

Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline.

IDENTITY

Citation

· Gormley EA, Lightner DJ, Burgio KL, Chai TC, Clemens JQ, Culkin DJ, Das AK, Foster HE Jr, Scarpero HM, Tessier CD, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. Linthicum (MD): American Urological Association (AUA); 2012 May. 36 p. [222 references]

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DEVELOPER

Developer Name

· American Urological Association (AUA)

Conflict Of Interest Policy

Conflict Of Interest Disclosure

PURPOSE

Objective

· To provide direction to clinicians and patients regarding how to recognize non-neurogenic overactive bladder (OAB), conduct a valid diagnostic process and approach treatment with the goals of maximizing symptom control and patient quality of life while minimizing adverse events and patient burden.

INTENDED AUDIENCE

Intended Users

· all types of providers who evaluate and treat OAB patients, including those in general practice as well as those who specialize in various branches of medicine

Care Setting

METHOD OF DEVELOPMENT

Rating Scheme

Evidence Quality Rating Scheme

- AUA categorizes evidence strength as Grade A (well-conducted RCTs or exceptionally strong observational studies), Grade B (RCTs with some weaknesses of procedure or generalizability or generally strong observational studies) or Grade C (observational studies that are inconsistent, have small sample sizes or have other problems that potentially confound interpretation of data).

Recommendation Strength Rating Scheme

- **STANDARDS** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken based on Grade A or Grade B evidence. **RECOMMENDATIONS** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken based on Grade C evidence. **OPTIONS** are non-directive statements that leave the decision to take an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears relatively equal or unclear; Options may be supported by Grade A, B or C evidence. **OPTIONS** generally reflect the Panel's judgment that a particular decision is best made by the clinician who knows the patient with full consideration of the patient's prior treatment history, current quality of life, preferences and values.

Qualifying Statement

Patient And Public Involvement

TARGET POPULATION

Inclusion Criterion

- non-neurogenic OAB

Exclusion Criterion

- individuals with symptoms related to neurologic conditions

KNOWLEDGE COMPONENTS

DEFINITIONS

Term: OAB

Term Meaning: urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of UTI or other obvious pathology

Term: urgency

Term Meaning: the complaint of a sudden, compelling desire to pass urine which is difficult to defer

Term: nocturia

Term Meaning: the complaint of interruption of sleep one or more times because of the need to void

Term: urgency urinary incontinence

Term Meaning: the involuntary leakage of urine, associated with a sudden compelling desire to void.

RECOMMENDATION: 1 - Diagnosis

Conditional: The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB and

exclude other disorders that could be the cause of the patient's symptoms; the minimum requirements for this process are a careful history, physical exam and urinalysis. {Rec_1:Cond_1 }

Decision Variable: {suspected} OAB

Value: true

Action: The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB and exclude other disorders that could be the cause of the patient's symptoms; the minimum requirements for this process are a careful history, physical exam and urinalysis.

Actor: clinicians

Verb: engage

Complement: in a diagnostic process to document symptoms and signs that characterize OAB and exclude other disorders that could be the cause of the patient's symptoms.

Deontic: should

Description: HISTORY: The clinician should carefully elicit the patient's bladder symptoms to document duration of symptoms and baseline symptom levels, to ensure that symptoms are not the consequence of some other condition and to determine whether the patient constitutes a complex OAB presentation that may require referral. Questions should assess bladder storage symptoms associated with OAB (e.g., urgency, urgency incontinence, frequency, nocturia), other bladder storage problems (e.g., stress incontinence episodes) and bladder emptying (e.g., hesitancy, straining to void, prior history of urinary retention, force of stream, intermittency of stream). The symptom of urgency as defined by the ICS is the "complaint of sudden compelling desire to pass urine which is difficult to defer." The interpretations of "sudden" and "compelling" are highly subjective and difficult to quantitate. Nevertheless, the clinician can simply ask if the patient has a problem getting to the bathroom in time, assuming the patient has normal mobility. Bladder function is related to amount and type of fluid intake. Excessive fluid intake can produce voiding patterns that mimic OAB symptoms. For this reason, an inquiry into fluid intake habits should be performed, including asking patients how much fluid and of what type (e.g., with or without caffeine) they drink each day, how many times they void each day and how many times they void at night. Patients who do not appear able to

provide accurate intake and voiding information should fill out a fluid diary. Urinary frequency varies across individuals. In community-dwelling healthy adults, normal frequency consists of voiding every three to four hours with a median of approximately six voids a day. Current medication use also should be reviewed to ensure that voiding symptoms are not a consequence of a prescribed medication, particularly diuretics. The degree of bother from bladder symptoms also should be assessed. If a patient is not significantly bothered by his/her bladder symptoms, then there would be less compelling reason to treat the symptoms. Degree of bother can affect different domains of daily activities related to work and leisure. Patients may avoid certain activities (e.g., travel, situations that do not allow easy access to a toilet) because of their bladder symptoms. Co-morbid conditions should be completely elicited as these conditions may directly impact bladder function. Patients with co-morbid conditions and OAB symptoms would be considered complicated OAB patients. These co-morbid conditions include neurologic diseases (i.e., stroke, multiple sclerosis, spinal cord injury), mobility deficits, medically complicated/uncontrolled diabetes, fecal motility disorders (fecal incontinence/constipation), chronic pelvic pain, history of recurrent urinary tract infections (UTIs), gross hematuria, prior pelvic/vaginal surgeries (incontinence/prolapse surgeries), pelvic cancer (bladder, colon, cervix, uterus, prostate) and pelvic radiation. The female patient with significant prolapse (i.e., prolapse beyond the introitus) also may be considered a complicated OAB patient. Patients with urgency incontinence, particularly younger patients, or a patient with extremely severe symptoms could represent a complicated OAB patient with an occult neurologic condition. A patient who has failed multiple anti-muscarinics to control OAB symptoms could also be considered a complicated OAB patient. If the history elicits any of these co-morbid conditions and/or special situations, then the clinician should consider referring these patients to a specialist for further evaluation and treatment.

Description: PHYSICAL EXAMINATION: A careful, directed physical exam should be performed. An abdominal exam should be performed to assess for scars, masses, hernias and areas of tenderness as well as

for suprapubic distension that may indicate urinary retention. Examination of lower extremities for edema should be done to give the clinician an assessment of the potential for fluid shifts during periods of postural changes. A rectal/genitourinary exam to rule out pelvic floor disorders (e.g., pelvic floor muscle spasticity, pain, pelvic organ prolapse) in females and prostatic pathology in males should be performed. In menopausal females, atrophic vaginitis should be assessed as a possible contributing factor to incontinence symptoms. The examiner should assess for perineal skin for rash or breakdown. The examiner also should assess perineal sensation, rectal sphincter tone and ability to contract the anal sphincter in order to evaluate pelvic floor tone and potential ability to perform pelvic floor exercises (e.g., the ability to contract the levator ani muscles) as well as to rule out impaction and constipation. Cognitive impairment is related to symptom severity and has therapeutic implications regarding goals and options. The Mini-Mental State Examination (MMSE) is a standardized, quick and useful assessment of cognitive function. An MMSE should be conducted on all patients who may be at risk for cognitive impairment to determine whether symptoms are aggravated by cognitive problems, to ensure that they will be able to follow directions for behavioral therapy and/or to determine the degree of risk for cognitive decline with anti-muscarinic therapy. In the Panel's experience, the ability of the patient to dress independently is informative of sufficient motor skills related to toileting habits.

Description: URINALYSIS: A urinalysis to rule out UTI and hematuria should be performed. A urine culture is not necessary unless indication of infection (i.e., nitrites/leukocyte esterase on dipstick, pyuria/bacteriuria on microscopic exam) is found and may be done at the discretion of the clinician. If evidence of infection is detected, then a culture should be performed, the infection treated appropriately and the patient should be queried regarding symptoms once the infection has cleared. If evidence of hematuria not associated with infection is found, then the patient should be referred for urologic evaluation.

Recommendation Strength: Clinical Principle

Logic:

If
{suspected} OAB is [true]
Then
The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB and exclude other disorders that could be the cause of the patient's symptoms; the minimum requirements for this process are a careful history, physical exam and urinalysis.

RECOMMENDATION: 2 - Diagnosis

Conditional: In some patients, additional procedures and measures may be necessary to validate an OAB diagnosis, exclude other disorders and fully inform the treatment plan. At the clinician's discretion, a urine culture and/or post-void residual assessment may be performed and information from bladder diaries and/or symptom questionnaires may be obtained.
{Rec_1:Cond_1 }

Decision Variable: selected patients with OAB

Action: at the clinician's discretion, a urine culture may be performed

Actor: clinicians

Verb: perform

Complement: a urine culture

Deontic: may

Description: URINE CULTURE: Urinalysis is unreliable for identification of bacterial counts below 100,000cfu/ml. In some patients with irritative voiding symptoms but without overt signs of infection, a urine culture may be appropriate to completely exclude the presence of clinically significant bacteriuria

Action: at the clinician's discretion, a post-void residual assessment may be performed

Actor: clinicians

Verb: perform

Complement: a post-void residual assessment

Deontic: may

Description: POST-VOID RESIDUAL (PVR): Measurement of the PVR is not necessary for patients who are receiving first-line behavioral interventions (see Guideline Statement 6 below) or for uncomplicated patients (i.e., patients without a history of or risk factors for urinary retention) receiving anti-muscarinic medications. Because anti-muscarinic medications can induce urinary retention, particularly in complicated

patients with retention risk factors, PVR should be assessed in patients with obstructive symptoms, history of incontinence or prostatic surgery, neurologic diagnoses and in other patients at clinician discretion when PVR assessment is deemed necessary to optimize care and minimize potential risks. It should be noted, however, that the occurrence of symptomatic urinary retention or asymptomatic elevations of postvoid residuals after the addition of anti-muscarinic agents occurs in a small proportion of patients; previously undiagnosed poor detrusor function may be unmasked in those individuals. PVR should be measured with an ultrasound bladder scanner immediately after the patient voids. If an ultrasound scanner is not available, then urethral catheterization may be used to assess PVR. For any patient on anti-muscarinic therapy, the clinician should be prepared to monitor PVR during the course of treatment should obstructive voiding symptoms appear. As there is considerable overlap between storage and emptying voiding symptoms, baseline PVRs should be performed for men with symptoms prior to initiation of anti-muscarinic therapy. Anti-muscarinics should be used with caution in patients with PVR >250-300 mL. Most randomized trials that evaluated anti-muscarinics for OAB treatment used a PVR of 150-200 mL as an exclusion criterion; the overwhelming majority of participants in these trials were women.

Action: at the clinician's discretion, information from bladder diaries may be obtained.

Actor: clinicians

Verb: obtain

Complement: information from bladder diaries

Deontic: may

Description: BLADDER DIARIES: Diaries that document intake and voiding behavior may be useful in some patients, particularly the patient who cannot describe or who is not familiar with intake and voiding patterns. Diaries also are useful to document baseline symptom levels so that treatment efficacy may be assessed. In particular, self-monitoring with a bladder diary for three to seven days is a useful first step in initiating behavioral treatments for OAB. At a minimum, the patient documents the time of each void and incontinence episode and the circumstances or reasons for the incontinence episode. Rating the degree

of urgency associated with each void and incontinence episode also can be useful. Adding measures of voided volumes can provide a practical estimate of the patient's functional bladder capacity in daily life and estimate the amount of overall fluid intake. Recording voided volumes also can be useful to differentiate between polyuria (characterized by normal or large volume voids) from OAB (characterized by frequent small voids). It is more burdensome, however, and is usually completed for only 24 to 48 hours. The bladder diary is a useful tool for both the clinician and the patient. In the evaluation phase, it provides information that can help the clinician plan appropriate components of intervention, particularly behavioral intervention. Recording the times that the patient voids provides a foundation for determining voiding intervals in bladder training programs. During the course of treatment, it can be used to monitor symptoms to track the efficacy of various treatment components and guide the intervention. For the patient, the self-monitoring effect of completing the diary enhances awareness of voiding habits and helps them recognize activities that can trigger incontinence. Twenty-four hour pad weights also can provide useful information regarding the severity of incontinence symptoms.

Action: at the clinician's discretion, information from symptom questionnaires may be obtained.

Actor: clinicians

Verb: obtain

Complement: information from symptom questionnaires

Deontic: may

Description: SYMPTOM QUESTIONNAIRES:

Validated symptom questionnaires have been utilized in OAB clinical trials to quantitate bladder symptom and bother changes with OAB therapies. Among these questionnaires are the Urogenital Distress Inventory (UDI), the UDI-6 Short Form, the Incontinence Impact Questionnaire (II-Q) and the Overactive Bladder Questionnaire (OAB-q). The rationale for utilization of these validated questionnaires is to quantitate and follow the patients' responses to OAB treatment as well as to obtain baseline and post-treatment levels of bother.

Reason: In some patients, additional procedures and measures may be necessary to validate an OAB diagnosis, exclude other disorders and fully inform the treatment plan.

Recommendation Strength: Clinical Principle

Logic:

If
selected patients with OAB
Then
(at the clinician's discretion, a urine culture may be performed
OR
at the clinician's discretion, a post-void residual assessment may be performed)
AND
(at the clinician's discretion, information from bladder diaries may be obtained.
OR
at the clinician's discretion, information from symptom questionnaires may be obtained.)

RECOMMENDATION: 3 - Diagnosis

Conditional: Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound should not be used in the initial workup of the uncomplicated patient. {Rec_2:Cond_2 }

Decision Variable: uncomplicated OAB patient

Value: true

Description: patients without a history of or risk factors for urinary retention

Action: do not use urodynamics in the initial diagnostic workup

Actor: clinicians

Verb: use

Complement: urodynamics in the initial diagnostic workup

Deontic: should not

Action: do not use cystoscopy in the initial diagnostic workup

Actor: clinicians

Verb: use

Complement: cystoscopy in the initial diagnostic workup

Deontic: should not

Action: do not use diagnostic renal and bladder ultrasound in the initial diagnostic workup

Actor: clinicians

Verb: use

Complement: diagnostic renal and bladder ultrasound in the initial diagnostic workup

Deontic: should not

Reason: Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound are not recommended in the initial diagnostic workup of the uncomplicated OAB patient. For complicated patients or refractory patients who have failed multiple OAB treatments, the choice of additional diagnostic tests depends on patient history and presentation and clinician judgment. In some cases, additional information may make clear that the patient has neurogenic OAB rather than non-neurogenic OAB and requires a different treatment plan. Patients with hematuria should be referred for a urologic work up. In the low-risk uncomplicated patient without microscopic hematuria, urine cytology is infrequently associated with atypia requiring further investigation, engendering costs and possibly resulting in morbidity. Urine cytology is not recommended in the routine evaluation of patients with uncomplicated OAB without hematuria who respond to therapy.

Recommendation Strength: Clinical Principle

Logic:

If
uncomplicated OAB patient is [true]
Then
do not use urodynamics in the initial diagnostic workup
AND
do not use cystoscopy in the initial diagnostic workup
AND
do not use diagnostic renal and bladder ultrasound in the initial diagnostic workup

RECOMMENDATION: 4 - Treatment

Conditional: OAB is not a disease; it is a symptom complex that generally is not a life threatening condition. After assessment has been performed to exclude conditions requiring treatment and counseling, no treatment is an acceptable choice made by some patients and caregivers. {Rec_3:Cond_3 }

Decision Variable: OAB

Value: true

Decision Variable: assessment has been performed to exclude conditions requiring treatment and counseling

Value: true

Action: no treatment is an acceptable choice made by some patients and caregivers

Reason: OAB is not a disease; it is a symptom complex that generally is not a life threatening condition.

Reason: Initiating treatment for OAB generally presumes that the patient can perceive an improvement in his or her quality of life. In patients who cannot perceive symptom improvements, treatment may not be appropriate, may be potentially unsafe or may be futile (e.g., in the very elderly or demented patient) except in patients for whom OAB symptoms present a significant health risk (e.g., risk for skin breakdown). It is important for clinicians who treat this problem to recognize this issue and to set feasible therapeutic goals with the patient and/or caregiver. The presence of an overactive bladder frequently accompanies other disorders such as deficiencies in cognition (i.e., dementia) and/or poor mobility, which can complicate treatment. To treat incontinence, optimally the patient must have a desire to be continent or have a desire for symptom improvement. In patients with cognitive deficits, this desire may not be present and family and/or caregivers may have difficulty understanding that simply giving a medication will not correct the problem. The other common situation associated with OAB is severely reduced mobility. Causes can range from dementia, severe arthritis, severe obesity, hemiparesis/plegia, and lower extremity amputations. In these situations, despite receiving an urge to urinate, the patient physically cannot get from their current position without assistance to a toileting facility. This cannot be corrected pharmacologically and should be recognized by the treating physician. In certain patients for whom hygiene and skin breakdown are major concerns, treatment may be considered regardless of the patient's perceptions when it is in the patient's best interests. In these patients, behavioral strategies that include prompted voiding and fluid management may be helpful. Pharmacologic treatments and invasive treatments, however, are generally not appropriate for these individuals. The Panel also recognizes that untreated incontinence can result in falls when a patient with compromised mobility attempts to move quickly to a toileting facility. The treating physician, the patient and the caregiver must weigh these risks when making the decision whether and how to treat OAB.

Recommendation Strength: Expert Opinion

Logic:

If
OAB is [true]
AND

assessment has been performed to exclude conditions requiring treatment and counseling is [true]

Then

no treatment is an acceptable choice made by some patients and caregivers

RECOMMENDATION: 5 - Treatment

Conditional: Clinicians should provide education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits vs. risks/burdens of the available treatment alternatives and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved. {Rec_4:Cond_4 }

Decision Variable: OAB

Value: true

Action: Clinicians should provide education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits vs. risks/burdens of the available treatment alternatives and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved.

Actor: clinicians

Verb: provide

Complement: education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits vs. risks/burdens of the available treatment alternatives and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved.

Deontic: should

Description: Prior to initiating treatment, the clinician should provide patient education regarding normal and abnormal bladder function, including voiding frequency and toileting behavior.

Reason: Explaining what is normal can help the patient understand how their condition diverges from normal and gives them a comparator (or goal) for judging their own progress in treatment. Education also empowers the patient to engage and participate in their treatment, which is essential when using interventions that rely on behavior change. Patients must understand that voiding is a behavior that can be managed and that successful OAB treatment requires a willing participant who is informed and engaged in the treatment process.

Reason: Patients should be informed that OAB is a symptom complex with a variable and chronic course that needs to be

managed over time, that it primarily affects quality of life, that there is no single ideal treatment and that available treatments vary in the effort required from the patient as well as in invasiveness, risk of adverse events and reversibility. An effective treatment plan depends on patients having realistic goals for treatment and a clear understanding of the risks and burdens of particular treatments. In this context, it is important to understand the patient's expectations of treatment, not only in terms of its outcome, but regarding what is required of them as well. Expectations are important because they affect motivation and adherence, and they can influence the patient's interpretation of treatment effects and satisfaction with outcomes.

Reason: Most OAB treatments can improve patient symptoms but not eliminate them. The available OAB treatments, with the exception of behavioral therapies, present risks for adverse events, some of which are serious. When initiating behavioral interventions, it is crucial that the patient understands that treatment progress and outcomes will depend on their active participation and persistence over time. It is also useful for them to understand several other aspects of behavioral change: progress is usually gradual, change can be irregular with good days and bad days and long-term change in symptoms depends on their long-term change in behavior.

Reason: Patients may decide that the symptomatic improvement achieved with a particular therapy (e.g., from 5 incontinence episodes per day to 3 incontinence episodes per day) is not worthwhile given the adverse events associated with that treatment (e.g., dry mouth and constipation associated with anti-muscarinic therapy) and choose to discontinue therapy despite symptomatic improvement. Choosing to forego treatment is a valid decision. It is the opinion of the Panel that patients seeking treatment initially and at any point in the treatment algorithm should be told that they may opt for no treatment with minimal adverse effects on their health and no impact on the success of later management should they choose to pursue treatment in the future.

Recommendation Strength: Clinical Principle

Logic:

If
OAB is [true]
Then
Clinicians should provide education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits vs. risks/burdens of the

available treatment alternatives and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved.

RECOMMENDATION: 6 - First Line Treatments: Behavioral Therapies

Conditional: Clinicians should offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as first line therapy to all patients with OAB. {Rec_5:Cond_5 }

Decision Variable: OAB

Value: true

Description: all OAB patients, including OAB patients who require a caregiver

Action: Clinicians should offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as first line therapy

Actor: clinicians

Verb: offer

Complement: behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as first line therapy

Deontic: should

Description: Behavioral therapies should be offered to all OAB patients, including OAB patients who require a caregiver; caregivers can be instructed in behavioral techniques in order to optimize patient symptom control (i.e., prompted voiding, timed voiding).

Reason: Behavioral treatments are designated as first-line treatments because they are as effective in reducing symptom levels as are anti-muscarinic medications, and they consist of many components that can be tailored to address the individual patient's needs and capacities. In addition, they are relatively non-invasive and, in contrast to medications, are associated with virtually no adverse events. They do require the active participation of the patient and/or of the patient's caregiver, however, as well as time and effort from the clinician.

Reason: Although most patients do not experience complete symptom relief with behavioral intervention, the literature indicates that most patients experience significant reductions in symptoms and improvements in quality of life. The literature provides clear support for the effectiveness of bladder training (incremental voiding schedules done with distraction and self-assertions) and behavioral training (pelvic floor muscle training with urge suppression techniques). Typical mean improvements range from 50% to 80%

reduction in the frequency of incontinence. Reductions in voiding frequency have also been documented in men and women.

Reason: There is also a good body of literature addressing the effects of weight loss on incontinence specifically. The most definitive trial reported that a 6-month behavioral weight loss intervention resulted in an 8.0% weight loss in obese women, reduced overall incontinence episodes per week by 47% (compared to 28% in the control group) and reduced urgency urinary incontinence episodes by 42% (compared to 26% in controls).

Reason: One study evaluated fluid management and reported that a 25% reduction in fluid intake reduced frequency and urgency. The Panel notes that when attempting intake reduction, baseline intake levels must be considered to determine whether reduction is appropriate. There is also evidence from a study of bladder training that reducing caffeine intake results in greater reductions in voiding frequency.

Reason: The literature review of comparative effectiveness randomized trials indicated that various types of behavioral treatment were generally either equivalent to or superior to medications in terms of reducing incontinence episodes, improving voiding parameters such as frequency and nocturia and improving QoL.

Reason: The Panel interpreted these data to indicate that behavioral therapies can result in symptomatic improvements similar to anti-muscarinics without exposing patients to adverse events. Evidence strength is Grade B because although the majority of studies were randomized trials and findings were generally consistent across studies (both randomized and observational), most of the randomized trials were of moderate quality, follow-up durations were short in most studies (12 weeks) and sample sizes were small.

Evidence Quality: Grade B; Benefits outweigh risks/burdens

Recommendation Strength: Standard

Logic:

If
OAB is [true]
Then
Clinicians should offer behavioral therapies (e.g.,
bladder training, bladder control strategies, pelvic floor
muscle training, fluid management) as first line therapy

RECOMMENDATION: 7 - First Line Treatments: Behavioral Therapies

Conditional: Behavioral therapies may be combined with anti-muscarinic therapies. {Rec_6:Cond_ 6 }

Decision Variable: OAB

Value: true

Action: behavioral therapies may be combined with anti-muscarinic therapies.

Actor: clinicians

Verb: combine

Complement: behavioral therapies and anti-muscarinic therapies.

Deontic: may

Reason: Behavioral and drug therapies are often used in combination in clinical practice to optimize patient symptom control and QoL. A limited literature indicates that initiating behavioral and drug therapy simultaneously may improve outcomes, including frequency, voided volume, incontinence and symptom distress. In patients who are not adequately improved on behavioral or drug therapy alone, there also is evidence that continuing the initial therapy and adding the alternate therapy using a stepped approach can produce additional benefit. Evidence strength is Grade C because of the limited evidence base consisting of relatively few trials, small sample sizes, and limited follow-up durations.

Evidence Quality: Grade C; Benefits outweigh risks/burdens

Recommendation Strength: Recommendation

Logic:

If

OAB is [true]

Then

behavioral therapies may be combined with anti-muscarinic therapies.

RECOMMENDATION: 8 - Second-Line Treatments: Anti-Muscarinics

Conditional: Clinicians should offer oral anti-muscarinics, including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium (listed in alphabetical order; no hierarchy is implied) as second-line therapy. {Rec_8:Cond_ 8 }

Decision Variable: OAB

Value: true

Action: Clinicians should offer oral anti-muscarinics, including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium (listed in alphabetical order; no hierarchy is implied) as second-line therapy.

Actor: clinicians

Verb: offer

Complement: Clinicians should offer oral anti-muscarinics, including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium (listed in alphabetical order; no hierarchy is implied) as second-line therapy.

Deontic: should

Risk/Harm: oral anti-muscarinics can commonly have non-life-threatening side effects such as dry mouth, constipation, dry or itchy eyes, blurred vision, dyspepsia, UTI, urinary retention and impaired cognitive function. Rarely, life-threatening side effects such as arrhythmias have been reported.

Risk/Harm: The Panel interpreted the oxybutynin and tolterodine data to indicate that the probability that a patient will experience dry mouth and/or constipation appears to be higher overall with the administration of oxybutynin compared to tolterodine.

Description: Due to the similar efficacy observed for all oral anti-muscarinic medications, the choice of medication for a particular patient depends on the patient's history of anti-muscarinic use, information regarding adverse events experienced in the past, the impact on the patient of adverse events, patient preferences, comorbidities, use of other medications and the availability of and resources to acquire specific medications. In addition, although there was no evidence of differential efficacy across medications, both qualitative analysis and meta-analysis of all randomized trial arms revealed different adverse event profiles for dry mouth and constipation. This information may be relevant if a patient is particularly sensitive to one of these adverse events.

Reason: The choice of oral anti-muscarinics as second-line therapy reflects the fact that these medications reduce symptoms but also can commonly have non-life-threatening side effects such as dry mouth, constipation, dry or itchy eyes, blurred vision, dyspepsia, UTI, urinary retention and impaired cognitive function. Rarely, life-threatening side effects such as arrhythmias have been reported. An extensive review of the randomized trials that evaluated pharmacologic therapies for OAB (including trials with placebo control groups as well as trials with active treatment comparison groups) revealed no compelling evidence for differential efficacy across medications. This finding is consistent with the conclusions of several published systematic reviews. Evidence strength was

Grade B because most trials were of moderate quality and follow-up durations were relatively short (i.e., 12 weeks).

Evidence Quality: Grade B; Benefits outweigh risks/burdens

Recommendation Strength: Standard

Logic:

If

OAB is [true]

Then

Clinicians should offer oral anti-muscarinics, including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine or trospium (listed in alphabetical order; no hierarchy is implied) as second-line therapy.

RECOMMENDATION: 9 - Second-Line Treatments: Anti-Muscarinics

Conditional: If an immediate release (IR) and an extended release (ER) formulation are available, then ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth. {Rec_7:Cond_ 7 }

Decision Variable: OAB

Value: true

Decision Variable: prescribing an anti-muscarinic

Value: true

Decision Variable: an extended release (ER) formulation is available

Value: true

Decision Variable: an immediate release (IR) formulation is available

Value: true

Action: ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth.

Benefit: lower rates of dry mouth

Actor: clinicians

Verb: prescribe

Complement: ER formulations over IR formulations

Deontic: should

Description: The decision to prescribe an IR vs. an ER formulation should be made in the context of the patient's prior experience with anti-muscarinics and the availability of medications, including insurer constraints, in order to minimize patient burden. Insurer constraints may be such that a patient may need to be prescribed an IR formulation and either have inadequate symptom control or have intolerable side effects prior to obtaining approval to be prescribed an ER formulation. The Panel notes that if a patient has

good symptom control and tolerable side effects on an IR formulation, then there is no need to change to an ER formulation.

Reason: A meta-analysis of adverse events indicated that the ER formulations of oxybutynin and tolterodine resulted in statistically significantly fewer patient reports of dry mouth than the IR formulations of both medications. Within each medication, there was no relationship with dose. There were insufficient trospium trial arms to meta-analyze the IR vs. ER formulations; however, a similar pattern was evident.

Reason: Because OAB is a chronic condition and treatment with anti-muscarinics generally would be required long-term, optimizing medication tolerability is critical to obtaining patient compliance. Adverse drug events, particularly dry mouth, are the major reasons that patients fail to comply with anti-muscarinic therapy; thus choosing the formulation with the lowest likelihood of adverse events may improve compliance. In addition, compliance with a once-daily treatment has been shown to be greater than with medications that are taken more than once a day.

Evidence Quality: Grade B; Benefits outweigh risks/burdens

Recommendation Strength: Standard

Logic:

If
OAB is [true]
AND
prescribing an anti-muscarinic is [true]
AND
an extended release (ER) formulation is available is [true]
AND
an immediate release (IR) formulation is available is [true]
Then
ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth.

RECOMMENDATION: 10 - Second-Line Treatments: Anti-Muscarinics

Conditional: Transdermal (TDS) oxybutynin (patch or gel) may be offered.
{ Rec_9:Cond_ 9 }

Decision Variable: OAB

Value: true

Decision Variable: history of dry mouth with oral agents

Value: true

Decision Variable: at risk of experiencing dry mouth with oral agents

Value: true

Action: Transdermal oxybutynin (patch or gel) may be offered instead of oral anti-muscarinics

Actor: clinicians

Verb: offer

Complement: Transdermal oxybutynin (patch or gel) instead of oral anti-muscarinics

Deontic: may

Reason: The Panel interpreted available data to indicate that transdermal oxybutynin (patch and gel) is effective in reducing incontinence episodes, in particular, with dry mouth rates that appear to be less than the meta-analyzed rates of 40.0% for oral oxybutynin ER and 68.0% for oral oxybutynin IR. Because the number of studies evaluating TDS oxybutynin was relatively few with different patient inclusion criteria (i.e., known responders to anti-muscarinic medications in some trials), the body of evidence strength was designated as Grade C.

Evidence Quality: Grade C; Benefits outweigh risks/burdens

Recommendation Strength: Recommendation

Logic:

If

OAB is [true]

AND

(history of dry mouth with oral agents is [true]

OR

at risk of experiencing dry mouth with oral agents is [true])

Then

Transdermal oxybutynin (patch or gel) may be offered instead of oral anti-muscarinics

RECOMMENDATION: 11 - Second-Line Treatments: Anti-Muscarinics

Conditional: If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication may be tried. {Rec_10:Cond_ 10 }

Decision Variable: OAB

Value: true

Decision Variable: taking an anti-muscarinic medication

Value: one

Decision Variable: inadequate symptom control

Value: true

Decision Variable: unacceptable adverse drug events

Value: true

Action: modify dose of current anti-muscarinic medication

Actor: clinicians

Verb: modify

Complement: dosage of current anti-muscarinic medication

Deontic: may

Action: prescribe a different anti-muscarinic medication

Actor: clinicians

Verb: prescribe

Complement: a different anti-muscarinic medication

Deontic: may

Reason: In the Panel's experience, patients who experience inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication may experience better symptom control and/or a more acceptable adverse drug event profile with another anti-muscarinic. In addition, in some patients, dose modification (i.e., reducing dose or reducing dose and combining medication with behavioral techniques) may achieve a better balance between efficacy and adverse drug events. A small literature composed of observational studies supports this experience, particularly when switching from an older medication to a newer medication. Patients who had prior unsatisfactory symptom control and/or unacceptable adverse events with tolterodine or oxybutynin reported better efficacy and/or more acceptable adverse event profiles with fesoterodine solifenacin or darifenacin. Based on the Panel's clinical experience and this limited literature, the Panel advises that clinicians should not abandon anti-muscarinic therapy if trial of one medication appears to fail or produces an unacceptable adverse event profile. There is no literature that addresses combination therapy of anti-muscarinics with each other or with other classes of medication such as tricyclics to manage non-neurogenic OAB.

Recommendation Strength: Clinical Principle

Logic:

If
OAB is [true]
AND
taking an anti-muscarinic medication is [one]
AND
(inadequate symptom control is [true])
OR

unacceptable adverse drug events is [true])
Then
modify dose of current anti-muscarinic medication
OR
prescribe a different anti-muscarinic medication

RECOMMENDATION: 12 - Second-Line Treatments: Anti-Muscarinics

Conditional: Clinicians should not use anti-muscarinics in patients with narrow angle glaucoma unless approved by the treating ophthalmologist and should use anti-muscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention. {Rec_11:Cond_ 11 }

Decision Variable: OAB

Value: true

Decision Variable: narrow angle glaucoma

Value: true

Decision Variable: use of anti-muscarinics approved by treating ophthalmologist

Value: false

Action: do not use anti-muscarinics

Actor: clinicians

Verb: prescribe

Complement: anti-muscarinics

Deontic: should not

Recommendation Strength: Clinical Principle

Logic:

If
OAB is [true]
AND
narrow angle glaucoma is [true]
AND
use of anti-muscarinics approved by treating ophthalmologist is [false]
Then
do not use anti-muscarinics

Conditional: Clinicians should not use anti-muscarinics in patients with narrow angle glaucoma unless approved by the treating ophthalmologist and should use anti-muscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention. {Rec_11:Cond_ 12 }

Decision Variable: OAB

Value: true

Decision Variable: impaired gastric emptying

Value: true

Decision Variable: history of urinary retention

Value: true

Action: use anti-muscarinics with extreme caution

Actor: clinicians

Verb: prescribe

Complement: anti-muscarinics with extreme caution

Deontic: should

Description: If the patient is at risk for or has a history of gastric emptying problems, then the patient should be seen by or receive clearance from a gastroenterologist. If the patient has a history of or is at risk of urinary retention, then urology consultation should be strongly considered. It is useful to obtain a post void residual in any patient the clinician suspects has a higher than normal risk of urinary retention. Anti-muscarinics are also contraindicated in patients using solid oral forms of potassium chloride, as the reduced gastric emptying potentially caused by the anti-muscarinics may increase the potassium absorption of these agents. If these patients can be switched to alternative forms of potassium chloride, then anti-muscarinic therapy may be possible with caution. In weighing the risks of anti-muscarinic therapy in high-risk patients, it is important to remember that OAB may compromise quality of life, but it is not a life-threatening condition. Clinicians, therefore, should exercise extreme caution in using treatments that may present life-threatening risks.

Recommendation Strength: Clinical Principle

Logic:

If
OAB is [true]
AND
(impaired gastric emptying is [true]
OR
history of urinary retention is [true])
Then
use anti-muscarinics with extreme caution

RECOMMENDATION: 13 - Second-Line Treatments: Anti-Muscarinics

Conditional: Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic therapy. Management may include bowel management, fluid management, dose modification or alternative anti-muscarinics. {Rec_12:Cond_13 }

Decision Variable: OAB

Value: true

Decision Variable: effective anti-muscarinic therapy

Value: true

Decision Variable: patient considering discontinuation

Value: true

Action: manage constipation and dry mouth before abandoning effective anti-muscarinic therapy

Actor: clinicians

Verb: manage

Complement: manage constipation and dry mouth before abandoning effective anti-muscarinic therapy

Deontic: should

Description: Management may include bowel management, fluid management, dose modification or alternative anti-muscarinics.

Description: Even before initiating anti-muscarinic therapy, patients should be educated about the possible effects of medication on bowel function and the roles of adequate dietary fiber and fluid, psyllium-based fiber supplements, regular exercise and normal bowel habits. Preparing for dry mouth might include advice on oral lubricants, avoiding mouthwashes with alcohol, taking small sips of water, sucking on sugar-free hard candies and chewing sugar-free gum. When dosing options are available, dose reduction can provide relief from side-effects while retaining some therapeutic effects. In older patients who may metabolize drugs differently, it is often advisable to start with a minimal dose and then increase it if it is tolerated well. With multiple drugs available for OAB, trying alternate anti-muscarinics may identify a medication that the patient can more easily tolerate.

Reason: One of the main limitations of anti-muscarinic therapy is that the majority of patients discontinue after a few weeks or months. Although there may be several factors involved in this decision, side effects are commonly cited as the reason for discontinuation. One way clinicians can help patients benefit from anti-muscarinic therapy is to proactively monitor for and manage common side-effects.

Recommendation Strength: Clinical Principle

Logic:

If

OAB is [true]

AND

effective anti-muscarinic therapy is [true]

AND
patient considering discontinuation is [true]
Then
manage constipation and dry mouth before abandoning
effective anti-muscarinic therapy

RECOMMENDATION: 14 - Second-Line Treatments: Anti-Muscarinics

Conditional: Clinicians must use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties. {Rec_13:Cond_ 14 }

Decision Variable: OAB

Value: true

Decision Variable: use of medications with anti-cholinergic properties

Value: true

Description: These medications include tricyclic antidepressants, those used in the treatment of Parkinsonism and other extra-pyramidal diseases and of Alzheimer's disease, and include benzotropine, biperiden HCl, galantamine, rivastigmine and trihexyphenidyl HCl. Certain anti-nausea medications and those with atropine-like properties, such as trimethaphan, methscopolamine bromide and ipratropium, may also potentiate these side effects. Providers also should exercise caution in patients who are prescribed acetylcholinesterase inhibitors such as donepezil. This list is not intended to be exhaustive; prescribers should be aware of precautions and contraindications for these medications.

Action: use caution in prescribing anti-muscarinics

Actor: clinicians

Verb: use caution in prescribing

Complement: anti-muscarinics

Deontic: must

Description: Providers also should exercise caution in patients who are prescribed acetylcholinesterase inhibitors such as donepezil. This list is not intended to be exhaustive; prescribers should be aware of precautions and contraindications for these medications.

Reason: The concurrent use of other medications with anti-cholinergic activity may potentiate the side effects of the anti-muscarinic class of OAB medications.

Recommendation Strength: Expert Opinion

Logic:

If
OAB is [true]
AND
use of medications with anti-cholinergic properties is
[true]
Then
use caution in prescribing anti-muscarinics

RECOMMENDATION: 15 - Second-Line Treatments: Anti-Muscarinics

Conditional: Clinicians should use caution in prescribing anti-muscarinics in the frail OAB patient. {Rec_14:Cond_ 15 }

Decision Variable: OAB

Value: true

Decision Variable: frail

Value: true

Description: patients with mobility deficits (i.e., require support to walk, have slow gait speed, have difficulty rising from sitting to standing without assistance), weight loss and weakness without medical cause and who may have cognitive deficits

Action: Clinicians should use caution in prescribing anti-muscarinics

Actor: clinicians

Verb: use caution

Complement: in prescribing anti-muscarinics

Deontic: should

Description: Clinicians should begin with the lowest possible dose and increase doses slowly while carefully assessing for the balance between symptom control and adverse events. The use of transdermal anti-muscarinics should be monitored to ensure that the skin where the medication is applied remains intact.

Description: In dementia patients, anti-muscarinics should be used with extreme caution or may be contraindicated entirely depending on the level of cognitive impairment.

Reason: In frail patients, defined as patients with mobility deficits (i.e., require support to walk, have slow gait speed, have difficulty rising from sitting to standing without assistance), weight loss and weakness without medical cause and who may have cognitive deficits (PR 37, 98, 315), the use of OAB medications may have a lower therapeutic index and a higher adverse drug event profile. OAB medication studies generally are not conducted in the frail elderly, resulting in a lack of data in this group. In the Panel's experience, however,

adverse drug events in addition to the typically reported events of dry mouth and constipation may occur, including impaired thermoregulation that can cause dangerous core temperature elevation.

Reason: Cognitive deficits, particularly memory difficulties, have been reported in response to anti-muscarinics, and clinical experience suggests that elderly patients may be particularly prone to these adverse effects. There is some suggestion that the newer agents (e.g., darifenacin) are less likely to produce cognitive deficits in elderly patients than are the older agents, but the literature is limited and the two-week drug administration period in these studies is not long enough to yield definitive conclusions. Key notes, however, that patients may not recognize that memory deterioration has occurred, making it essential for the clinician, family members and caregivers to monitor for these effects. In addition, polypharmacy is common in community dwelling patients who are frail, placing them at higher risk for adverse drug events, including impaired cognition. In dementia patients, anti-muscarinics should be used with extreme caution or may be contraindicated entirely depending on the level of cognitive impairment. The clinician should consider these possibilities in prescribing anti-muscarinics to frail patients and reassess the balance between benefits and risks/burdens with the patient, caregiver and/or family on a regular basis and/or when functioning appears to change. In patients who cannot tolerate anti-muscarinics or for whom these medications are not appropriate, behavioral strategies that include prompted voiding and fluid management may be helpful.

Recommendation Strength: Clinical Principle

Logic:

If
OAB is [true]
AND
frail is [true]
Then
Clinicians should use caution in prescribing anti-muscarinics

RECOMMENDATION: 16 - Second-Line Treatments: Anti-Muscarinics

Conditional: Patients who are refractory to behavioral and medical therapy should be evaluated by an appropriate specialist if they desire additional therapy. {Rec_15:Cond_ 16 }

Decision Variable: refractory OAB

Value: true

Description: The Panel defines the refractory patient as the patient who has failed a trial of symptom-appropriate behavioral therapy of sufficient length to evaluate potential efficacy and who has failed a trial of at least one anti-muscarinic medication administered for 6 to 12 weeks. Failure of an anti-muscarinic medication may include lack of efficacy and/or inability to tolerate adverse drug effects. The Panel notes that this definition is a minimum definition; individual clinicians and patients may decide that it is in the best interests of the patient to persevere with behavioral and/or anti-muscarinic therapy for longer periods, to combine behavioral and anti-muscarinic therapies to achieve better efficacy, or to try alternate anti-muscarinics before judging that a patient is refractory.

Decision Variable: desire additional therapy

Value: true

Action: patients should be evaluated by an appropriate specialist

Actor: patients

Verb: be evaluated by

Complement: an appropriate specialist

Deontic: should

Description: Behavioral therapies present no risks to patients and anti-muscarinics present risks that cease when the medication is stopped. The remaining treatment levels present increasing risks to patients that must be balanced with potential efficacy. Before a patient is exposed to these therapies, a comprehensive evaluation should be conducted to ensure that the patient's symptoms are attributable to OAB and not to some other disease process that requires other kinds of treatment and the patient's desire for further treatment should be ascertained.

Reason: Behavioral therapies present no risks to patients and anti-muscarinics present risks that cease when the medication is stopped. The remaining treatment levels present increasing risks to patients that must be balanced with potential efficacy.

Recommendation Strength: Expert Opinion

Logic:

If
refractory OAB is [true]
AND
desire additional therapy is [true]

Then
patients should be evaluated by an appropriate
specialist

RECOMMENDATION: 17 - FDA-Approved Neuromodulation Therapies

Conditional: Clinicians may offer sacral neuromodulation (SNS) as third-line treatment in a carefully selected patient population characterized by severe refractory OAB symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure. {Rec_16:Cond_17 }

Benefit Harm Assessment: Given the negative effects on quality of life associated with severe incontinence and frequency, the Panel judged that benefits of SNS in the appropriate patient outweighed the risks/burdens and notes that patients should be carefully counseled regarding the risks/burdens. Evidence strength is Grade C because of the predominance of observational designs, the small sample sizes, the limited number of unique patient groups (i.e., there are multiple reports on the same patient groups followed over time) and limited information regarding the protocols used by patients to maintain symptom control.

Decision Variable: severe refractory OAB symptoms

Value: true

Decision Variable: candidate for second-line therapy

Value: false

Decision Variable: willing to undergo a surgical procedure

Value: true

Action: Clinicians may offer sacral neuromodulation (SNS) as third-line treatment

Actor: clinicians

Verb: offer

Complement: sacral neuromodulation (SNS) as third-line treatment

Deontic: may

Risk/Harm: In contrast to PTNS studies (see discussion under Guideline Statement 18), SNS studies reported frequent adverse events, including pain at the stimulator site (3.3 to 19.8% of patients), pain at the lead site (4.5 to 19.1% of patients), lead migration (2.2 to 8.6% of patients), infection/irritation (2.2 to 14.30% of patients), electric shock (5.5 to 7.9% of patients) and need for surgical revision (6.25 to 39.5% of patients). In most studies, the need for surgical revision occurred in greater than 30% of patients. There is some evidence that newer, less invasive surgical procedures and tined devices may be associated with fewer adverse events.

Leong (2011) reported that although 90% of patients reported satisfaction with SNS, 56% reported adverse events, particularly pain at the stimulator site and when the stimulator was turned on and daily life limitations, such as difficulty passing through airport metal detectors and inability to undergo magnetic resonance imaging (MRI).

Description: The Panel notes that patients should be counseled that the device requires periodic replacement in a planned surgical procedure and that the length of time between replacements depends on device settings. Patients also must be willing to comply with the treatment protocol because treatment effects typically are only maintained as long as the therapy is maintained and have the cognitive capacity to use the remote control to optimize device function. In addition, patients must accept that the use of diagnostic MRIs is contraindicated in individuals with the device implanted.

Reason: The Panel interpreted available data to indicate that in carefully selected patients, SNS is an appropriate therapy that can have durable treatment effects but in the context of frequent and moderately severe adverse events, including the need for additional surgeries.

Evidence Quality: Grade C; Benefits outweigh risks/burdens

Recommendation Strength: Recommendation

Logic:

If
(severe refractory OAB symptoms is [true]
OR
candidate for second-line therapy is [false])
AND
willing to undergo a surgical procedure is [true]
Then
Clinicians may offer sacral neuromodulation (SNS) as
third-line treatment

RECOMMENDATION: 18 - FDA-Approved Neuromodulation Therapies

Conditional: Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third-line treatment in a carefully selected patient population. {Rec_17:Cond_18 }

Decision Variable: moderately severe baseline incontinence

Value: true

Decision Variable: moderately severe baseline frequency

Value: true

Decision Variable: willingness to comply with the PTNS protocol

Value: true

Decision Variable: resources to make frequent office visits in order to obtain treatment

Value: true

Action: Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third-line treatment

Actor: clinicians

Verb: offer

Complement: peripheral tibial nerve stimulation (PTNS) as third-line treatment

Deontic: may

Reason: The Panel interpreted available data to indicate that PTNS can benefit a carefully selected group of patients characterized by moderately severe baseline incontinence and frequency and willingness to comply with the PTNS protocol. Patients must also have the resources to make frequent office visits in order to obtain treatment because treatment effects dissipate once treatment ceases. As a group, the PTNS studies constitute Grade C evidence because of the predominant observational designs, varying patient inclusion criteria and short follow-up durations for most studies.

Evidence Quality: Grade C; Balance between benefits and risks/burdens uncertain

Recommendation Strength: Option

Logic:

If
moderately severe baseline incontinence is [true]
AND
moderately severe baseline frequency is [true]
AND
willingness to comply with the PTNS protocol is [true]
AND
resources to make frequent office visits in order to
obtain treatment is [true]
Then
Clinicians may offer peripheral tibial nerve stimulation
(PTNS) as third-line treatment

RECOMMENDATION: 19 - Non-FDA-Approved: Intradetrusor injection of onabotulinumtoxinA

Conditional: Clinicians may offer intradetrusor onabotulinumtoxinA as third-line treatment in the carefully-selected and thoroughly-counseled patient who has been refractory to first- and second-line OAB treatments. The patient must be able and

willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization if necessary. {Rec_18:Cond_ 19 }

Decision Variable: refractory to first-line OAB treatments

Value: true

Decision Variable: refractory to second-line OAB treatments

Value: true

Decision Variable: thoroughly counseled

Value: true

Decision Variable: able and willing to return for frequent post-void residual evaluation

Value: true

Decision Variable: able and willing to perform self-catheterization if necessary.

Value: true

Action: Clinicians may offer intradetrusor onabotulinumtoxinA as third-line treatment

Actor: clinicians

Verb: offer

Complement: intradetrusor onabotulinumtoxinA as third-line treatment

Deontic: may

Description: Patients considering onabotulinumtoxinA treatment must be counseled regarding the possible need to perform self-catheterization for long periods (or to have a caregiver perform catheterization) and should be willing to accept this possibility.

OnabotulinumtoxinA treatment also may require access to a clinician who can measure PVR on a periodic basis if necessary. Further, effects diminish over time for most patients; therefore, patients also should be informed that repeat injections are likely to be necessary to maintain symptom reduction. The Panel also believes that this procedure should be performed by experienced personnel familiar with intravesical injection techniques.

Reason: The Panel designated intradetrusor onabotulinumtoxinA treatment as an option because although most studies reported improvements in measured parameters, rates of adverse events that could compromise quality of life or lead to serious illness were extremely high in some trials, making the balance between benefits and risks/burdens unclear. In addition, at the time of this writing, intradetrusor onabotulinumtoxinA is not FDA-approved for treatment of non-neurogenic OAB.

Reason: The Panel interpreted available data to indicate that, although onabotulinumtoxinA injections can improve symptoms, the risk of adverse events that could require secondary intervention is substantial (e.g., an untreated UTI, undiagnosed urinary retention). Evidence strength is Grade C because follow-up durations were short in the best-designed studies (ranging from 4 to 12 weeks for the RCTs), most of the available studies were observational designs without control groups, doses and injection sites varied across studies, adverse event reporting was extremely variable and the total number of patients evaluated in the randomized trials was small (approximately 400).

Evidence Quality: Grade C; Balance between benefits and risks/burdens uncertain

Recommendation Strength: Option

Logic:

If
refractory to first-line OAB treatments is [true]
AND
refractory to second-line OAB treatments is [true]
AND
thoroughly counseled is [true]
AND
able and willing to return for frequent post-void residual evaluation is [true]
AND
able and willing to perform self-catheterization if necessary. is [true]
Then
Clinicians may offer intradetrusor onabotulinumtoxinA as third-line treatment

Notes: The available literature on intravesical use of onabotulinumtoxinA is reviewed below; the Panel focused this treatment Option on injections into the detrusor specifically because most studies assessed this injection location. There is insufficient evidence at present to comment on the relative efficacy of injections into other intravesical locations.

RECOMMENDATION: 20 - Additional Treatments

Conditional: Indwelling catheters (including transurethral, suprapubic, etc.) are not recommended as a management strategy for OAB because of the adverse risk/benefit balance except as a last resort in selected patients. {Rec_19:Cond_ 21 }

Decision Variable: urinary incontinence has resulted in the development and progression of decubiti

Value: true

Code Set: {true}

Decision Variable: urinary incontinence is the predominant disability affecting activities of daily living and therefore may result in institutionalization

Value: true

Decision Variable: medical management of burdensome OAB is not feasible, effective nor recommended

Value: true

Description: as in the patient with severe cognitive deficits or mobility issues

Action: As a last resort, an indwelling catheter may be considered.

Actor: clinicians

Verb: consider

Complement: an indwelling catheter (including transurethral, suprapubic, etc.) as a last resort

Deontic: may

Reason: In situations where the medical management of burdensome OAB, as outlined above, is not feasible, effective nor recommended, as in the patient with severe cognitive deficits or mobility issues, then other management options may need to be considered. Management with diapering and absorbent garments is always preferred to indwelling catheterization because of the high risk of indwelling catheter-associated UTIs, urethral erosion/destruction and urolithiasis. Intermittent catheterization may be an option when concomitant incomplete bladder emptying is present leading to overflow incontinence; however, this approach generally requires either patient willingness and ability or significant caregiver support.

Recommendation Strength: Expert Opinion

Logic:

If
urinary incontinence has resulted in the development
and progression of decubiti is [true]

OR

urinary incontinence is the predominant disability
affecting activities of daily living and therefore may
result in institutionalization is [true]

OR

medical management of burdensome OAB is not
feasible, effective nor recommended is [true]

Then

As a last resort, an indwelling catheter may be considered.

RECOMMENDATION: 21 - Additional Treatments

Conditional: In rare cases, augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB patients may be considered. {Rec_20:Cond_22 }

Decision Variable: severe OAB

Value: true

Decision Variable: refractory OAB

Value: true

Decision Variable: complicated OAB

Value: true

Action: In rare cases, augmentation cystoplasty or urinary diversion may be considered.

Actor: clinicians

Verb: consider

Complement: augmentation cystoplasty or urinary diversion

Deontic: may

Reason: In general, surgery is not recommended for OAB patients except in extremely rare cases. The vast majority of case series that document the effects of augmentation cystoplasty and diversion focus on neurogenic patients. Little is known regarding the impact of these procedures on non-neurogenic OAB patients and, particularly, on their quality of life. There are substantial risks to these procedures, however, including the likely need for long-term intermittent self-catheterization and the risk of malignancy.¹⁹⁹ In the Panel's judgment, therefore, a surgical approach to OAB treatment is appropriate only in the extremely rare patient.

Logic:

If
severe OAB is [true]
OR
refractory OAB is [true]
OR
complicated OAB is [true]

Then
In rare cases, augmentation cystoplasty or urinary diversion may be considered.

RECOMMENDATION: 22 - Follow-Up

Conditional: The clinician should offer follow up with the patient to assess compliance, efficacy, side effects and possible alternative treatments. {Rec_21:Cond_23 }

Decision Variable: OAB

Value: true

Action: The clinician should offer follow up with the patient to assess compliance, efficacy, side effects and possible alternative treatments.

Actor: clinicians

Verb: offer

Complement: follow up to assess compliance, efficacy, side effects and possible alternative treatments.

Deontic: should

Description: The purpose of follow-up is to assess compliance with treatment protocols, query patients regarding symptom improvements and any adverse events and present information about possible alternative treatments to patients who have insufficient symptom improvement and/or intolerable adverse events. There are many ways to measure symptom changes, including voiding diaries with or without frequency-volume charts and patient-rated global response scales for urgency, urgency incontinence, incontinence, frequency and nocturia. In addition, validated OAB-specific instruments may be used to assess the impact of OAB symptoms on quality of life. Ideally, clinicians should obtain baseline measures using the same instruments in order to chart progress. Patients should be encouraged to persist with a particular treatment for four to eight weeks; this time period will identify the majority of responders.

Description: Clinicians and any clinical personnel engaged in follow-up should be aware that the various treatment options for OAB have different requirements for efficacy and different adverse event probabilities and severities. For example, the efficacy of some treatments (e.g., behavioral therapies, neuromodulation) depends greatly on treatment compliance, and the efficacy must be balanced against possible adverse events. For other treatments, such as the use of anti-muscarinics, adverse events are common but vary in severity across patients. Patients should be informed about and subsequently queried regarding dry mouth and its severity (i.e., sufficient to impair alimentation), constipation, fecal retention and any possible central nervous system (CNS) effects. Queries of the patient and caregiver regarding CNS effects are particularly important in elderly or frail patients; clinical experience suggests that CNS effects can be severe enough to

cause loss of independent living skills in some patients. Non-responders to anti-muscarinics should be tried on at least one other anti-muscarinic and/or dose modification attempted to determine if a better balance between efficacy and adverse events occurs. If adverse events are severe enough to compromise patient quality of life, then strategies to manage specific adverse events, such as ameliorating constipation with appropriate bowel management, should be implemented before abandoning anti-muscarinic treatment.

Description: For therapies collectively labeled as neuromodulation, including sacral neuromodulation and peripheral tibial nerve stimulation, pre- and post-therapy measures are essential to assess efficacy. The before-and-after evaluation should include baseline assessment with a voiding diary and assessment of urgency as well as a global response assessment. Adverse events such as pain and collateral stimulation should be assessed, and sacral neuromodulation wound complications should be evaluated.

Description: Patients treated with intradetrusor onabotulinumtoxinA should be followed for the possibility of increased PVRs and the need for self-catheterization. Patients who have undergone surgical treatments (e.g., augmentation cystoplasty with or without sling, supravescical diversion) or permanent or semi-permanent catheter placements also should be followed regularly for symptom level, QoL and any complications. Patients who are using incontinence pads, regardless of whether or how they are being treated, should be followed for appropriate skin care and skin integrity.

Recommendation Strength: Expert Opinion

Logic:

If

OAB is [true]

Then

The clinician should offer follow up with the patient to assess compliance, efficacy, side effects and possible alternative treatments.

ALGORITHM: