DIAGNOSIS AND TREATMENT OF OVERACTIVE BLADDER (Non-Neurogenic) IN ADULTS: AUA/SUFU GUIDELINE

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Purpose: The purpose of this guideline is to provide a clinical framework for the diagnosis and treatment of non-neurogenic overactive bladder (OAB).

Methods: The primary source of evidence for the original version of this guideline was the systematic review and data extraction conducted as part of the Agency for Healthcare Research and Quality (AHRQ) Evidence Report/Technology Assessment Number 187 titled *Treatment of Overactive Bladder in Women* (2009).[1] That report searched PubMed, MEDLINE, EMBASE, and CINAHL for English-language studies published from January 1966 to October 2008 relevant to OAB. AUA conducted additional literature searches to capture treatments not covered in detail by the AHRQ report (e.g., intravesical onabotulinumtoxinA) and relevant articles published between October 2008 and December 2011. Insufficient evidence was retrieved regarding diagnosis; this portion of the guideline, therefore, is based on Clinical Principles and Expert Opinion. The review yielded an evidence base of 151 treatment articles after application of inclusion/exclusion criteria. The AUA update literature review process, in which an additional systematic review is conducted periodically to maintain guideline currency with newly-published relevant literature, was conducted in February 2014. This review identified an additional 72 articles relevant to treatment. These publications were used to create the majority of the treatment portion of the guideline. When sufficient evidence existed, the body of evidence for a particular treatment was assigned a strength rating of A (high), B (moderate) or C (low). Additional treatment information is provided as Clinical Principles and Expert Opinion when insufficient evidence existed. See text and algorithm for definitions and detailed diagnostic, management and treatment frameworks.

Guideline Statements

Diagnosis:

1. 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. *Clinical Principle*

2. 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. *Clinical Principle*

3. Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound should not be used in the initial workup of the uncomplicated patient. *Clinical Principle*

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4. 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. *Expert Opinion*

5. 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. *Clinical Principle*

Treatment:

First-Line Treatments:

6. 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. *Standard (Evidence Strength Grade B)*

7. Behavioral therapies may be combined with pharmacologic management. *Recommendation (Evidence Strength Grade C)*

Second-Line Treatments:

8. Clinicians should offer oral anti-muscarinics or oral β_3-adrenoceptor agonists as second-line therapy. *Standard (Evidence Strength Grade B)*

9. 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. *Standard (Evidence Strength Grade B)*

10. Transdermal (TDS) oxybutynin (patch [now available to women ages 18 years and older without a prescription]* or gel) may be offered. *Recommendation (Evidence Strength Grade C)*Revised June 11, 2013*

11. 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 or a β_3-adrenoceptor agonist may be tried. *Clinical Principle*

12. 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. *Clinical Principle*

13. 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. *Clinical Principle*

14. Clinicians must use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties. *Expert Opinion*

15. Clinicians should use caution in prescribing anti-muscarinics or β_3-adrenoceptor agonists in the frail OAB patient. *Clinical Principle*

16. Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy. *Expert Opinion*

Third-line Treatments:

17. Clinicians may offer intradetrusor onabotulinumtoxinA (100U) 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. *Standard Option (Evidence Strength Grade B C)*

18. Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third line treatment in a carefully selected patient population. *Recommendation (Evidence Strength Grade C)*

19. 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. *Recommendation (Evidence Strength – Grade C)*

20. Practitioners and patients should persist with new treatments for an adequate trial in order to determine whether the therapy is efficacious and tolerable. Combination therapeutic approaches should be assembled methodically, with the addition of new therapies occurring only when the relative efficacy of the preceding therapy is known. Therapies that do not demonstrate efficacy after an adequate trial should be ceased. *Expert Opinion*

Additional Treatments:

21. 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. *Expert Opinion*

22. In rare cases, augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB patients may be considered. *Expert Opinion*

Follow-Up:

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

Introduction

Section 1: Purpose

This guideline's purpose is 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. The strategies and approaches recommended in this document were derived from evidence-based and consensus-based processes. There is a continually expanding literature on OAB; the Panel notes that this document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to OAB evolves and improves, the strategies presented here will require amendment to remain consistent with the highest standards of clinical care. This document was created to serve as a guide for 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.

Section 2: Methodology

The primary source of evidence for the first version of this guideline was the systematic review and data extraction conducted as part of the Agency for Healthcare Research and Quality (AHRQ) Evidence Report/Technology Assessment Number 187 titled *Treatment of Overactive Bladder in Women* (2009).[1] That report, prepared by the Vanderbilt University Evidence-Based Practice Center (EPC), searched PubMed, MEDLINE, EMBASE and CINAHL for English-language studies published from January 1966 to October 2008 relevant to OAB and excluded non-relevant studies, studies with fewer than 50 participants and studies with fewer than 75% women. AUA conducted an additional literature search to capture articles published between October 2008 and December 2011. In addition, because the Panel wished to consider data for male as well as female patients, studies excluded by the AHRQ report because there were fewer than 75% women participants were extracted and added to the database. Studies that focused primarily on nocturia were also added to the database. Given that the AHRQ report included limited information regarding use of neuromodulation therapies, including sacral neuromodulation (SNS) and peripheral tibial nerve stimulation (PTNS) (also known as posterior tibial nerve stimulation) and limited information regarding the use of intravesical onabotulinumtoxinA to treat non-neurogenic OAB patients, additional searches were performed to capture this literature and relevant data were added to the database. The AUA update literature review process, in which an additional systematic review is conducted periodically to maintain guideline currency with newly-published relevant literature, was conducted in February 2014. This review identified an additional 72 articles relevant to treatment. These articles were added to the database, and AUA's qualitative and quantitative analyses were updated as appropriate.

Data from studies published after the literature search cut-off will be incorporated into the next version of this guideline. Preclinical studies (e.g., animal models), pediatric studies, commentary and editorials were eliminated. Review article references were checked to ensure inclusion of all possibly relevant studies. Multiple reports on the same patient group were carefully examined to ensure inclusion of only nonredundant information.

OAB Diagnosis. The review revealed insufficient publications to address OAB diagnosis from an evidence basis; the diagnosis portions of the algorithm (see Figure 1), therefore, are provided as *Clinical Principles* or as *Expert Opinion* with consensus achieved using a modified Delphi technique if differences of opinion emerged.[2] A *Clinical Principle* is a statement about a component of clinical care that is widely agreed upon by urologists or other expert clinicians for which there may or may not be evidence in the medical literature. *Expert Opinion* refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge and judgment for which there is no evidence.

OAB Treatment. With regard to treatment, a total of 151 articles from the original search processes met the inclusion criteria; an additional 72 relevant articles were retrieved as part of the update literature review process and also have been incorporated. The Panel judged that these were a sufficient evidence base from which to construct the majority of the treatment portion of the algorithm. Data on study type (e.g., randomized controlled trial, controlled clinical trial, observational study), treatment parameters (e.g.,

dose, administration protocols, follow-up durations), patient characteristics (i.e., age, presence of specific symptoms such as urgency, urgency incontinence and/or frequency, detrusor overactivity documented by urodynamics), adverse events, and primary outcomes (as defined by study authors) were extracted. The primary outcomes for most studies were reductions in frequency, urgency incontinence, incontinence and urgency.

The quality of individual studies was assessed by the EPC using accepted criteria to determine the quality of internal and external validity. The criteria and rating scheme are described in detail in the published report The same system was used to assess the quality of additional included studies.

Table 1: AUA Nomenclature
Linking Statement Type to Level of Certainty and Evidence Strength *[Updated Version]*

Standard: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A (high quality; high certainty) or B (moderate quality; moderate certainty) evidence
Recommendation: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade C (low quality; low certainty) evidence
Option: Non-directive statement that leaves the decision regarding an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or appears uncertain based on Grade A (high quality; high certainty), B (moderate quality; moderate certainty), or C (low quality; low certainty) evidence
Clinical Principle: a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature
Expert Opinion: a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

Introduction

The categorization of evidence strength (ES) is conceptually distinct from the quality of individual studies. Evidence strength refers to the body of evidence available for a particular question and includes consideration of study design, individual study quality, consistency of findings across studies, adequacy of sample sizes and generalizability of samples, settings and treatments for the purposes of the guideline. 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).

AUA Nomenclature: Linking Statement Type to Evidence Strength. The AUA nomenclature system explicitly links statement type to body of evidence strength and the Panel's judgment regarding the balance between benefits and risks/burdens.[3] ***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 (high level of certainty) or Grade B (moderate level of certainty) 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 (low level of certainty) 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 (high certainty), B (moderate certainty) or C (low certainty) 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.

Limitations of the Literature. The Panel proceeded with full awareness of the limitations of the OAB literature. For example, despite the relatively large number of randomized controlled trials (RCTs) with placebo control groups and randomized designs with active controls that assessed pharmacologic OAB treatments, the overwhelming majority of trials followed patients for only 12 weeks. Additional

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