Editorial

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Future directions in overactive bladder treatment: Personalized medicine can be applied?

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The treatment of overactive bladder (OAB) is usually started with behavioral treatments [1]. If behavioral treatments are not effective or are only partially effective, oral antimuscarinics or oral β3-adrenoceptor agonists can be offered as a second-line therapy. If symptom control is inadequate or intolerable adverse events are encountered, a dose modification or switching to another antimuscarinic medication or other β3-adrenoceptor agonist can be tried. As a third-line therapy, intradetrusor injection of onabotulinumtoxinA or peripheral tibial nerve stimulation may be offered in carefully selected patients. Sacral neuromodulation (SNS) is another option for third-line therapy in patients with severe, refractory OAB symptoms who are ready to undergo surgical treatment. Currently, pharmacotherapy is a mainstay of treatment, but one study reported a high rate of non-persistence after the first prescription (44.5%; defined as a gap of >45 days between successive prescription fills or a switch to any other OAB medication) [2], meaning that treatment had been performed insufficiently.

The precise pathogenesis of OAB might be multifactorial and remains to be clarified, and OAB symptoms are various. Individuals differ in their sensitivity to drug treatment for a combination of pharmacodynamic and pharmacokinetic reasons. In clinical practice, drug selection should be individualized, taking into account a patient's comorbidities and concomitant medications as well as the available dosages and safety profiles of the various agents. Therefore, the treatment strategy for OAB needs to be individualized. The President's Council of Advisors on Science and Technology defines personalized medicine as the tailoring of medical treatment to the individual characteristics of each patient, classifying individuals into subpopulations that differ in their susceptibility to a particular disease or response to a specific treatment so that preventive or therapeutic interventions can then be focused on those who will benefit, sparing expense and side effects for those who will not [3]. With advances in genome and biomarker assays and targeted therapeutics, personalized medicine enables more accurate diagnosis, better prognostication of patients at risk for more aggressive disease, and identification of who will respond to a treatment. These innovations supporting personalized medicine are expected to result in optimal management while minimizing potential adverse effects and morbidity.

The treatment paradigm of OAB has markedly changed with the introduction of mirabegron and intradetrusor onabotulinumtoxinA. Unlike the mechanism of action of antimuscarinics, mirabegron relaxes the detrusor muscle during the storage phase by activation of β3-

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adrenoceptors, resulting in an increase in bladder capacity. Mirabegron 50 mg showed significant improvements in mean numbers of incontinence episodes and micturitions from baseline versus placebo at weeks 4, 8, and 12 that were maintained throughout 12 months [4]. Mirabegron does not affect the contractility of the detrusor muscle and thus can be used in patients with detrusor overactivity with impaired contractility. Intradetrusor injection of onabotulinumtoxinA can be offered to OAB patients who are refractory to antimuscarinics. Recent research has demonstrated improved drug delivery (e.g., liposome-encapsulated onabotulinumtoxinA); thus, treatment with onabotulinumtoxinA is likely to be facilitated in the future.

In accordance with the alternation of mainstream pharmacotherapy, the concept of refractory OAB should be changed: from the current "inadequate response to antimuscarinics" to "inadequate response to combination therapy with antimuscarinics and mirabegron." Furthermore, treatment modalities are becoming more diverse as medical treatments advance. Gene therapy has been applied in various ways and has shown potential as a useful modality for the treatment of OAB. Antisense oligonucleotides were shown to block overexpression of nerve growth factor in bladder urothelium, which suppressed bladder overactivity [5]. Optogenetics combines optics with genetics, and light illumination is utilized to modulate neuronal inhibition or excitation through exogenous light-activated proteins [6]. Optogenetics has been applied to investigate diseases of the central nervous system and other organ systems (e.g., heart, pancreas). Optogenetics has potential as a modality of OAB treatment through inhibition of the detrusor muscle or control of the neural system. The current mode of SNS operates via continuous electrical activity without arousing long-term neuroplastic changes. Future technologies are expected to provide miniature or rechargeable batteries and enable closed-loop conditional stimulation as a method to acquire better efficacy without adverse electric-field effects [6].

In recent decades, efforts have been made to investigate biomarkers of OAB, and several urinary markers (e.g., nerve growth factor, adenosine triphosphate) are promising. Although there is no established biomarker as yet, future studies of biomarkers are expected to offer better understanding of OAB and enable diagnosis and prediction of treatment outcome.

Personalized medicine is already rapidly becoming mainstream and is expected to grow to 5% to 10% of the entire pharmaceutical market over the next 10 years [7]. In the era of diversification of treatment modality and the discovery of biomarkers of OAB, it is expected that optimal treatment for each patient will become a reality. As we come to better understand patients with OAB through advances in our understanding of the genome and biomarkers, and with advanced therapeutics, the treatment paradigm of OAB will move to being personalized, predictive, preventive, and participatory.

CONFLICTS OF INTEREST

The author has nothing to disclose.

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