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Review Article

Medical treatment of female overactive bladder syndrome and treatment-related effects

Sheng-Mou Hsiao ^{a,b,c}, Ho-Hsiung Lin ^{a,b,*}^a Department of Obstetrics and Gynecology, Far Eastern Memorial Hospital, Banqiao, New Taipei, Taiwan^b Department of Obstetrics and Gynecology, National Taiwan University College of Medicine and Hospital, Taipei, Taiwan^c Graduate School of Biotechnology and Bioengineering, Yuan Ze University, Taoyuan, Taiwan

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The age-adjusted prevalence of overactive bladder syndrome (OAB) in Taiwan is approximately 16.9%. Currently, a variety of treatments are available for female OAB. However, different treatments have different treatment-related effects that may lead to significant adverse effects and ineffective treatment. In this article, we reviewed the tools that can be used to evaluate the efficacy of OAB treatments, such as a variety of questionnaires, serum or urine biomarkers, bladder diaries and urodynamic studies. In addition, we reviewed the medications used for female OAB treatment, such as antimuscarinics, beta-3 agonists, onabotulinumtoxinA intradetrusor injections, topical vaginal estrogen therapy and bladder instillation of liposome-encapsulated onabotulinumtoxinA. We focused on their efficacy and any treatment-related effects. The information in this review should be useful as a guide to the treatment of female OAB patients.

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Introduction

Overactive bladder syndrome (OAB) is characterized by urinary urgency with or without incontinence and is frequently associated with urinary frequency and nocturia.¹

Urgency is the core symptom of OAB.² The age-adjusted prevalence of OAB in Taiwan is 16.9%.³

Because acetylcholine-induced stimulation of the muscarinic receptors of the detrusor muscle is involved in involuntary bladder contraction,⁴ several antimuscarinics

* Corresponding author. Department of Obstetrics and Gynecology, National Taiwan University College of Medicine and Hospital, No. 8 Chung-Shan South Road, Taipei, 100, Taiwan. Fax: + 886 2 2311 4965.
E-mail address: hhlin@ntuh.gov.tw (H.-H. Lin).

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are currently marketed for the treatment of OAB.^{5–7} In addition, mirabegron, a beta-3 agonist, can relax the detrusor smooth muscle during the bladder storage phase and increase bladder capacity.^{8,9}

Comparisons of the efficacy of antimuscarinics and mirabegron have been reported^{8,9}; however, detailed treatment-related effects have not been reviewed. Thus, the main aim of this review article is to examine the efficacy and treatment-related effects of the treatments of female OAB after reviewing the tools used to assess female OAB treatments.

Tools to evaluate female OAB treatment

Questionnaires

The Overactive Bladder Symptoms Score (OABSS),¹⁰ the modified Indevus Urgency Severity Scale (IUSS),^{11,12} the International Prostate Symptom Score (IPSS),¹³ the Urogenital Distress Inventory (UDI-6), the Incontinence Impact Questionnaire (IIQ-7),¹⁴ the King's Health Questionnaire,¹⁵ the Patient Perception of Bladder Condition questionnaire (PPBC),¹⁶ bladder diaries and urodynamic studies have been used to assess treatment efficacy.⁵

The OABSS, which represents the sum of daytime frequency, nighttime frequency, urgency and urgency incontinence symptoms, was developed by Homma et al.,¹⁰ and the Chinese version has been validated in Taiwan.^{2,17} The OABSS could serve as an alternative for assessing OAB patients.² The OABSS baseline was found to be the only predictor of responsiveness to antimuscarinics.¹⁸ OABSS ≥ 7 was the optimal cutoff value for predicting a response to therapy with a receiver operating characteristic area under the curve of 0.79.¹⁸

The original IUSS was developed by Nixon et al.¹¹ The urgency severity scale produces scores of 0, 1, 2, or 3, which are defined as no, mild, moderate, and severe urgency, respectively.¹¹ In the modified IUSS, urgency with urinary incontinence is assigned a score of 4.^{12,19} A high IUSS score is strongly associated with detrusor overactivity¹² and associated with better therapeutic efficacy of solifenacin treatment.¹⁹ IUSS has been used to assess the efficacy of antimuscarinics or onabotulinumtoxinA intradetrusor injection in OAB patients.^{19–21}

The IPSS is a questionnaire that evaluates the symptom severity of benign prostatic hyperplasia,¹³ and it has been used to assess women with lower urinary tract symptoms.^{22–26} We found that an IPSS voiding-to-storage subscore ratio (IPSS-V/S) of ≥ 1.33 had the best predictive value for female voiding dysfunction among women with lower urinary tract symptoms and that the IPSS-storage subscore can be used to evaluate storage dysfunction in women.²⁶

The UDI-6 and the IIQ-7 were developed to assess the impact of urinary incontinence on health-related quality of life. In the original article, the UDI-6 and the IIQ-7 were validated by women with urodynamic stress incontinence or detrusor overactivity.^{14,27} The UDI-6 and the IIQ-7 were used to assess women with urinary incontinence related to stress or OAB.^{6,7,28}

The King's Health Questionnaire was developed by Kelleher et al. and has been used to assess the quality of life of women with urinary incontinence,¹⁵ including women with stress urinary incontinence²⁹ and OAB.^{9,30,31}

The PPBC, a single-item global patient-reported measure, was developed by Coyne et al. for the assessment of patients with OAB.¹⁶ PPBC is frequently used with other questionnaires, such as the OABSS, for the assessment of OAB.^{17,18}

Among the above questionnaires, the OABSS is a simple and useful alternative to a bladder diary,^{32,33} although the OABSS may overestimate daytime and nighttime frequency.³² The OABSS was found to be well correlated with the PPBC ($\rho = 0.56$), the IPSS ($\rho = 0.41–0.45$) and the IPSS quality of life score ($\rho = 0.47–0.55$).^{34,35} In addition, the OABSS was superior to the PPBC and the IPSS in terms of test-retest reliability.³⁶ Thus, the OABSS is a better tool than the PPBC and the IPSS for assessing female OAB in clinical practice.

Serum biomarker

The serum level of C-reactive protein, which is mainly used as a general biomarker of acute or chronic inflammation and infection, is elevated in patients with OAB,^{37,38} particularly in OAB wet patients.³⁹ Thus, inflammation is thought to be involved in the development of OAB.^{37,38} However, C-reactive protein levels cannot be used as a tool to diagnose OAB in women with lower urinary tract symptoms given its small area under the receiver operating characteristic curve.³⁹

Urine biomarker

The level of urine nerve growth factor is elevated in women with OAB and decreases after treatment with antimuscarinics.^{21,40} However, urine nerve growth factor is not a good tool for the diagnosis of OAB given its lack of sensitivity.⁴⁰ Urine nerve growth factor also fails to reflect changes in bladder conditions based on subjective symptoms⁴¹ and cannot assess the therapeutic efficacy of antimuscarinics or the recurrence of OAB symptoms.⁵

Bladder diary

Bladder capacity can be determined from a bladder diary, uroflowmetry, or filling cystometry.⁴² We found that on days 1–3, the average maximum daytime voided volumes excluding the first morning void (DVVmaxavg mean = 263 mL) exhibited the highest correlation with the strong-desire volume during filling cystometry (mean = 261 mL; $\rho = 0.51$, $P < 0.001$). In addition, on days 1, 2, and 3, the daytime maximum voided volumes excluding the first morning void (DVVmax) were all significantly associated with the strong-desire volume ($\rho = 0.43–0.46$, all $P < 0.001$).⁴³ In addition, the post-treatment changes from baseline in DVVmaxavg were significantly correlated with changes in the strong-desire volume ($\rho = 0.32$).⁴³ Thus, DVVmaxavg or day 1 DVVmax could be used as a good surrogate measurement of bladder capacity.⁴³

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