

The management of overactive bladder syndrome: a review of the European Association of Urology Guidelines



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Practice Points

- Currently, recommendations for the management of overactive bladder (OAB) can be found within the guidelines for urinary incontinence and male lower urinary tract symptoms.
- A voiding diary is invaluable in the assessment of patients presenting with OAB symptoms, corroborating symptom severity, estimating functional bladder capacity and identifying those with polyuria.
- An individualized approach to treatment is prudent to optimize efficacy while minimizing adverse effects of treatments, starting with lifestyle modification and behavioral therapies.
- Antimuscarinics are the mainstay of pharmacotherapy with proven efficacy but are associated with poor tolerability and poor persistence due to side effects.
- Antimuscarinics are an appropriate option in men with predominate storage lower urinary tract symptoms but caution should be taken if bladder outlet obstruction is suspected (a raised postvoid residual >200 ml).
- Intravesical botulinum toxin A is an efficacious option after failure of pharmacotherapies but is associated with a significant incidence of retention/urinary tract infection, while the long-term effects are unknown and it remains unlicensed for use in OAB.
- β 3-adrenoceptor agonists are a newly available class of pharmacotherapy for OAB that are likely to be included in future guidelines.

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SUMMARY Overactive bladder syndrome is a common and highly bothersome problem in the general adult population and a major source of health expenditure in industrialized nations. Much research has been undertaken to advance the understanding of the symptom syndrome and develop optimal management strategies. Although, currently, treatment options are increasing, it is often the case that treatment is inefficacious, impractical or associated with intolerable side effects. The latest European Association of Urology guidelines provides evidence-based recommendations for the diagnosis and management of overactive bladder syndrome within the guidelines for urinary incontinence in women and men as well as non-neurogenic male lower urinary tract symptoms. Their aim is to improve the standard of care of patients with lower urinary tract symptoms. In this article we review the latest guidance and discuss the evidence behind the recommendations, and the practical aspects of their application, as well as their limitations.

Overactive bladder (OAB) is a common and bothersome symptom complex affecting men and women of all ages. It is estimated to affect between 10 and 20% of the population with an even distribution between males and females, although the etiology differs between the sexes [1–3]. The defining feature of OAB is urinary urgency. OAB often has a chronic course and impacts adversely upon the health-related quality of life (QoL) of sufferers who are more likely to be depressed and unemployed than age- and gender-matched controls [4]. The economic costs of OAB run into the billions of dollars per year in healthcare expenditure and financial implications of lost productivity [5,6].

‘Overactive bladder’ was first used as a term in 1988 [7], as applied to a syndrome defined urodynamically by the presence of detrusor overactivity (DO) – nonvolitional bladder contractions during bladder filling. OAB is now defined in symptom-based terms as “urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection (UTI) or other obvious pathology” [8]. The current definition reflects the fact that DO is not always present and yet patients still have bothersome symptoms. Additionally, a definition based upon symptoms is particularly appropriate for use in a primary care settings where urodynamic studies are often not available.

Urgency is the most important defining feature of the syndrome and is defined as “the sudden and compelling desire to pass urine which is difficult to defer” [8]. It is a matter of debate whether the sensation is an ‘all-or-nothing’ event akin to

a light switch being turned on or off or rather reflects a gradual build up of feeling of increasing intensity much like a rheostat [9]. What is clear is that patients are often unable to reach the toilet on time and consequently suffer leakage, this is known as urgency urinary incontinence (UUI) [10]. Urgency must be differentiated from urge which is a physiological sensation experienced by normal individuals when the bladder becomes full [11], urgency is pathological, characterized by a fear of urine leakage [11].

Urinary incontinence (UI) is defined as “the complaint of involuntary loss of urine” [8] and is broadly divided in to three main categories: stress urinary incontinence (SUI), “the complaint of involuntary leakage on effort or exertion or on sneezing or coughing”; UUI, “the complaint of involuntary loss of urine associated with urgency” [8]; and mixed urinary incontinence (MUI), “the complaint of involuntary leakage associated with urgency and also with exertion, effort, sneezing or coughing” [8]. A further category is mixed symptoms, which is SUI with accompanying urgency. Patients with OAB may have any of these categories of UI, termed OAB-wet; when UI is absent the term OAB-dry is used.

Despite being the subject of much research OAB remains both incompletely understood and challenging to manage, with no ideal therapeutic approaches. As such, both patients and doctors often take a nihilistic approach to the problem [12–14]. The development of evidence-based guidelines seeks to dispel such attitudes and promote best practice in diagnosis and treatment. Here we review the current European Association of Urology (EAU) guidelines on the management

of both non-neurogenic male lower urinary tract symptoms (LUTS) [15] and male and female urinary incontinence [16] and the implications they have for contemporary clinical practice.

Guidelines

The EAU is the official body representing national urology societies across Europe. The guidelines office of the EAU is responsible for the development and dissemination of evidence-based guidelines for the diagnosis and management of urological diseases and are widely read and widely cited in the literature. Guidelines are developed by an expert panel through an independent systematic review of the literature based on population, intervention, comparator and outcome questions.

Action-based recommendations using a modified Oxford system and treatment-based algorithms are developed through consensus discussions. The reader is referred back to the relevant evidence, including an annotation regarding the strength of the recommendation. OAB is not represented by a specific guideline, instead recommendations relating to OAB are present in different guidelines, for non-neurogenic male LUTS (Figure 1) and UI (Figures 2 & 3). The latest guidelines, published in 2012, will be discussed [15,16].

Assessment & diagnosis

The guidelines recommend that at presentation a history is taken and an examination is performed. It is important to emphasize the significance of

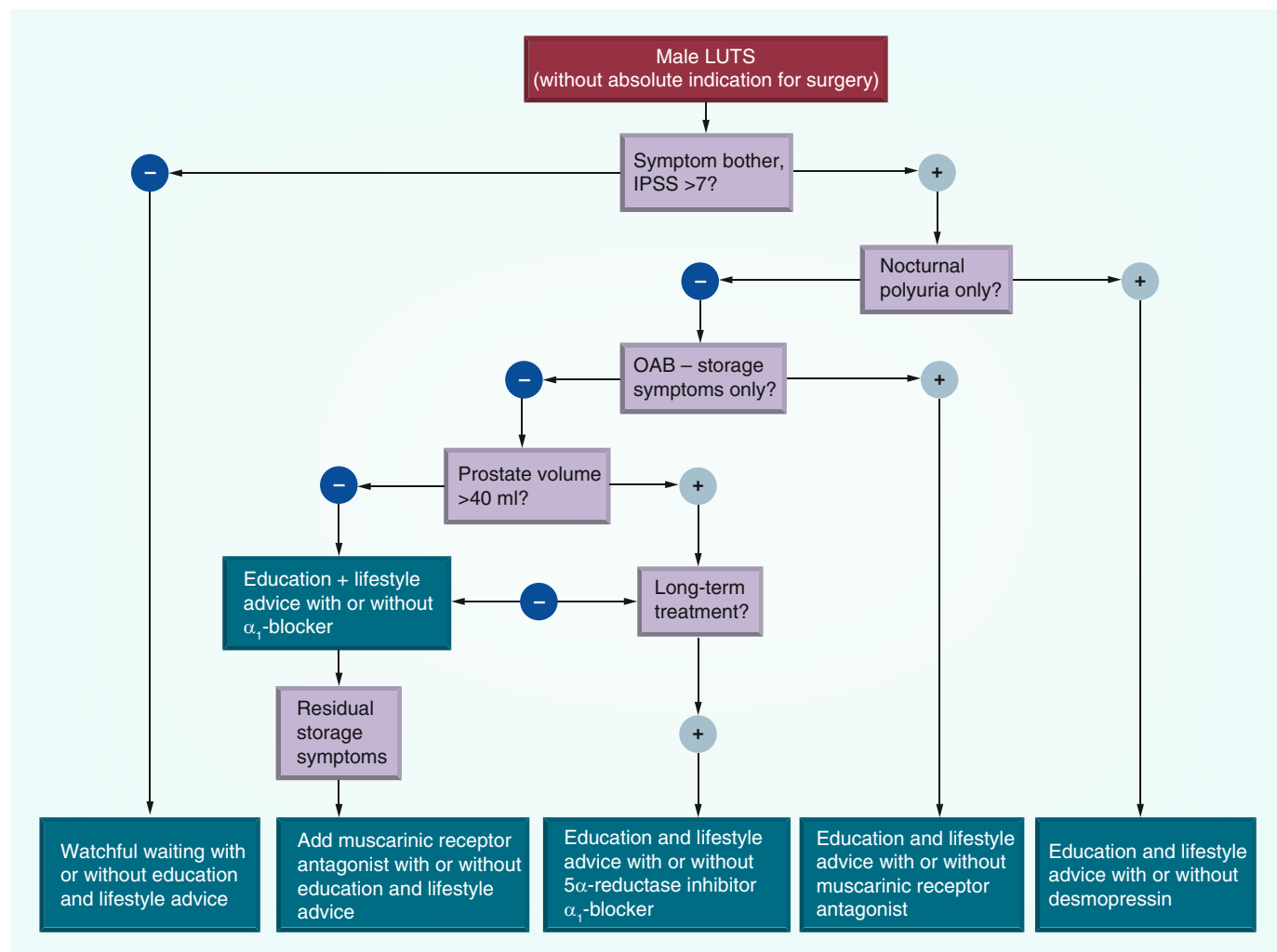


Figure 1. Treatment algorithm for male lower urinary tract symptoms including overactive bladder. IPSS: International prostate symptom score; LUTS: Lower urinary tract symptoms; OAB: Overactive bladder. Reproduced with permission from [103].

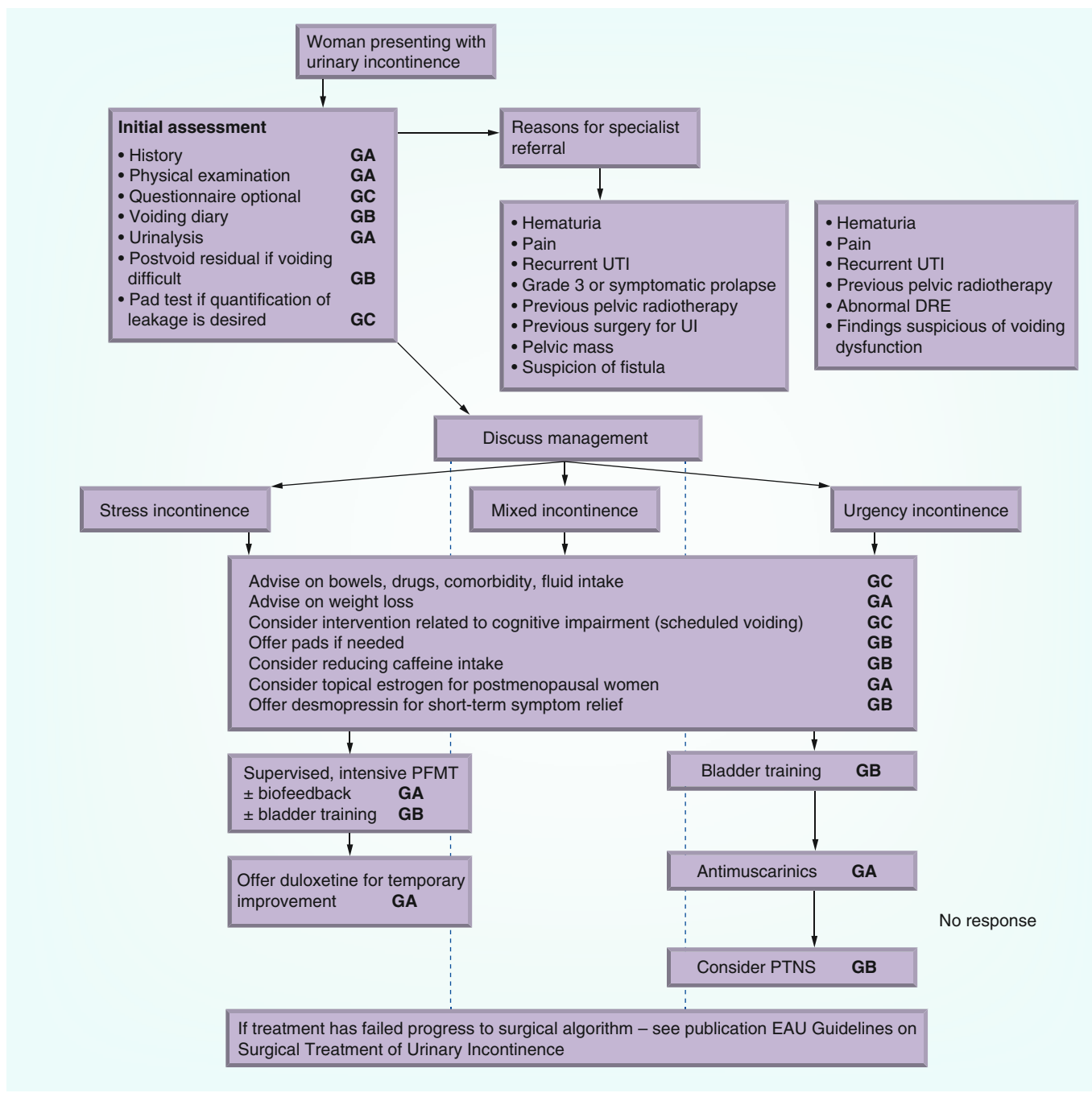


Figure 2. Nonsurgical management of female urinary incontinence. GA, GB and GC refer to grades of recommendations. DRE: Digital rectal examination; EAU: European Association of Urology; PFMT: Pelvic floor muscle training; PTNS: Percutaneous tibial nerve stimulation; UI: Urinary incontinence; UTI: Urinary tract infection. Reproduced with permission from [86] © Elsevier (2012).

this to exclude other pathologies, both benign and malignant, before symptoms are attributed to OAB. The history should focus on voiding and storage LUTS, symptom severity and impact on QoL, as well as enquire into risk factors (e.g., neurological disease) and the presence of

other conditions (e.g., endocrine) that may lead to similar symptoms. Physical examination should include abdominal examination and digital rectal examination of the prostate in males. While in women, vaginal examination for estrogen status and presence of pelvic organ prolapse (as there

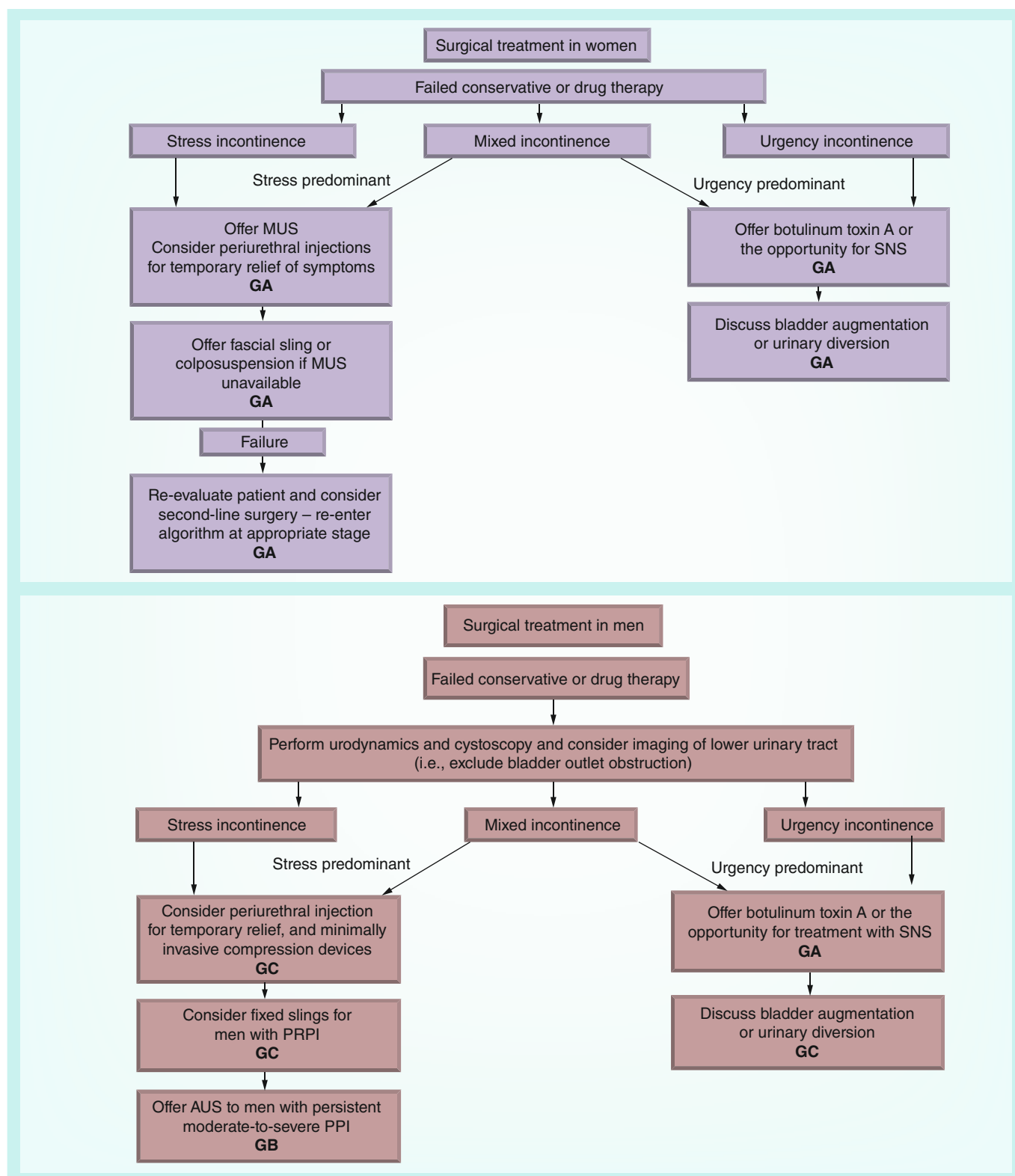


Figure 3. Surgical management of urinary incontinence. GA, GB and GC refer to grades of recommendations. AUS: Artificial urinary sphincter; MUS: Mid-urethral sling; PPI: Postprostatectomy incontinence; PRPI: Postradical-prostatectomy urinary incontinence; SNS: Sacral nerve stimulation. Reproduced with permission from [86] © Elsevier (2012).

is evidence that cystocele worsens urgency [17] and cough testing for the presence of leakage is important.

■ Symptom questionnaires & patient-reported outcome measures

Symptom bother is an important determinant of whether patients with OAB seek treatment [18]. Evaluating symptom severity and impact upon QoL is vital in the initial assessment and monitoring response to treatment. A multitude of questionnaires have been developed to assess OAB symptom severity, bother and QoL [19]. To improve comparability, a short standardized OAB questionnaire has been produced by the international consultation on incontinence [20], although in practice it is not widely used to date. As such, guidelines leave it to the care provider's discretion as to whether they are used, however, in practice, most questionnaires are lengthy and time consuming and have been used in a research setting. Certainly, a shorter questionnaire was shown to have utility in identifying patients with bothersome OAB in primary care [21].

■ Voiding diaries

A voiding diary is recommended for the evaluation of both men and women with UI and where there is a history of urinary frequency or nocturia in men with LUTS. Voiding diaries are primarily a semi-objective measure that helps substantiate the severity of symptoms, which can be overestimated by some patients [22] and underestimated by some physicians [23]. Additionally, voiding diaries provide information on the maximum voided volume and the 24 h and nocturnal urine production, essential in determining patients suffering with symptoms due to urine overproduction from those with a reduced bladder capacity. Voiding diaries can also be used to assess response to treatment and may also have an intrinsic therapeutic benefit by helping patients realize adverse drinking habits [22].

The UI guideline highlights the consensus on the terminology of voiding diaries [8,24]. Micturition time charts are defined as a record of only the timing of micturitions over a 24-h period, frequency–volume charts note the time and volumes voided and bladder diaries expand upon this by including information on fluid intake, urgency and severity of incontinence episodes as well as pad used. However, no specific recommendations on the type of voiding diary are

made in clinical practice. We find the bladder diary provides the most useful information and facilitates an informed discussion with the patient on management. The recommended length that a diary is to be recorded for is 3 days. There is no advantage in extending the recording period beyond this time and longer diaries may in fact be associated with poorer compliance [25–27] and are generally used in a research setting [28].

■ Urinalysis & urine culture

Urinalysis is recommended in all patients presenting with LUTS to exclude UTI or hematuria before symptoms are attributed to OAB. Urine microscopy and culture is indicated to confirm the bacterial growth and sensitivities if urinalysis is positive. Although the guidelines suggest that a normal urinalysis in the majority of patients can effectively exclude UTI it must be noted that urinalysis may not be reliable for identification of low bacterial counts ($<10^5$ CFU/ml) which may be considered as diagnostic of UTI [29]. Hence, where a UTI is clinically suspected but urinalysis is normal, a urine culture is entirely appropriate.

■ Postvoid residual

Ultrasound is a simple, accurate and non-invasive method of estimating the postvoid residual (PVR) in patients with LUTS [30]. It is not deemed necessary as routine practice in all patients with OAB but is recommended in groups at risk of urinary retention (i.e., those where a reduced functional bladder capacity leading to OAB is due, in whole or in part, to a raised PVR). These groups include men with OAB, especially before consideration is given to antimuscarinic (anti-M) therapy. Other groups include women with voiding dysfunction and patients with complicated incontinence (previous incontinence surgery or neurological disease).

■ Urodynamics

Urodynamics is the collective term given to encompass both the invasive and noninvasive tests that provide objective measures of LUT function [31]. Pressure flow studies (PFS) are essential for the urodynamic diagnosis of LUT disorders such as DO and bladder outlet obstruction (BOO). The aim of PFS is to reproduce the patient symptoms and provide a pathophysiological explanation. In practice, the vast majority of patients with OAB do not need to undergo PFS as evidence suggests they do not

influence treatment outcome of conservative therapies in UI [32]. PFS are recommended in guidelines for when the outcome may influence the choice of surgery or when surgery for UI is being considered in patients with OAB or a history, previous incontinence surgery. In contemporary practice, patients with OAB typically undergo PFS after failure of anti-M, to confirm the presence of DO before further therapies.

Treatment

OAB symptoms are bothersome and affect QoL but are not life threatening. This should be borne in mind when treatment is being considered, specifically with therapies that have potentially adverse side effects or risks. How motivated and how likely to comply with treatment a patient will be are also important considerations, as is the patient's ability, whether cognitive, emotional or physical, to deal with any treatment-emergent adverse events. Patients should be educated from the outset that OAB is often a chronic symptom syndrome, where approximately a third of sufferers become refractory to first-line treatments [33], so that they have realistic expectations of therapy. Treatment goals should be identified and individualized to the particular patient and circumstances. For instance, in elderly patients with dementia who may not have the ability to perceive an improvement in symptoms, a more appropriate aim may be to prevent skin breakdown due to incontinence, which may best be achieved through containment devices rather than pharmacotherapy.

Management approaches in OAB progress from lifestyle measurements, behavioral and physical therapies, pharmacotherapies through to minimally invasive treatments such as intradetrusor botulinum toxin and neuromodulation, with very few patients requiring more invasive procedures such as bladder augmentation. In practice, a stepwise progression is not appropriate in all patients.

■ Conservative management: lifestyle interventions, behavioral & physical therapies

It is recommended to advise patients to reduce fluid intake if they drink excessively (usually considered >2.5 l/day) although in practice OAB patients often 'under drink' for fear of leakage. Reducing caffeine intake is also recommended, although remains somewhat controversial due

to the equivocal findings of the small short-term studies available [34,35], while a larger longer-term study showed that caffeine intake was not a risk factor for UI progression [36]. Additionally, women who are overweight should be advised to reduce their weight as this may improve UI.

Behavioral therapies are suggested initially as they are noninvasive and generally not associated with adverse effects while having equivalent efficacy to antimuscarinic agents. Bladder training (or bladder drill) is recommended in the UI guidelines as first-line therapy to patients with UUI and MUI. In practice it is also used for patients with urgency and frequency but no incontinence. It involves following a scheduled program aimed at improving an individual's control over LUT function by progressively increasing the intervals between voids (using distraction or urgency suppression techniques) as well as modifying adverse drinking habits [37]. The process is facilitated by the use of a bladder diary. Bladder training necessitates intact cognitive function and a well-motivated individual to achieve significant benefits. Improvements will invariably diminish once therapy is stopped. In patients with impaired cognition but who can void independently a timed voiding approach where the patient is prompted to void by the caregiver is recommended.

Pelvic floor muscle training (PFMT) has established efficacy in the treatment of SUI and MUI and it is recommended that patients are offered supervised PFMT for at least 3 months. In the context of UUI the aim of PFMT is to result in an improvement in urge suppression through potentiating of the guarding reflex; the current guidelines however do not specifically recommend their use in UUI. A recently published systematic review of 13 trials concluded that physiotherapy techniques may be beneficial for the treatment of UUI although the data is considered limited and further studies are required [38].

■ Pharmacotherapy

Anti-Ms

Anti-Ms are recommended as an initial treatment option for patients with UUI in the incontinence guidelines and in men with moderate-to-severe LUTS who have predominately storage symptoms in the male LUTS guidelines. In practice anti-Ms are also often indicated in women with OAB but no UUI. They are traditionally thought to work through antagonism of muscarinic M_3

receptor leading to the inhibition of smooth muscle contraction [39,40]. Muscarinic receptors have also been found in the urothelium and afferent nerves suggesting anti-Ms may also work through an effect on the afferent system [41].

Anti-Ms have well-established efficacy in improving symptoms over placebo. Tolterodine, solifenacin, propiverine, darifenacin, oxybutynin, trospium and fesoterodine were reviewed comprehensively in two systematic reviews with meta-analyses, with decreases of 0.5–1.3 voids per day and 0.4–1.1 in instances of UI [42,43]. Dry rates for anti-M therapy in OAB-wet patients (especially when coupled with bladder retraining) are reported to be as high as 30–60%, although the use of dry rates as an efficacy end point may not be reliable due to interstudy variations in diary duration, baseline frequency of UI and the population analyzed [44]. In terms of urodynamic outcomes, the volume at first desire to void increased by 70 ml and bladder capacity increased by 90–100 ml. These improvements translated into better health-related QoL scores for all agents.

Extended-release (ER) preparations have efficacy while having a better side-effect profile than immediate-release (IR) preparations. The guidelines recommend offering IR or ER formulations of anti-Ms as an initial treatment option for adults with UUI and, if IR formulations of anti-Ms are unsuccessful for adults with UUI, ER preparations should be offered as second-line treatment. No recommendation is made with regard to dose titration, balancing efficacy and side effects, which may be more beneficial for some patients. Evidence suggests that when flexible dosing is offered as a treatment option, those with the most severe symptoms at baseline derive the greatest benefit from dose increases [45]. Considering the use of transdermal oxybutynin if oral anti-Ms cannot be tolerated due to dry mouth is recommended due to the lower rates of dry mouth than with oral anti-Ms, but has a higher rate of withdrawal overall due to adverse skin reaction (~7–14%).

Although anti-Ms have enduring benefit improving symptoms, at 2 years with good adherence [46], discontinuation rates are as high as 71% at 6 months. Poor persistence may occur due to side effects or lack of perceived efficacy. Dry mouth is the most commonly reported adverse event at 30%, followed by pruritus in 15% compared with 8 and 5%, respectively, in placebo arms. In practice, pruritus is most

commonly reported in patch users. Additionally, UTI, constipation, urinary retention and impaired cognitive function may also occur. In view of issues with efficacy and tolerability, the guidelines recommend offering and encouraging review of benefit within 1 month to patients started on anti-Ms for UUI.

There is no strong evidence for differential efficacy across medications due to the dearth of head-to-head comparisons of the different agents at their most effective doses. Consequently the guidelines do not make a recommendation for any particular agent over others. The advantage of trying a different agent in event of poor efficacy or tolerability is not clear, although is commonly practiced before transition to more invasive therapies. There is some evidence to suggest that darifenacin has a lower rate of CNS side effects than other agents [47]; although the level of evidence for there being much difference between the contemporary agents apart from oxybutynin is deficient.

Imipramine

Imipramine, a tricyclic antidepressant, is considered by some to be a useful drug for the treatment of OAB, especially when combined with anti-M agents, although this has not been adequately assessed in clinical trials [48] and is not recommended in the guidelines, in particular because of its recognized cardiotoxicity, especially in the elderly.

Mirabegron: the first β_3 -agonist

It has recently been recognized that in the bladder, β_3 -adrenoceptors are predominantly located in detrusor muscle and facilitate urine storage by inducing detrusor relaxation [49]. β_3 -adrenoceptor agonists represent a new class of agents with a distinct mechanism of action [50–52]. Mirabegron is the first-in-class to have completed Phase III registrational trials and, following approval in Japan and the USA, represents a new oral agent for OAB treatment. Recent Phase III trials have demonstrated efficacy and safety of mirabegron for up to 12-week therapy [101,102]. This drug was launched for use in the UK at the beginning of March 2013 and it will be interesting to see how it performs in UK clinical practice. This agent is not covered in the existing guidelines as the Phase II and Phase III clinical results have yet to be published in full [53–55]. It brings the potential of an alternative therapeutic class into the

clinical armamentarium. This has the advantage of avoiding anti-M side effects and provides an alternative to anti-M therapy, particularly in patients who have not responded to anti-M drugs or who have failed to tolerate them.

Desmopressin

Nocturia is highly bothersome and an important component of OAB. Desmopressin acetate is a synthetic analog of arginine vasopressin that is recommended for use in nocturia due to nocturnal polyuria in the male LUTS guidelines and for the short-term relief of UI in the incontinence guidelines. It acts as a selective V2 receptor agonist and induces an antidiuretic effect without having vasopressor effects associated with V1 agonism. The clinical outcome is the production of lower volumes of more concentrated urine [56]. While the evidence for the use of desmopressin in reducing nocturia episodes and improving QoL is substantial, its role in reducing nocturnal incontinence episodes is largely unknown [57]. Leakage could occur due to SUI when the patient gets up to go to the toilet or due to UUI caused by DO, a reduction in nocturnal urine production would theoretically reduce the risk of these events occurring in patients with coexistent nocturnal polyuria. The main risk of desmopressin treatment is hyponatremia (serum sodium <130 mmol/l), which occurs in approximately 3% of patients [58], usually within the first week of treatment and is more common in older individuals, females and with higher doses. As such, serum sodium levels should be checked at baseline (within 36 h) and within several days and monitored subsequently (usually 3-monthly).

■ Special considerations in men

Both OAB and BOO due to benign prostatic hyperplasia become more prevalent with age and many patients will have both conditions. In men, OAB is commonly associated with DO in 69 and 90% of individuals with OAB-dry and OAB-wet, respectively [59]. Approximately half of men with LUTS/benign prostatic hyperplasia demonstrate DO as well as BOO [60,61] and in 27% of such men undergoing outlet surgery, DO persists postoperatively, suggesting a separate etiopathogenesis [62]. Similarly, storage LUTS persist in a third of patients after outlet surgery [63]. The treatment algorithm suggests that in men with both voiding and storage symptoms, the former should be treated first with

α -blockers (with the addition of 5 α -reductase inhibitors in men with larger prostates [over 30–40 g]) and should the storage symptoms persist, typically after a 4–6 week trial following treatment with an α -blocker, anti-Ms should be considered. Alternatively, OAB may be entirely unrelated to prostate disease, occurring solely due to bladder dysfunction [64], in such patients, OAB symptoms occur in the absence of voiding LUTS and primary anti-Ms are recommended after lifestyle and behavioral interventions.

Although the evidence for the efficacy of anti-Ms is robust, there are some caveats. The majority of studies have excluded men with larger PVRs (usually >200 ml) who would be at a higher risk of urinary retention. Prostate volumes (when measured) were generally low. Most trials extended to only 3 months, which may not be long enough to provide a realistic picture of the risk of urinary retention. The guidance does not specifically address these points in terms of recommendations but in practice caution must be taken in men with a PVR >200 ml and those at risk of retention (previous retention or large prostates) and a regular check of PVR is certainly warranted. In men with confirmed BOO, caution is recommended in prescribing anti-Ms.

■ Special considerations in the elderly

Anti-M treatment should be considered with caution in the elderly and frail who may often have cognitive impairment, mobility problems and tendency toward constipation. Additionally, attention should be given to the potential for drug interactions given the higher prevalence of polypharmacy in this group. The potential benefit of anti-Ms should be balanced against the risk of adverse effects and particularly the risk of impairment of cognitive function, the guidelines recommended an objective assessment of mental function before treating patients whose cognitive function may be at risk. The avoidance of use of oxybutynin IR in patients with cognitive dysfunction is also recommended due to strong evidence that this agent worsens mental functioning [65,66]. There is some suggestion that the newer agents reduce the risk of cognitive impairment in the elderly, particularly trospium, as it is not thought to cross the blood–brain barrier in significant quantities, and darifenacin which has a particularly high affinity for the M3 receptor over M1 subtype. Although it must be borne in mind that in most studies the agents were

administered for 2 weeks only, detracting from any definitive conclusions. As such, caution is recommended in using solifenacin, darifenacin and tolterodine in patients with cognitive dysfunction while considering the use of trospium in these patients is recommended.

In practice, when managing elderly patients, a sensible approach is to begin with the lowest possible dose, increasing in small increments while carefully monitoring the balance between efficacy and side effects. Trospium is an option recommended by the guidelines in patients with known cognitive dysfunction, as this agent, a quaternary amine, does not cross the blood–brain barrier in significant amounts, and therefore has minimal central anticholinergic activity [67], although there is no data to support that this is the case in patients without intact cognition. Very little data exists for individual anti-M agents in patients with cognitive deficits. A recent study published in 2013 assessed the impact of solifenacin and oxybutynin (not included in the guidelines), and found that both agents had no impact on five standard composite outcomes of cognitive function in elderly individuals with mild cognitive impairment [68]. In a secondary analysis of the data, oxybutynin was shown to lead to significant decreases in power and continuity of attention at 1–2 h postdosing while solifenacin showed no detectable impact. A prior study of oxybutynin in elderly female nursing home patients with mild-to-severe dementia showed the agent to be safe, well tolerated and not to cause delirium with no difference in confusion assessment method score between oxybutynin and placebo at up to 28 days follow-up [69]. Other studies where patients who were receiving cholinesterase inhibitors were administered anti-Ms showed no adverse effect on cognition [70,71]. It is recommended that mental function be checked in patients on anti-Ms if cognitive dysfunction is a risk. Importantly, patients themselves may not realize when memory or cognitive function has become impaired, and so caregivers should be alerted to this possibility.

■ Intravesical botulinum toxin A

If anti-Ms have failed to sufficiently control UUI, intravesical botulinum toxin A (BTA) injection is recommended in the guidelines. BTA is a neurotoxin that binds to the presynaptic terminal of the neuromuscular junction and inhibits the release of acetylcholine, resulting in impairment of

detrusor contraction, apparent clinically 24–72 h after injection [72]. The action is not permanent and muscular function returns after several months due to the formation of new functional synapses. BTA may also work on the sensory system by inhibiting neurotransmitter release from the urothelium, which may be the explanation for improvement in urgency. Peak efficacy is reported at 4 weeks with significant beneficial impact upon patient symptoms, QoL, voiding diary variables and urodynamic parameters [73].

No recommendations are given with regard to suggested time intervals between treatments as the need varies between individuals but typically symptoms return after 9 months. The treatment continues to be efficacious for up to ten treatments.

The guidelines also make no recommendations with regard to dosage. We advocate a lower starting dose of 100 U of onabotulinum toxin A (OBTA) for OAB based on the currently available literature [74] and this has been submitted to the regulatory authorities as the recommended licensed dose. It is important to note that each preparation of BTA is a separate chemical entity and the doses and data for different agents cannot be used interchangeably. A dose of 200 U OBTA, although increasing cystometric capacity by 72%, decreases detrusor voiding pressures and is associated with a nearly 40% risk of voiding problems. A large study also demonstrated that a dose of 150 U was not additionally beneficial in improving symptoms while increasing the risk of voiding problems [75]. Other important considerations where no recommendations are made are injection site, volume and number, due to lack of available evidence. Intratriggeral injections do not appear to precipitate ureteric reflux and may be an important target area in some patients. Questions remain as to whether a greater volume and number of injections leads to greater improvements.

OBTA is associated with a raised PVR in 20–43% of patients although this resolves as the effect dissipates. The guidelines recommend that patients be warned of the possible need to self-catheterize and the associated risk of UTI, and to ensure that patients are willing and able to do so. UTI occurs in 13–44% of cases. OBTA remains unlicensed for OAB in the UK and the long-term effects are largely unknown; it is recommended that patients be told this when considering therapy.

■ Peripheral tibial nerve stimulation

Percutaneous tibial nerve stimulation is recognized as an option to improve symptoms in women with UUI who have failed pharmacotherapy, although not as a cure. A nerve is stimulated using a needle inserted above the medial ankle and treatment typically lasts 30 min. Most of the evidence for percutaneous tibial nerve stimulation comes from observational studies in patients with OAB symptoms not responsive to anti-M where response rates as high as 81% have been found. The randomized trials, conducted in females found benefit at 12 weeks and a lack of significant side effects [76–78] with sustained effects at 1 year [77]. However, the disadvantages are the expense and need for repeated treatments for sustained efficacy and additionally, longer-term efficacy data is lacking. In practice patients opting for this approach should have the time, motivation and resources to attend for regular treatments.

■ Sacral neuromodulation

Sacral neuromodulation is recommended as an option in patients with refractory UUI before more invasive options such as bladder augmentation and urinary diversion are considered. An implantable device is used to generate electrical pulses to modulate the neural reflexes governing lower urinary tract function. A two-stage implantation technique is now used whereby a definitive lead is placed through the S3 foramen, then utilized for both a test and permanent phase. Tined leads are used to prevent displacement and the insertion is done using a percutaneous technique. A greater than 90% improvement in symptoms occurs in 50% of patients [79,80] and is sustained for 3 years [81]. Studies extending beyond 5 years show similar sustainment of outcomes [82,83]. The disadvantage of the approach is that it requires a surgical procedure, which has complications such as pain at implant site, migration of lead, infection and device failure. Consequently, the need for revision is significant, over 30% in most studies. Clearly patients should be willing to comply with treatment and have the cognitive and physical ability to operate the device. Patients should be carefully selected and counseled for the procedure.

■ Surgical options

Surgery is considered to be a final option by the guidelines due to its irreversible nature and significant morbidity; in practice a tiny proportion of patients with OAB will end up undergoing

surgery. Offering augmentation cystoplasty is recommended after BTA and sacral neuromodulation have been discussed and patients should be counseled regarding the likelihood of needing intermittent catheterization. The risk of metabolic complications and urinary tract infection are significant. Detrusor myomectomy is associated with less short-term complications but is not recommended due to the poor long-term results and should now be considered as obsolete. Urinary diversion recommended for patients looking for a permanent solution with severe refractory symptoms who will accept a stoma. Both urinary diversion and augmentation cystoplasty are associated with a small risk of malignancy and it is recommended patients are warned of this and that lifelong follow up is undertaken. The mortality of augmentation cystoplasty is quoted at 0–2.7% [84].

Conclusion & future perspective

Guidelines in OAB have been developed in order to improve the diagnosis and management of the symptom syndrome. The EUA guidelines are primarily aimed at those working within the specialty of urology and considerable efforts have gone into producing the recent updates aiming to improve the standard of care in Europe. The current guidelines are, in general, reflective of the contemporary evidence and concepts of best clinical practice. The guidance is hindered by the focus on UI, which may not be a feature in all patients with OAB. In this respect a guidance that is specific to OAB, as has been produced by American Urological Association [85], may be more pertinent. A drawback with international guidelines is the difficulty with local implementation given variations in availability of treatments or reimbursements for treatments. In this context, national and local guidelines are required to make aspects of international guidelines locally relevant and applicable.

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