injection of Botulinum (Botox®) to treat urinary incontinence in patients with neurological conditions suffering from OAB was approved by the Food and Drug Administration (FDA) in 2011, even though this treatment is not licensed for this condition by the EMA. However, in the same year, it was approved in 12 European countries for UI in adults with DO resulting from neurogenic bladder.[82,83] Two clinical studies investigating the efficacy and safety of Botox in patients with Parkinson's disease (PD) and assessing the risks and benefits of longterm use for OAB/UUI have just been recently completed, the findings are yet to be published.[84,85]

Vanilloid receptors agonists

Vanilloid receptors are present on afferent sensory neurons innervating the detrusor and urethra. Capsaicin and Resiniferatoxin (RTX) are two drugs of this category. While the first suppresses involuntary detrusor contraction following chronic spinal cord lesion above the sacral segments, the second leads to a rapid improvement or disappearance of UI in up to 80% of selected patients and a 30% decrease in their daily urinary frequency.[86]

Hormonal treatment

Oestrogen treatment for UI can be given orally, vaginally or even intravesically. Oestrogen preparations have been used for many years in the treatment of urinary incontinence, however, oestrogen treatment, either alone or combined with progestogen, has achieved only poor results in UI.[87] From a review of 8 controlled and 14 uncontrolled prospective trials, it was concluded that oestrogen therapy was not an efficacious treatment for stress incontinence but may be useful for symptoms of urgency and frequency.[88]

Desmopressin (DDVAP) is a synthetic analogue of vasopressin (also known as antidiuretic hormone), which increases water re-absorption in the renal collecting ducts without increasing blood pressure. It can be taken orally, nasally or by injection. Desmopressin has been used primarily in the treatment of nocturia and nocturnal enuresis in children[89] and adults.[90] More recently nasal desmopressin has been reported as a 'designer drug' for the treatment of daytime urinary incontinence.[91] Desmopressin is safe for long term use; however the drug should be used with care in the elderly due to the risk of hyponatraemia.[12]

RESEARCH IN INCONTINENCE

Urinary incontinence, a common and distressing condition among women, remains an issue medical, social and hygienic issue. Population studies estimate that 20-30% of women are affected but only 7-12% perceive it as a problem[92] having a significant effect on quality of life (QoL). There is still a lot to be done to tackle this situation, especially in the developing countries. Basic research, epidemiology and clinical research including socioeconomic studies are the main areas where recommendations were made. For pharmacotherapy, most recently, a new area has emerged investigating the potential role of stem cells in the treatment of urinary incontinence.[93] Stem cells are classically thought to aid in tissue repair via their ability for multilineage differentiation and self-renewal. They may also exert a therapeutic effect via the secretion of bioactive factors that direct other stem and progenitor cells to the area of injury, and that also possess antiapoptotic, antiscarring, neovascularization, and immunomodulatory properties.[94] Their potentiality to restore function vias direct effects on the underlying mechanisms leading to incontinence or voiding dysfunction has been evaluated in preclinical animal models and clinical trials, especially for SUI.[95-97]

Mesenchymal Stem Cells (MSCs), Muscle-Derived Stem Cells (MDSCs), Adipose-Derived Stem Cells (ADSCs) and Urine-Derived Stem Cells (USCs) are the sources of stem cells investigated for therapeutic benefit in urologic applications.[95,97-99] Clinical trials reported improvement in SUI, through great reduction in pad weight, diary-reported leaks and even a complete achievement of continence in women, with no serious adverse events (pain, bruising at biopsy or injection sites).[95]

To date, stem cells have shown promising results for the treatment of voiding dysfunction. Applications in SUI and OAB have demonstrated success in both preclinical animal trials and limited clinical trials. This research area needs to be further well investigated in order to bring a hope to the millions of women suffering from UI, and whom pharmacotherapy remains the ideal option.

CONCLUSION

Urinary continence in the female is a medical condition maintained by a series of complex mechanisms, which allow the pressure in the urethra to exceed that in a receptive bladder. Clinical evidences have shown that UI reduces both social interactions and physical activities, decreases quality of life. Associated with stigma and shame, UI women become in long term isolated from the communities, affecting the possibility to seek and to engage into treatment. Nowadays, there are various

management and treatments methods. For women who cannot afford or tolerate surgical therapies, varieties of conservative treatments and pharmacotherapies are very much available. To date, clinical data have shown the significant benefits of these therapies. Recently, potential and promising areas have been arising in pharmacotherapy, giving alternative options to women seeking non-surgical treatment. However, with few controversial data, further well designed studies with high quality are required to tackle this problem.

Abbreviations

ADL: Activities of daily living; ADSCs: Adipose-derived stem cells; BMI: Body mass index; BUN: Blood urea nitrogen; CNS: Central nervous system; DOI: Detrusor overactivity incontinence; EMA: European medicines agency; EPI: Estimated percent improvement; ER: extended release; FDA: Food and drug administration; ICS: International continence society; IR: Immediate release; ISI: Incontinence stress index; LSA: Life space assessment; LUTS: Lower urinary tract symptoms; MDSCs: Muscle-derived stem cells; MSCs: Mesenchymal stem cells; MUI: Mixed urinary incontinence; OAB: Overactive bladder; OCD: Obsessive-compulsive disorder; PD: Parkinson's disease; PFMT: Pelvic floor muscle training; PSQ: Patient satisfaction question; PUI: Phantom urinary incontinence; PVR: Post-void residual; QoL: Quality of life; RUIS: Revised urinary incontinence scale; SUI: Stress urinary incontinence; UDI-6: Urogenital distress inventory; UI: Urinary incontinence; UTI: Urinary tract infection; USCs: Urine-derived stem cells; USI: Urodynamic stress incontinence; UUI: Urge urinary incontinence; WHO: World Health Organization.

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